Chapter 4
Physical Changes During Pubertal Transition

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Introduction

Puberty is a period of life during which secondary sex characteristics develop and the gonads reach their endocrine and exocrine maturity. The duration of the pubertal transition is approximately 3–4 years, and at the end of the process, slightly before the body growth ceases, individuals are able to reproduce.

Physical events during puberty reflect the profound endocrine changes in the hypothalamus, pituitary, gonads and adrenal glands. Adolescent reawakening of the hypothalamic–pituitary–gonadal (HPG) axis is preceded by a gender-specific secretion of gonadotropins and sex hormones during foetal life as well as in the postnatal period (minipuberty) [1]. The hormonal peaks during early infancy are followed by a prepubertal HPG quiescence that takes several years. HPG reactivation during adolescence is crucial for the development of puberty, but the underlying mechanisms are not completely understood.

Onset of Puberty: Adrenarche and Gonadarche

The fundaments of pubertal development are two independent but chronologically related processes—*adrenarche* and *gonadarche* [2].

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Adrenarche

Adrenarche is a phenomenon of adrenal zona reticularis activation leading to increased secretion of dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulphate (DHEAS) [3]. Prepubertally low adrenal androgens begin to rise at around 6–7 years of age and continue to increase in accordance with age and pubertal stages in boys and girls [4]. The development of adrenarche contributes to the appearance of several androgen-dependent phenotypic features after the age of 8–9 years such as occurrence of pubic (*pubarche*) and axillary (*axillarche*) hair, accelerated statural growth, stimulation of apocrine sweat and sebaceous glands associated with adult-type body odour and acne in some children [3, 5, 6]. According to traditional understanding, adrenarche is a process specific for humans and some primates; however, some data describe similar morphological and steroid changes in rat adrenal glands [7, 8]. Adrenal androgens might influence bone development and behaviour, but nevertheless physiological significance of adrenarche remains unknown [9, 10].

Adrenarche is independent of gonadal development and could occur even in patients with gonadal dysgenesis [11]. However, patients with Turner syndrome and ovarian failure showed earlier onset of adrenarche contrasting with significantly delayed pubarche in comparison to healthy girls [12]. These results demonstrate that pubic hair growth depends not only on adrenal hormonal production but also on the gonadal function, and thus terms *adrenarche* and *pubarche* could not be used interchangeably [2, 12]. Adrenal gland maturation is not crucial for puberty, and patients with central precocious puberty could undergo sexual development before the onset of adrenarche [13].

Gonadarche

The pubertal key step is the reactivation of gonadotropin-releasing hormone (GnRH) pulse generator leading to the increased gonadotropin levels and subsequent activation of ovarian or testicular hormonal production. The complex neuroendocrine mechanisms that trigger the GnRH neuron function in the hypothalamus result in the development of gametogenesis and fertility during pubertal maturation [reviewed in 14–18]. The physical expression of HPG reactivation is the enlargement of testicular and ovarian volume (*gonadarche*). The elevated steroid hormones in girls induce the onset of breast development (*thelarche*).

Profound changes in hypothalamus–pituitary–gonadal system, activation of adrenal glands as well as stimulation of somatotrophic axis are the main factors responsible for physical changes in boys and girls during puberty.

Physical Changes in Girls

Breast Development

During puberty, the system and local effects of estrogens, growth hormone (GH) and insulin-like growth factor-1 (IGF1) stimulate the breast cell proliferation in maturing healthy girls [19]. Endocrine and paracrine interrelations induce mammary gland development that progresses through several stages from preadolescent state to mature breast (Fig. 4.1).

Usually, the phenotypic changes are evaluated by a visual rating method developed in the late 1960s and widely known as "Tanner stages" [20]. The long preadolescent period (Stage B1) is followed by an initial breast development at the onset of puberty (Stage B2) characterized by a specific mound-like elevation of the breast and papilla as well as slight areolar enlargement. Further growth of the breast and areola without separation of their contours is typical for stage B3. The progression through B4 stage is marked by a formation of secondary mound due to areola and papilla elevation above the breast level. Restoration of areola to the general contour as well as overall breast enlargement indicates adult breast development (Stage B5) [20–22].

Thelarche is an important sign of the puberty onset and it is usually observed in girls at the age of 10 years. However, progression toward Tanner B2 stage could occur at different time in girls from diverse racial and ethnic groups and from various geographic locations (Table 4.1) [22–33]. A Johannesburg study (1976–1977) showed that thelarche occurred at similar mean age of 11.5 years for black and white girls [34]. Twenty years later in the USA, the mean age of breast development onset was strikingly decreased especially in African-American girls (8.87 ± 1.93 years) [26]. Similar secular trend was observed in European countries, but 15 years later [35]. Danish girls examined in 1990s developed B2 stage at the age of 10.88 years, not earlier than their peers investigated in 1960s [29]. However, a study conducted in 2006–2008 within the same geographical region showed significantly earlier breast development (mean age 9.86 years) [36]. The same process of earlier female pubertal development was observed also in Asian countries in the last 50 years [37, 38], but the reasons remained unexplained. Obesity and endocrine-disrupting chemicals could affect pubertal maturation; however, other factors including ethnic differences, psychosocial environment and family conditions might be also of clinical importance [33, 39–41].

The transition from one breast stage to another takes about 12–18 months, while the whole breast maturation continues approximately 4–4.5 years [22, 25, 32, 33]. The appearance of pubertal signs in girls less than 8 years is traditionally considered as precocious sexual development, while the lack of breast development by 13 years is a sign of delayed or absent sexual maturation [42, 43].

