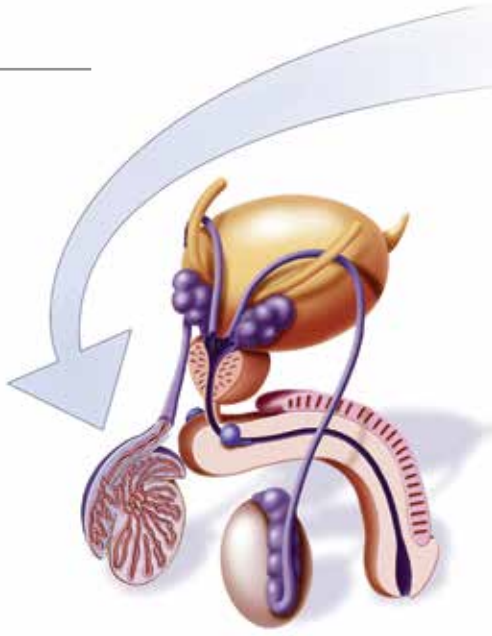
Disorders of pubertal timing in young people



VALLI VELAYUTHUM MB BS, FRACP
RACHANA DAHIYA MB BS, BSc(Hons), FRACP, PhD

Precocious or delayed puberty can cause major concern to young people and their families and may signify underlying pathology. Detailed history taking and examination, including assessment of pubertal status, followed by investigation of bone age and, if indicated, hormone levels can help GPs decide the next step. Depending on the presentation, management ranges from reassurance and monitoring to urgent investigation and referral to a paediatric endocrinologist.

KEY POINTS

- Puberty involves the development of secondary sexual characteristics and reproductive function, associated with acceleration and completion of linear growth.
- Accurate assessment of the stage of puberty depends on inspection and palpation to assess breast development in girls and testicular volume in boys.
- Precocious puberty is defined as puberty beginning before the age of 8 years in girls and 9 years in boys; it is usually idiopathic in girls but may be a sign of underlying pathology, especially in boys.
- Delayed puberty is puberty beginning after the age of 13 years in girls and 14 years in boys; it is mainly constitutional but may also result from primary gonadal failure and defects of hypothalamic or pituitary function.
- Early referral of young people with precocious or delayed puberty is important for timely investigation, management and prevention of short stature and psychosocial problems.

Puberty is a crucial phase of rapid linear growth and physical changes in the transition from childhood to adulthood. Variations from normal in the timing and progression of puberty can signify underlying disease and may also have major psychological and social impacts on young people and affect their final height. GPs are usually the first point of contact when young people have disordered pubertal development. Timely investigations and, when indicated, referral are prudent to exclude an underlying tumour or other organic disease. Assessing concerns about puberty requires knowledge of normal pubertal development. Terms applied to the different stages of puberty are defined in Box 1.