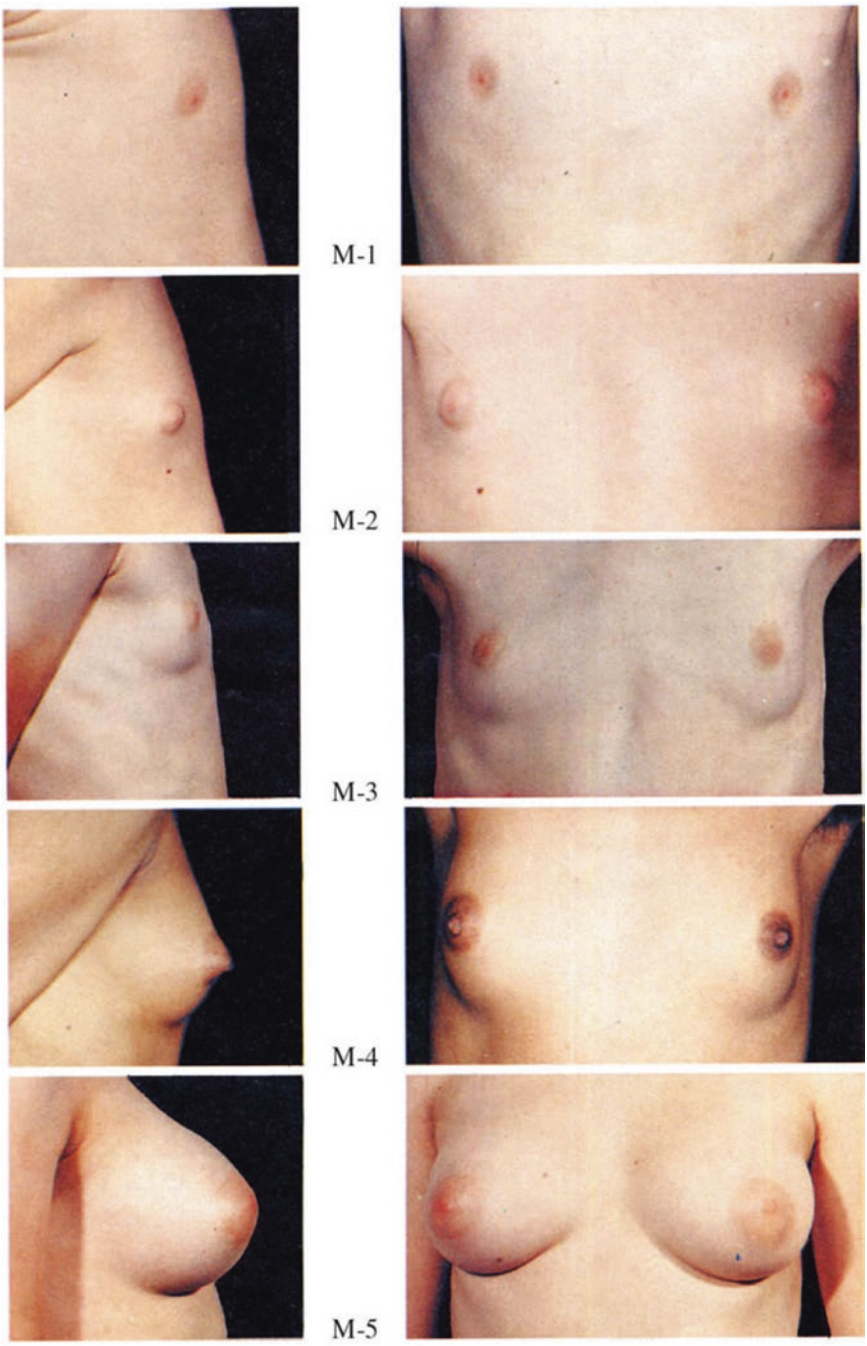

Fig. 4.1 Breast development in girls. M1–M5 correspond to breast stages B1–B5 in the text. [Reprinted from Biro F, Dorn L. Issues in Measurement of Pubertal Development. In: Preedy VR, editor. Handbook of Anthropometry: Physical Measures of Human Form in Health and Disease. New York, NY: Springer Science + Business Media; 2012:237–251. With permission from Springer Science + Business Media]

Table 4.1 Average age (mean or median) of breast (B2–B5) and pubic hair (PH2–PH5) development as well as peak height velocity (PHV) and menarche (M) in girls from different countries [22–33, 57]

Country	Authors	B2	B3	B4	B5	PH2	PH3	PH4	PH5	PHV	M
USA	Reynolds and Wines (1948) (l)	10.8	11.4	12.2	13.7	11.0	11.9	12.5	13.9		12.90
UK	Marshall and Tanner (1969) (l)	11.15	12.15	13.11	15.33	11.69	12.36	12.95	14.41	12.14	13.47
UK	Billewicz et al. (1981) (l)	10.78	12.04	13.07	13.97					12.16	13.37
Sweden	Lindgren (1996) (c)	10.8	11.7	13.0	14.8	11.2	12.3	13.4	14.9		
USA	Herman-Giddens et al. (1997) (c)[a]	9.96	11.30			10.51	11.53				12.88
USA	Herman-Giddens et al. (1997) (c)[b]	8.87	10.19			8.78	10.35				12.16
USA	Sun et al. (2002)[a] (c)	10.38	11.75	13.29	15.47	10.57	11.80	13.0	16.33		
Lithuania	Zukauskaite et al. (2005) (c)	10.2	11.3	13.9		11.2					
Denmark	Juul et al. (2006) (c)	10.88	12.40	13.54	14.66	11.29	12.39	13.51	14.49		13.42
Turkey	Bundak et al. (2008) (l)	10.3	11.7	12.3	12.8	11.2	11.8	12.3	12.8	11.3	12.2
Bulgaria	Tomova et al. (2009) (c)										12.0
Iran	Rabbani et al. (2010) (c)	10.10	11.62	13.55	14.92	9.83	11.60	13.27	14.96		12.55
UK	Christensen et al. (2010a) (l)	10.19	11.66	13.19		10.95	11.99	12.88			12.87
USA	Susman et al. (2010) (l)	9.8	11.3	12.7	14.2	10.2	11.5	12.7	14.2		

c cross-sectional, *l* longitudinal

[a]White

[b]Afro-Americans

Androgen-Dependent Hair Growth

Androgen-dependent hair growth in women results from the neuroendocrine hypothalamic–pituitary–adrenal and gonadal changes leading to increased DHEAS and testosterone levels [33].

Pubarche

Pubic hair (PH) growth is an important phenotypic sign of sexual maturation. Magnetic resonance imaging data has shown an increase of adrenal volume in accordance with the chronological age and pubic hair stages in children [44]. However, adrenal androgen levels are not associated with adrenal size, and no hormonal cut-off values specific for pubarche have been estimated, because of pronounced interindividual variability [44, 45].

The widely accepted method for evaluation of pubic hair development is Tanner staging (Fig. 4.2) [20–22]. Stage PH1 indicates preadolescent state without pubic hair, while the sparse growth of straight slightly pigmented hair mainly along the labia characterized next pubic hair stage PH2. The progression of puberty is marked by the growth of darker, coarser and curled hair that spreads over the junction of the pubes and could be detected on white–black photographs (PH3). Stage PH4 resembles the adult pattern, but the covered area is still considerably smaller than in grown-up women, and it does not spread over the inner thighs. The adult female pubic hair is distributed in the form of an inverse triangle (PH5) [21, 22].

Usually, initial breast development occurs several months earlier than pubic hair growth, but in some girls pubarche could be the first sign of true sexual maturation [2, 22]. According to the study of Biro et al., 58.6 % of the investigated female participants showed synchronous breast and pubic hair development, while in the rest separate "thelarche" or "pubarche" pathway of pubertal onset occurred [2]. The Avon Longitudinal Study of Parents and Children reported that in 46.3 % of girls, breast and pubic hair development began at the same time, while in 42.1 % of participants, B2 stage preceded pubic hair development (thelarche pathway), and in 11.6 % of girls, the opposite sequence of events was observed (pubarche pathway) [46]. According to other authors, only 17.1 % of girls underwent synchronous breast and pubic hair development, while most of the girls (66.2 %) developed breast stage 2 before pubic hair growth [33]. The pubarche pathway of sexual development was rarely found in North Europe, but not so unusual in the USA and Turkey [30, 33, 45]. Thelarche pathway in girls was associated with increased weight gain during early childhood, increased prevalence of obesity at the age of 8 years, greater proportion of body fat at the onset of puberty and increased prevalence of obese mothers [2, 46, 47]. The pubarche pathway was related to significantly increased DHEAS levels, while no differences in estradiol and testosterone levels in comparison to the thelarche