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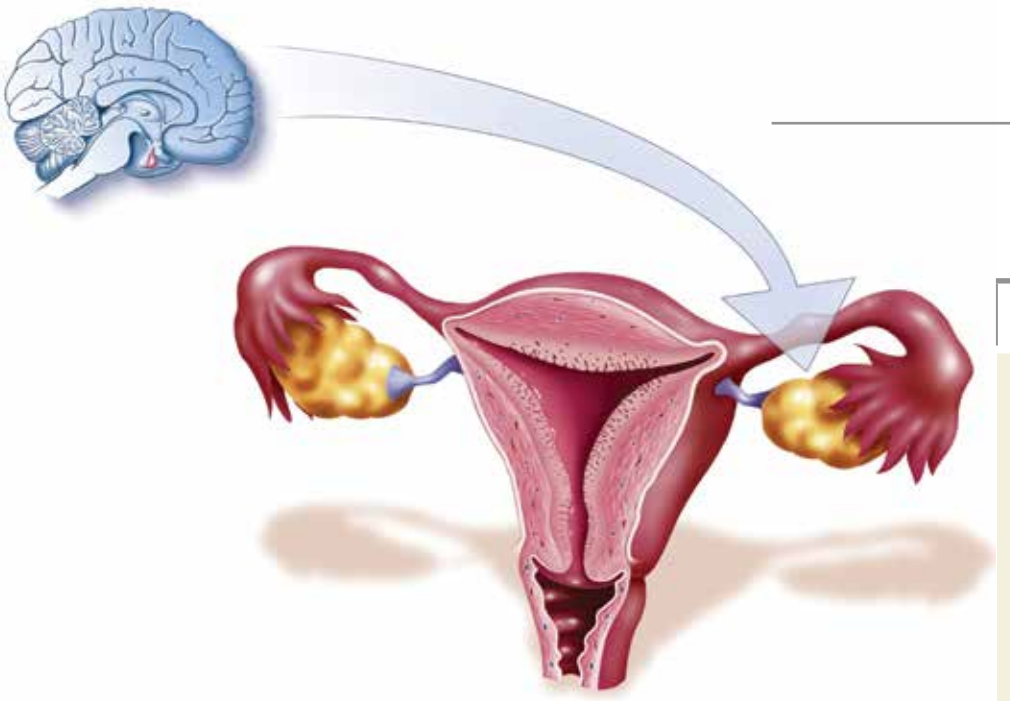
Dr Velayuthum is a Paediatric Endocrinology Fellow at Westmead Children's Hospital, Sydney, NSW.
Dr Dahiya is a Consultant Paediatric Endocrinologist at Lady Cilento Children's Hospital and Greenslopes Private Hospital, Brisbane; and Senior Lecturer at The University of Queensland, Brisbane, Qld.

Normal pubertal development

Hormonal changes of puberty

Normal puberty begins between the ages of 8 and 13 years in girls and 9 and 14 years in boys, with activation of the hypothalamic–pituitary–gonadal axis (Figure 1).[1] Pulsatile secretion of gonadotrophin-releasing hormone (GnRH) from the hypothalamus begins around a year before pubertal changes, initially only during sleep, and is crucial for normal pubertal development. GnRH secretion leads to increased amplitude and frequency of pulses of the gonadotrophins, luteinising hormone (LH) and follicle stimulating hormone (FSH), secreted from the anterior pituitary gland. The gonads are then triggered to produce sex steroids – testosterone in boys and oestradiol in girls – eventually stimulating gametogenesis.

Testosterone causes growth of the external genitalia and body hair, rapid linear growth, increased muscle mass and deepening of the voice. Oestradiol is responsible for thelarche (onset of breast development), increased growth velocity, bone maturation and menarche. The interplay of oestradiol and progesterone is required for regular menstrual cycles and normal reproductive function. FSH



promotes the growth of ovarian follicles, oestradiol production and breast development in girls and spermatogenesis and testosterone production in boys. LH is essential for ovulation and maintenance of the corpus luteum in girls and testosterone production from Leydig cells in boys.

Timing and sequence of puberty

In Caucasian and Hispanic children, puberty begins at a mean age of 9.5 to 10.5 years in girls and 11.5 years in boys.[2] Children of African origin start puberty approximately a year earlier. These age thresholds are 1.5 to two years earlier than described in the past. Factors thought to contribute to this earlier onset of puberty include genetics, endocrine disruptors, premature birth and diet. Overall, 50 to 75% of the variation in pubertal timing, particularly age at menarche, can be attributed to genetics.

Obesity has been associated with earlier puberty in both girls and boys, but morbidly obese boys may present with delayed puberty. Furthermore, chronic health problems, underweight and stress can delay puberty. The duration of puberty generally ranges from 1.5 to five years, with an average of four years.

Puberty in girls usually begins with thelarche (breast budding), although in 15% it begins with pubarche. This is followed by a growth spurt. Menarche typically occurs one to three years after breast budding, at an average age of 12 to 13 years. Asymmetric breast development in girls is common and does not need further investigation.