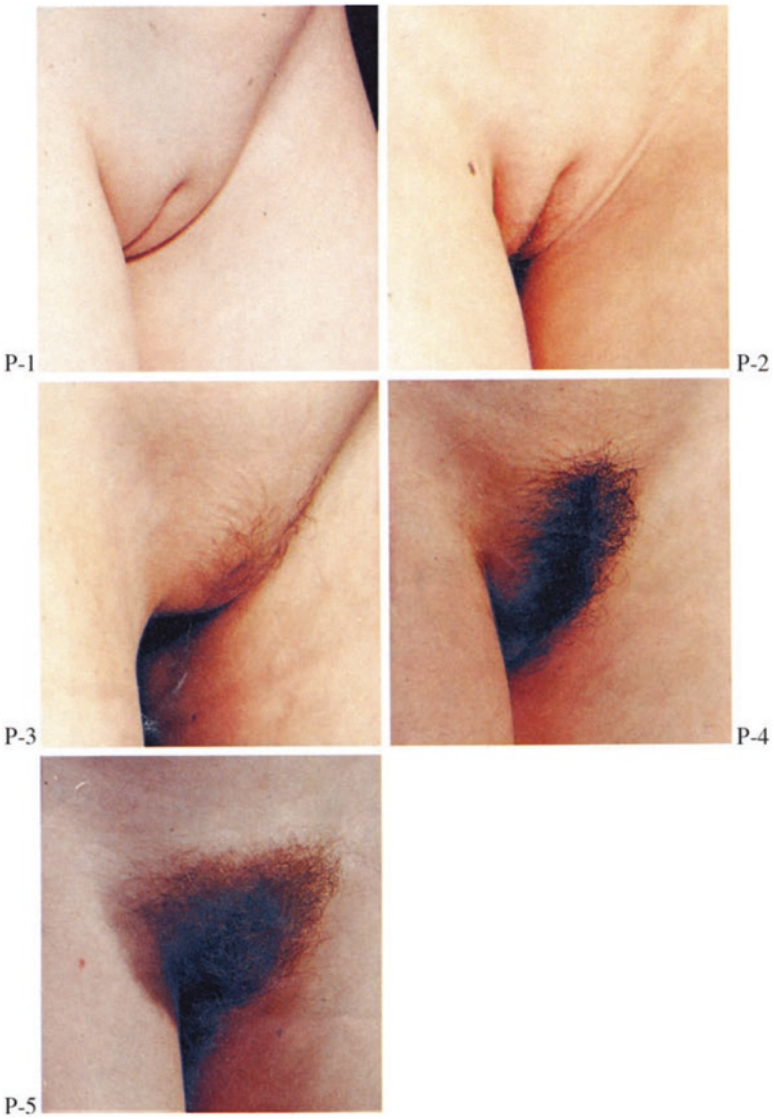

Fig. 4.2 Pubic hair development stages (P-1–P-5). [Reprinted from Biro F, Dorn L. Issues in Measurement of Pubertal Development. In: Preedy VR, editor. Handbook of Anthropometry: Physical Measures of Human Form in Health and Disease. New York, NY: Springer Science+Business Media; 2012:237–251. With permission from Springer Science+Business Media]

pathway were established [2]. The age of progression through the pubic hair stages according to different studies is shown on Table 4.1. Duration of pubic hair development takes approximately 3.5–4 years but could differ substantially among studies (Table 4.1).

Axillarche

Axillarche is another important sign of increased androgen levels. Herman-Giddens et al. described a three-level scale for axillary hair (AH) estimation including stage 1, no hair (AH1); stage 2, sparse curly or straight hair (AH2); and stage 3, mature adult-type hair (AH3) [26]. Accordingly, the mean age of AH2 in black and white girls was 10.08 and 11.80 years, respectively, or 1.3 years after entering stage PH2 for both races [26]. Axillary hair appeared later in English and Lithuanian girls at the age of 12.53 and 12.7 years, respectively [24, 28]. Lithuanian girls developed axillarche 1.5 years after pubarche, while in Turkish girls axillary hair (AH2) emerged only several months after pubic hair onset (PH2) [28, 30]. The transition between the initial stage AH2 and mature axillary hair (AH3) took about a year (0.9–1.22 years) [24, 30]. In some populations, full axillary hair growth was observed in only 75 % of girls within B5 and PH5 stages [48].

Internal and External Genitalia Development

Internal Genitalia

The average ovarian volume rises from 1.01 cm^3 in prepubertal girls to 2.60 cm^3 in Tanner stage 2, while in the Tanner stage 5, it reaches 7.24 cm^3 [49]. Significant changes in ovarian morphology with increased prevalence of polycystic ovaries during puberty have been described by some but not all authors [50, 51].

The uterine volume in newborns regresses postnatally in accordance with the cessation of placental estrogens and remains consistently small until the age of 7 years [52, 53]. Thereafter, it increases gradually in accordance to age, pubertal stages and estradiol levels [50, 52, 53]. The change in uterine volume could be considered as the earliest pubertal event in girls, since it occurs before the appearance of breast development or pubic hair [50, 52]. The female maturation is associated also with a concomitant increase of uterine fundo-cervical ratio and mean endometrial thickness [54].

Menarche

The pubertal hormonal changes ensure the adequate development of internal genitalia and lead to the appearance of the first menstrual bleeding in healthy girls (*menarche*). Usually, menarche occurs between 12.0 and 13.5 years of age, but it could

vary among ethnical groups and in different study periods [55]. In the nineteenth and twentieth centuries, the mean age of menarche has decreased significantly, while nowadays the secular trend begins to slow down [56–59]. According to Marshall and Tanner, menarche is a late pubertal event occurring about 2.3 years after the onset of breast development mostly during stage B4 [22]. Interestingly, in recent studies menarche appears between stages B3 and B4, but again about two and a half years after the onset of puberty [30–32]. A lack of menarche by the age of 15 years as well as more than 3 years after thelarche could be accepted as abnormality and needs clinical evaluation [60].

The median length of the first cycle after menarche is shown to be approximately 34 days, and the first few postmenarcheal years are characterized by a pronounced irregularity with mixed short and long intervals between menstrual cycles [61, 62]. Different studies conducted in the second half of the twentieth century have found that a transition toward more regular menstrual pattern occurs about 5–7 years after menarche at the chronological age of approximately 20 years [61, 63, 64]. A study measuring 24-h urine pregnanediol output as a marker of luteal activity found that the presence of ovulatory cycles depended on the postmenarcheal age. Ovulation was observed in 22.9 % of girls in the first postmenarcheal year, but in 71.8 % of adolescents 5–8 years from the menarche [64]. However, recent studies showed that 65 % of adolescent girls had an established adult-type pattern (10 or more menstruations) even in the first postmenarcheal year [65]. Regular ovulatory cycles in some girls soon after menarche suggest faster HPG maturation in contemporary environment [66].

External Genitalia

Female external genitalia undergo significant transformation during puberty such as deposition of subcutaneous fat in the mons pubis and labia majora and enlargement of the labia minora, introitus, vagina, vaginal fornices and cervix [67, 68]. A small increase in clitoral dimensions was also observed during puberty [69]. The vaginal changes include thickening and stratification of the epithelium, hormone-dependent deposition of intracellular glycogen, increase in cervico-vaginal secretion as well as a shift in vaginal biocoenosis with raised prevalence of lactobacilli and acidification of the vaginal milieu [67, 68, 70]. The complex pubertal transformation of internal and external genitalia allows the achievement of full sexual maturity and ability to reproduce.

Growth and Skeletal Maturation

Pubertal Height Spurt

The pubertal growth spurt is an important event during the complex maturation process between infancy and adulthood. Growth velocity is low in the preadolescent years but accelerates rapidly during midpuberty due to increased interaction between

growth hormone (GH), insulin-like growth factor 1 (IGF-1), gonadal steroid hormones and insulin [71, 72]. GH pulse amplitude increases significantly before pubertal onset in girls and reaches a peak at midpubertal stages [73]. Thereafter, GH secretion rate declines to prepubertal values at breast stage 5 [74]. Pubertal development is associated also with increased growth hormone receptor gene expression and decreased levels of growth hormone-binding protein [75]. In healthy girls, IGF-1 and insulin levels show a parallel stepwise increase between each Tanner stage from prepuberty to breast stage 4, and decline afterward [76].

In accordance with the hormonal changes, normal pubertal growth is characterized by acceleration, deceleration and cessation leading to a total height gain of approximately 25 cm during female puberty [71, 77]. The height velocity begins to rise at the mean age of 9 years and peaks in 11–12-year-old girls at Tanner breast stage 3 [22, 30, 77]. After reaching the maximal value of average 8.3 cm/year, the growth velocity decreases to nearly zero at the age of 16 years [77, 78]. Peak height velocity (PHV) is achieved approximately 1 year before the onset of menstruation [22, 30].

Pubertal Weight Changes

The pubertal growth spurt is accompanied by an increased bone mineralization as well as a significant weight gain. The bone mineral density shows a significant raise in girls during Tanner stage B3 and continues to increase in stages B4 and B5 [79]. The peak weight velocity reaches 7.81 kg/year and occurs several months after the PHV at the average age of 12.78 years [80]. The changes in body composition shape a specific for adult women fat distribution. Bioelectrical impedance analysis revealed a constant increase in fat mass percentage in adolescent girls that was independent of their initial body weight and corresponded with a stable increase of leptin levels during pubertal transition [81]. Magnetic resonance imaging showed that intra-abdominal and subcutaneous fat areas increased in adolescent girls, while their intra-abdominal to subcutaneous ratio decreased [82]. Beyond fat tissue distribution, different musculoskeletal changes in laxity, flexibility and strength of lower limbs during the female adolescent growth have been observed [83].

Physical Changes in Boys

Testicular Development and Spermarche

Testicular Development

Reactivation of HPG axis in boys stimulates the endocrine and exocrine testicular functions leading to increased steroid hormone production from the Leydig cells as well as spermatogenesis. An adequate development of secondary sexual characteristics

indicates the presence of sufficient testosterone concentrations, while an increase of testicular volume reflects the enlargement of the seminiferous tubules following the follicle-stimulating hormone (FSH) concentration raise [84, 85]. Tanner stages are widely accepted as a visual rating method for evaluation of pubertal male genitalia: G1 reflects the preadolescent state, while the G2 stage shows the initial pubertal development with an increase of the testicular volume and scrotum as well as a discrete scrotal skin reddening; G3 stage is characterized by penile growth and further enlargement of the testis and scrotum; G4 stage is distinguished by the enlargement of the penis with a glance shaping; and further testis and penile growth leads to the adult appearance of male genitalia known as G5 stage [86].

The increase of testicular volume is the first physically detectable sign of puberty in boys and could be manually measured by Prader or other type of orchidometer (see Chap. 15: Fig. 15.2) [84, 87, 88]. Such objective measurement of the testicular increase can detect more precisely the onset and development of puberty compared to subjective estimation of the Tanner genital stages. Testicular volumes evaluated by orchidometer have shown high correlation coefficients with ultrasonographic measurements as well as with the actual size of testes from orchidectomized patients determined by the gold standard (water displacement of the surgical specimen) [88, 89]. Determining of the gonadal size is more accurate using ultrasound technique, but the latter is rarely used in epidemiological studies because of the greater cost and complexity [88, 89].

A testicular volume of 3 ml or greater is usually considered as a hallmark of pubertal transition, even though some authors use the volume of 4 ml [90–92]. According to longitudinal data of Bulgarian boys, the mean age of reaching testicular volume of 3 ml is 11.50 (9–14) years for the right testis and 11.63 (9–14) years for the left testis [93]. Thus, the development of the right testis overtakes that of the left testis with approximately 1–2 months. Similarly, the boys in neighbouring Greece started pubertal transition at the mean age of 11 years, while the corresponding age in Turkish children was 11.6 years [91, 94].

The sexual development in North-European children began at the mean age of 11.92 years in 1991–1993, but significantly earlier at the mean age of 11.66 years in children investigated 15 years later [95]. A pronounced secular trend was described recently in a US study [92]. Gonadal enlargement begins earlier in boys who are overweight and obese than in normal weight children, while the slowest pubertal development was observed in underweight boys [96]. Thus, the increased prevalence of overweight nowadays could be one of the most important reasons for the earlier pubertal development of both sexes. Different other factors might influence the maturation process, such as heredity, general health condition, nutrition, physical activity, habits, environmental pollution and socio-economic state [35, 97–100].

Usually, the increase of the testicular volume precedes the development of pubic hair as the first sign of sexual maturation in boys (testicular pathway), but in some adolescents the opposite sequence of events have been observed (pubarche pathway). According to a transversal study in Bulgarian boys, pubarche occurred at the average age of 11.40 years, several months after gonadarche (mean age of 11.23 years)

[96]. A Danish longitudinal study showed that 59 % of boys entered puberty by the usual testicular pattern, 24.6 % by the pubarche pathway, and in 16.4 % pubic hair and testicular enlargement appeared synchronously [45]. According to other studies, only 1.4–3.8 % of US boys underwent synchronous pubertal development, 91.1–95.1 % entered puberty by the testicular pathway and 1.1–7.5 % by the pubarche pathway [33, 101]. On the contrary, the Fels longitudinal study reported synchronous pattern of development in 75.3 % of investigated boys [47]. Distinct pathways of maturation in boys were not associated with differences in the pubertal body mass index or androgen levels [45, 47].