Puberty in boys usually begins with testicular enlargement (to 3 mL or more in volume or 2.5 cm or more in length), although in a small proportion (less than 10%) it begins with pubarche. The bulk of

1. DEFINITIONS OF PUBERTY TERMS

Puberty: stage of development and maturation of secondary sexual characteristics and reproductive function

Adolescence: the second decade of life (age 10 to 19 years), which includes puberty and major psychosocial and neurocognitive development

Gonadarche: initiation of sex hormone production from the gonads (testes and ovaries)

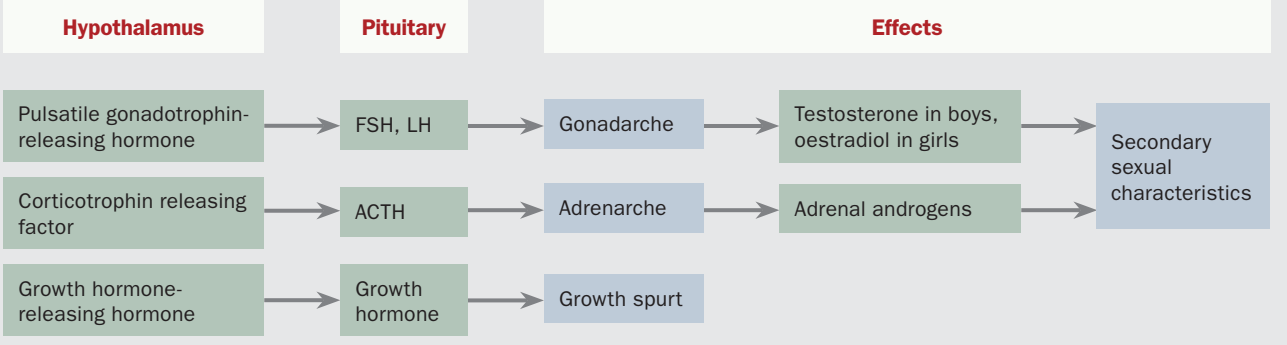
Thelarche: onset of breast development in girls

Gynaecomastia: breast development in boys; pubertal gynaecomastia is present in 50% of boys and regresses within two years

Adrenarche: development of androgen-dependent body changes such as axillary or pubic hair growth, body odour and acne

Pubarche: onset of pubic hair growth

Menarche: onset of menstrual bleeding



Abbreviations: ACTH = adrenocorticotrophic hormone; FSH = follicle stimulating hormone; LH = luteinising hormone.

Figure 1. Normal pubertal events.