The gonadal development continues approximately 4.5–5 years, and boys reach genital stage 5 at the mean age of 15 years. Unlike pubertal onset, the age at stage G5 has not been changed in the last 50 years [85]. The appearance of genital stages according to various studies in different countries is shown at Table 4.2 [25, 29, 33, 86, 90, 92, 94–96, 101–108]. Sexual development before 9 years is considered precocious, while the lack of testicular enlargement by the age of 14 years indicates a pubertal delay [42, 43].

Spermarche

Maturation of germ cells during puberty is associated with a first appearance of spermatozoa in the urine (*spermarche*) as well as with onset of ejaculation (*ejaculatarche* or *oigarche*). The sperm in the urine (*spermaturia*) could be observed in the earlier stages of male pubertal development and even in prepubertal boys [103, 109]. Spermatozoa were found more frequently in urine samples collected in early than in late puberty suggesting different underlying mechanisms [110]. According to Pedersen et al., spermaturia might result from a spontaneous flow to the urethra in the beginning adolescence in contrast to postejaculatory peristaltic flow observed in late pubertal boys and adults [110].

The average age of spermarche varies between 13.4 and 14.5 years according to different studies [103, 111–113]. However, the passive spermatozoa flow in urine does not reflect the profound psychosomatic changes leading to a conscious ejaculation. According to some authors, the first conscious ejaculation (FCE) is the pubertal milestone in boys corresponding to menarche in girls [114]. The FCE occurs at the mean chronological age of 13.17–14.25 years and at the average bone age of 13.5 years [108, 114, 115].

Data from primate species show that first pubertal ejaculates might not contain spermatozoa. During the maturation process, the ejaculate volume as well as sperm count and motility increases [116]. The low quality of sperm in pubertal chimpanzee has been associated with insufficient epididymal maturation as well as impaired balance between seminal and prostatic secretions [116]. Similar data in boys was reported by Janczewski and Bablok: first ejaculations were characterized by small volumes and very high prevalence of azoospermia (over 80 %) [117]. During pubertal development sperm characteristics improved in parallel with the increase of testicular volume and androgen-dependent hair growth. An optimal spermatozoa quality was reached approximately 21 months after the first ejaculation [117, 118]. Thus,

Table 4.2 Average age (mean or median) of genital (G2–G5) and pubic hair (PH2–PH5) development as well as gonadarche (Go), peak height velocity (PHV) and spermarche/ejacularche (Sp/Ej) in boys from different countries [25, 29, 33, 86, 90, 92, 94–96, 101–108]. *c* – cross-sectional; *l* – longitudinal. Gonadarche (Go) – development of testicular volume ≥ 3 ml (* >3 ml)

Country	Authors	Go	G2	G3	G4	G5	PH2	PH3	PH4	PH5	PHV	Sp/Ej
USA	Reynolds and Wines (1951) (l)		11.5	12.7	13.4	17.3	12.2	13.3	13.9	16.1		
UK	Marshall and Tanner (1970) (l)		11.64	12.85	13.77	14.92	13.44	13.90	14.36	15.18	14.06	
Switzerland	Largo and Prader (1983) (l)	11.8	11.2	12.9	13.8	14.7	12.2	13.5	14.2	14.9		
UK	Nielsen et al. (1986) (l)										13.80	13.4
Turkey	Yenioğlu et al. (1995) (c)		11.6	13.3	14.4	15.8	12.2	13.3	14.6	15.8		
USA	Biro et al. (1995) (l)	12.18					12.79	13.74	14.63	15.19		
Sweden	Lindgren (1996) (c)		11.6	13.5	14.1	15.1	12.7	13.5	14.3	15.5		
Greece	Papadimitriou et al. (2002) (c)	11.0	11.0	12.2	13.3	14.2	11.5	12.7	13.4	14.1		
USA	Karpati et al. (2002) (c)		9.9	12.2	13.6	15.8	11.9	12.6	13.6	15.7		
Denmark	Juul et al. (2006) (c)*	11.92	11.83	13.30	14.31	15.39	11.88	13.45	14.28	15.56		
Greece	Pantsiotou (2007) (l)		10.3	11.9	12.9		10.8	12.4	13.0		13.2	
USA	Susman et al. (2010) (l)		10.3	12.3	13.4	14.8	11.3	12.6	13.6	15.0		

(continued)

Table 4.2 (continued)

Country	Authors	Go	G2	G3	G4	G5	PH2	PH3	PH4	PH5	PHV	Sp/Ej
Denmark	Sørensen et al. (2010) (c)*	11.66	11.59	13.13	13.61	14.31	12.38	13.25	13.67	14.45		
Bulgaria	Tomova et al. (2011, 2015) (c)	11.23					11.40	12.60	13.93	15.82		13.27
USA	Herman-Giddens et al. (2012) (c) /White/	9.95	10.14	12.49	13.72	15.57	11.47	12.89	13.76	15.83		
USA	Herman-Giddens et al. (2012) (c) /Afro-americans/	9.71	9.14	11.58	13.04	15.51	10.25	11.79	13.06	15.72		

spermarche and ejaculatory are not completely identical events, and the presence of first conscious ejaculation is not equal to mature spermatogenesis.

Androgen-Dependent Hair Growth, Voice Changes and Penile Development

Pubarche

The gradual increase of androgen levels in pubertal boys ensures the development of secondary sexual characteristics including pubic, axillary and facial hair growth. The pubic hair pattern between stages PH2 and PH5 is similar in boys and girls, but in most men the triangular pubic hair typical for mature women spreads further along the linea alba (PH 6) [86]. The mean age at PH2 varies in different ethnic and racial groups: 10.9 years in German boys [119], 11.4 years in Saudi Arabia [120], 11.50 years in Italy [121], 12.0 years in Thailand [122] and 12.67 in China [123]. The latest US study has found that PH2 emerges nowadays approximately 6–12 months earlier than in the twentieth century, but definitive conclusions could not be drawn [92, 101].

The progression of pubic hair growth according to Tanner stages in several countries and in different periods is shown on Table 4.2. The duration of pubic hair development between PH2 and PH5 is about 4 years.

Axillarche

The axillary hair stages in boys might be described by the same three-level scale as in girls (AH1–AH3), although some authors have used a more complicated four-level scale [92, 99]. Axillarche emerges at the age of 12 years in Greek and Bulgarian boys (average age 12.2 and 12.28 years, respectively) [94, 124], but 1–2 years later in other ethnic groups: 13.55 years in Egypt, 14.32 and 14.4 in boys from the UK and Sweden [24, 25, 125]. The progress from the appearance of axillary hair to AH3 stage takes at least 1 year [25]. Thus, adult-type axillary hair growth is observed rarely in boys younger than 15 years, and in many adolescents this stage developed beyond the age of 17 years [94, 100].

Facial Hair Growth

Facial hair is an important secondary sexual feature of men. Development of facial hair passes through several stages from absent (FH1) to adult-type abundant hair growth on the cheeks and chin (FH4) [24, 100]. The intermediate steps include the appearance of slightly long and pigmented hair at the upper lip (FH2) and the spreading of hair growth on the upper part of the cheeks and below the lower lip (FH3) [24, 100]. FH2 occurs 6–16 months after the axillarche at the age of 14 years, while the

subsequent progression toward FH3 takes about 2 years [24, 100]. Adult-type FH4 develops rarely in adolescents boys and is more typical for young men (over 18–20 years).

Voice Break

Increased androgen production in pubertal boys leads to an enlargement of the laryngeal cartilages, muscles and ligaments mainly in posterior–anterior length with protrusion of the Adam's apple resulting in a drop of the average voice pitch of about one octave [126, 127]. On the contrary, female larynx undergoes milder hormone-dependent changes predominantly in height leading to only one-third octave decrease of the lower terminal pitch in normoandrogenic girls [126, 127]. Thus, voice break (V) is an important event in the late puberty of boys. Voice change could be measured through voice recording and sound analysing computer system or simply by three- or four-level voice scales. Most pubertal studies use three-level scale describing the voice as unbroken (V1), not fully broken (V2) or completely broken (V3) [24, 128]. The onset of voice break (V2) occurs at the mean age of 13.7–14.0 years [129, 130]. Decrease of the mean speaking frequency corresponds to the pubic hair development, and the greatest change has been observed between PH2 and PH3 stages [131].

A longitudinal study of UK men born in 1946 showed that boys with more advanced voice-breaking status at the age of 14 years grew faster than the others in early infancy and maintained higher body mass index as adolescents and adults [128]. Some studies found a secular trend in the age of voice break as a marker of accelerated pubertal development [129]. Different nutritional and social factors could have influenced the voice change in modern children such as the prevalence of obesity, diet quality, maternal unhealthy habits as well as socio-economic level of the family [99, 132, 133].

Penile Growth

Normal penile growth is determined mostly by the increased androgen secretion and enhanced androgen receptor protein expression in the critical periods of male development including gestation, early postnatal months and pubertal transition [134, 135]. The penile length increases slightly during childhood, while rapid growth occurs during adolescence [107, 136]. Longitudinal data show that between 9 and 14 years, the penile length in boys increases with 60 % [93]. The highest rise in the mean penile length could be observed between pubic hair stages PH1 and PH2 in Japan children, but later (between PH2 and PH4) in Bulgarian (Fig. 4.3) and Brazilian boys [107, 136, 137]. Cross-sectional and longitudinal data in Bulgarian boys show that the maximal increase in penile size coincides with the rapid growth of testicular volumes between 12 and 14 years [93, 107]. Interestingly, the average penile size is bigger at the end of sexual maturation in rural compared to urban Bulgarian male population [107].

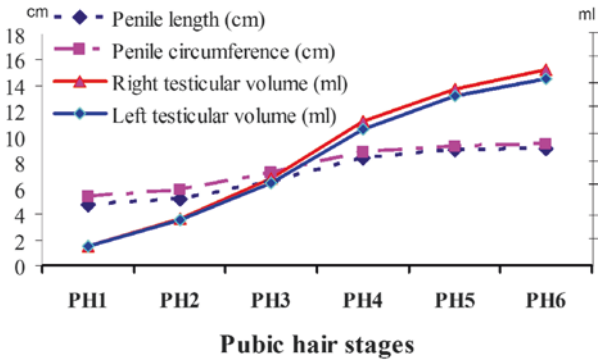

Fig. 4.3 Increase in the testicular volumes and penile size of Bulgarian boys in accordance with the progression through the Tanner pubic hair stages. [Based on data from [107]

Growth and Skeletal Maturation

Pubertal Height Spurt

The height in children is comparable in both sexes, but pubertal growth is more pronounced in boys than in girls leading to a higher adult height in men compared to women. In prepubertal children, mean growth hormone production is similar in both sexes, while during pubertal transition, GH secretion rises first in girls and then in boys [74]. Accordingly, height velocity in boys begins to increase 1–2 years later than in girls [77]. Peak height velocity in male adolescents reaches 9.79 cm/year at the mean chronological age of 14.12 years corresponding to genital stage 4 [80]. The increased growth velocity during puberty leads to an overall height gain of about 27.5–30 cm in maturing boys [77, 107]. Thereafter, the growth velocity decreases, and the epiphyseal closure limits further growth usually after the age of 17 years [71].