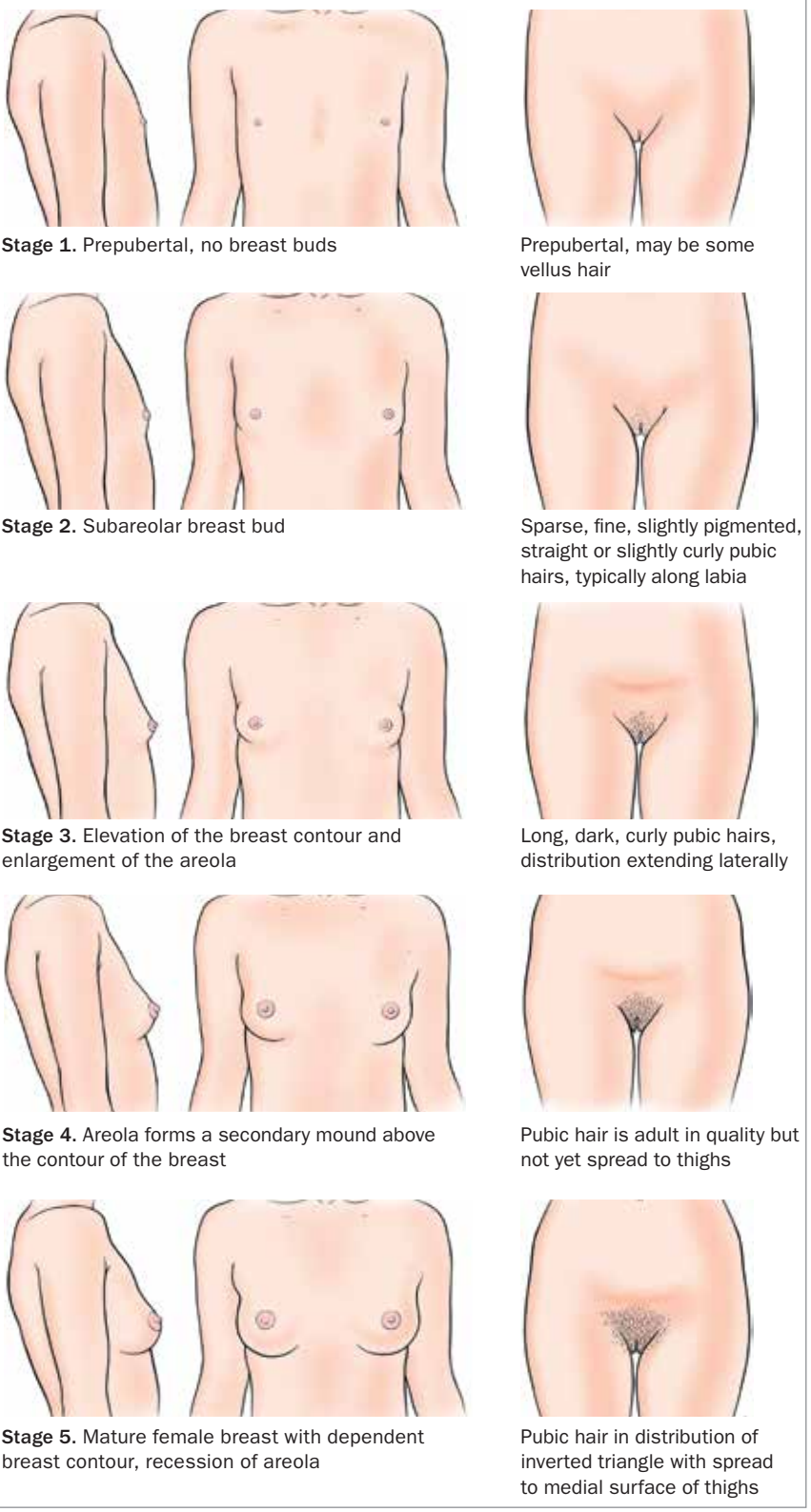


Figure 2. Tanner staging system for pubertal development in females.

testicular enlargement is attributed to the growth of seminiferous tubules, whereas the androgen-producing Leydig cell mass is small. The penis increases first in length, followed by width, and then pubarche occurs. A growth spurt occurs at a sexual maturity stage of 3 or 4 on the Tanner scale. Nocturnal sperm emissions begin after the growth spurt.

Peak height velocity in girls is 8 to 12 cm per year, occurring at a Tanner stage of 2 to 3 or an average age of 11.5 to 12 years. In boys, peak height velocity is 9 to 14 cm per year and occurs at an older age, at a Tanner stage of 3 to 4 or an average age of 13.5 to 14 years.[3,4] Growth in girls slows after menarche and stops at around the age of 16 years. In boys, growth stops at around the age of 18 years. Growth during puberty contributes 17 to 18% of final adult height.[4]

Assessment of puberty

Accurate staging of puberty is essential in the assessment of young people with pubertal disorders. The Tanner scale for puberty staging classifies sexual maturity into five stages based on development of breasts and pubic hair in girls and pubic hair and genitalia in boys (Figures 2 and 3).[5,6] Tanner stage 1 corresponds with prepuberty and stage 5 corresponds with adult development. Tanner staging may not be clear in patients with obesity or certain syndromes that cause dysmorphology.

Palpation should be used to distinguish between lipomastia (adipose tissue on the chest) and glandular breast tissue when assessing early pubertal breast development. The area around the nipple should be palpated with the second, third and fourth fingers, starting on either side of the areola and then proceeding outwards in circular motions until a discrete firm mass is identified that is distinct from the surrounding fat.

In boys, the first stage of puberty is enlargement of the testes to more than 3 mL in volume or 2.5 cm in length. This can be assessed with an orchidometer or by measuring the length of the testes.

Precocious puberty

Precocious puberty is defined:

- in girls, as the onset of thelarche before the age of 8 years or menarche before the age of 9.5 years
- in boys, as testicular enlargement before the age of 9 years.

The earlier the presentation, the higher the likelihood of underlying pathology, but rapid progression should also raise concerns. Precocious puberty can present with increased growth velocity, but advancement of bone age and earlier fusion of growth plates under the influence of oestradiol and its precursors, testosterone, dehydroepiandrosterone sulfate (DHEAS) and androstenedione results in reduced adult height.

Precocious puberty can be classified into benign variants and central and peripheral forms. Causes of precocious puberty are summarised in Box 2.

Benign variants

Some children have a single aspect of pubertal development (incomplete precocity) and no other signs of puberty (Box 2). This may represent early true precocious puberty or may be self-limiting or regress over time. Determination of bone age (x-ray of left hand and wrist) may be sufficient to differentiate between isolated premature thelarche or adrenarche and true puberty. If the bone age is concordant with the chronological age and no further progression of puberty is found on follow up then the parents can be reassured that their child has a benign variant of puberty and will go through true puberty at the normal age.

Premature thelarche is early breast development in girls in the absence of other signs of puberty. It usually occurs in girls under 3 years of age or between 6 and 8 years of age. There is subtle idiopathic overactivation of the hypothalamic–pituitary–gonadal axis, with FSH levels in the upper end of the prepubertal range. In girls aged under 2 years, this may be a continuation of the mini-puberty of infancy. Antral follicles may be found on ovarian ultrasound examination.

Final height, growth velocity and bone age are usually unaffected in incomplete precocity. Reassurance is sufficient management in most cases. However, 10% of girls with premature thelarche may progress to true precocious puberty. Girls with increasing breast development or advanced bone age require close follow up with clinical examination, measurement of gonadotrophin levels and pelvic ultrasound examination to assess for ovarian cysts or enlargement and to measure uterine dimensions and endometrial thickness.

Premature adrenarche is the early development of pubic or axillary hair secondary to adrenal androgen production with no evidence of increased growth velocity or advanced bone age. Risk factors include a history of premature or small-for-gestational age birth and obesity. Exaggerated premature adrenarche with bone age advancement may indicate excess androgen exposure or adrenal pathology and could progress to true precocious puberty. Vigilant monitoring is necessary, with clinical examination and referral to a paediatric endocrinologist when rapid advancement of adrenarche or puberty is found.

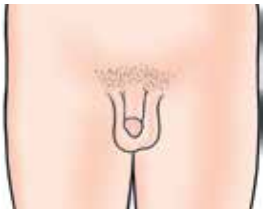
Girls with premature adrenarche are at increased risk of developing polycystic ovary syndrome. Both boys and girls with premature adrenarche have reduced insulin sensitivity and may develop type 2 diabetes mellitus in the future.[7-9]

Central precocious puberty

Central, or gonadotrophin-dependent, precocious puberty is caused by premature activation of the hypothalamic–pituitary–gonadal axis and occurs in one in 5000 to 10,000 children. A basal LH level higher than 0.3 IU/L indicates central precocious puberty, but an undetectable LH level does not exclude early puberty.[10] LH elevation occurs mostly during sleep, with levels peaking in the lower adult range (more than 1.0 IU/L) and falling below 0.6 IU/L during the day.[11] An LH/FSH ratio greater than 0.66 on an LH-releasing hormone stimulation test indicates progressive

Stage 1. Prepubertal; testes <3 mL. May be some vellus hair similar to hair on abdomen

Stage 2. Enlargement of testes and scrotum, little or no enlargement of penis. Sparse, fine, straight or slightly curly pubic hairs typically at base of penis



Stage 3. Enlargement of testes and scrotum, thinning of scrotal skin, penis grows in length. Long, dark, curly pubic hairs, distribution extending laterally

Stage 4. Further enlargement of testes and scrotum, penis grows in length and diameter, scrotal skin darkens. Pubic hair adult in quality but not yet spread to thighs

Stage 5. Mature male genitalia. Pubic hair spread to medial surface of thighs but not to linea alba or abdomen

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Figure 3. Tanner staging system for pubertal development in males.

puberty, whereas a lower ratio suggests nonprogressive puberty.[12]

Central precocious puberty is idiopathic in 80 to 90% of cases in girls, but underlying pathology is found in 40 to 75% of boys (Box 2).[11]

Central precocious puberty presents in girls with increased growth velocity, early breast development and menarche, and in boys with testicular and genital development, growth spurt, voice deepening and increased muscle mass. Headaches, visual disturbance, vomiting and gait abnormalities associated with central precocious puberty may indicate the presence of an intracranial tumour.