Pubertal Weight Gain

Pubertal weight gain in boys is associated with the accelerated linear growth and increase of bone and muscle mass, while no significant raise in percentage of fat mass has been found [81, 98]. Nevertheless, in comparison to girls, boys accumulate greater amounts of fat intra-abdominally, and their intra-abdominal to subcutaneous ratio increases during puberty leading to the sex-specific android distribution of fat tissue [82]. Peak weight velocity coincides with the peak height velocity and reaches 8.64 kg/year at the mean age of 14.27 years [80]. Thereafter, weight velocity decreases in the later stages of pubertal development [80, 81].

Other Changes

Beyond changes in growth, genital development and body composition, pubertal development in boys is associated with blood and metabolic alterations, such as increased haemoglobin and haematocrit values, as well as decreased total and high-density lipoprotein cholesterol levels [138, 139]. Sexually specific changes have been described also in brain development, cognition and behaviour of male adolescents. Especially, the brain amygdala–hippocampus complex could be significantly influenced by the steroid levels during puberty [140]. Animal studies have shown that pubertal increase of sex steroid hormones might alter the sensory associations and could induce strong motivation to seek out reproductive opportunities by modulating different brain zones including reward-related brain structures such as nucleus accumbens and dopaminergic pathways to the prefrontal cortex [reviewed in 141]. Thus, the physical changes in puberty are associated with mental alterations that both aim to create an optimal ability and willingness to reproduce.

Conclusions

The first pubertal signs appear at the mean age of 10 years in girls and approximately 1–2 years later in boys. The progression between B2 and B5 stages takes about 4 years in girls, while the genital development in boys needs a little longer (approximately 4.5 years). Most girls reach B5 stage at the age of 14, while most boys complete their genital development after the age of 15 years.

Menarche occurs at the mean age of 12.8 years, while the mean age of spermarche or ejacularche is about a year later. The peak height velocity is achieved early in girls, mostly at stage B3 or about a year before menarche. On the contrary, peak height velocity is a midpubertal event in boys occurring at the stage G4 and very close to the time of ejacularche. The appearance of menarche or ejacularche does not mean complete fertility potential, since anovulatory cycles in the first postmenarcheal year as well as low sperm quality in the first ejaculate samples are frequent. The timing and duration of pubertal events could vary among different ethnic groups, but nevertheless, the sequence of events underlying pubertal development is similar in boys and girls worldwide as shown on the classical figure by Marshall and Tanner (Fig. 4.4) [86, 107].

The transitional period is also the time of great worry. Adolescents as well as their parents and often doctors observing them are concerned if the children develop normally. Therefore on reasonable time intervals, norms for growth, weight and pubertal physical characteristics should be established as we did with our comprehensive study on boys [107] in order to have an actual basis for comparison and evaluation of the changes in every single case.

Sexual development is a complex process of specific physical and psychical changes that transform healthy children into mature men and women who are motivated and capable to create offspring.

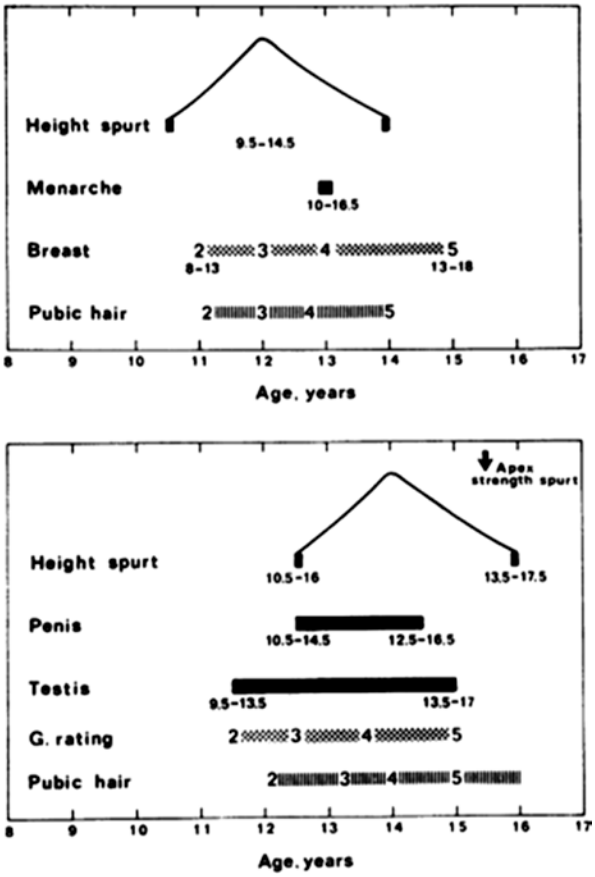

Fig. 4.4 The classical diagrams of the sequence of events at puberty created by Marshall and Tanner. [Reprinted from Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in boys. Arch Dis Child. 1970; 45(239):13–23. With permission from BMJ Publishing Group Ltd]

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