2. CAUSES OF PRECOCIOUS PUBERTY

Benign variants
- Premature thelarche
- Premature adrenarche
- Nonprogressive or intermittently progressive precocious puberty

Central precocious puberty (gonadotrophin-dependent)
- Idiopathic (80 to 90% of cases in girls, 25 to 60% of cases in boys)
- Hypothalamic hamartomas
- Central nervous system tumours (optic and hypothalamic gliomas, pinealomas, astrocytomas, ependymomas)
- Central nervous system irradiation
- Cerebral palsy, hydrocephalus, cysts, trauma, midline defects such as optic nerve hypoplasia
- Exogenous sex steroid exposure
- Pituitary gonadotrophin-secreting tumours (very rare)

Peripheral precocious puberty (gonadotrophin-independent)

Girls
- Ovarian cysts
- Ovarian tumours (e.g. granulosa cell tumour)

Boys
- Leydig cell tumours
- HCG-secreting tumours
- Familial male-limited sexual precocity

Both sexes
- Primary hypothyroidism
- Exogenous sex steroids or mimetic compounds
- Adrenal pathology (e.g. congenital adrenal hyperplasia, adrenal tumour)
- McCune–Albright syndrome

Abbreviation: HCG = human chorionic gonadotrophin.

Peripheral precocious puberty

Peripheral, or gonadotrophin-independent, precocious puberty is caused by anomalous secretion of sex steroids independent of gonadotrophin production (Box 2). The sex steroid may be appropriate for the sex (isosexual) or cause virilisation of girls or feminisation of boys (contrasexual). LH and FSH levels are suppressed in children with peripheral precocious puberty. The hypothalamic–pituitary–gonadal axis can be activated by withdrawal of sex steroids, resulting in central precocious puberty.

Girls who have McCune–Albright syndrome (the triad of peripheral precocity, irregular café-au-lait spots and fibrous dysplasia of bone, caused by constitutive activation of LH and FSH receptors due to a mutation in the *GNAS* gene) may present with menarche before breast development. Adrenal causes of peripheral precocity and familial-male limited sexual precocity (testotoxicosis caused by activation of the LH receptor gene) are associated with suppression of testicular enlargement.

Congenital adrenal hyperplasia is a cause of peripheral precocious puberty that is important to recognise. Australia is one of the few first world countries that does not test for this condition in neonatal screening despite the high risk of mortality. Congenital adrenal hyperplasia can cause virilisation of female infants, with clitoromegaly (clitoral length over 1 cm), hyperpigmentation of the genitalia, salt-wasting, hypoglycaemia, hypotension, shock and death. An infant with the salt-wasting form of congenital adrenal hyperplasia may present in the second or third week of life with poor feeding, lethargy, vomiting and diarrhoea. Those with the virilising form can present later with precocious puberty and lethargy, pallor and tremors during illness.

Children with either form of congenital adrenal hyperplasia have low cortisol levels and require hydrocortisone treatment; those with the salt-wasting type also require treatment with salt replacement in infancy and fludrocortisone for aldosterone deficiency. An elevated 17-hydroxyprogesterone level (caused by 21-hydroxylase deficiency) is the best way to diagnose this condition but testing takes time. Low cortisol levels with high androgen levels and low serum sodium, high serum potassium and high urinary sodium levels are another indicator of congenital adrenal hyperplasia. If congenital adrenal hyperplasia is suspected then the child should be referred immediately to a paediatric endocrinologist or, if acutely unwell, to the emergency department.

Diagnosis of precocious puberty

Clinical assessment

In children with suspected precocious puberty, history taking should cover:
- order and timing of development of secondary sexual characteristics
- pubertal history of parents and siblings
- past history of neurological problems, including cerebral palsy, spina bifida or cranial tumours, or radiotherapy
- past exposure to oestrogen, androgens or mimetic compounds, including soy, lavender and tea tree oils.

Examination in these children should assess for:
- growth – height, weight, growth velocity and midparental height. Two or three growth measurements over at least a six-month period are essential for calculating growth velocity. The normal growth rate for different age groups is shown in the Table. Midparental height (MPH) is calculated using the formulas:
  MPH (girls) = (father's height + mother's height – 13)/2 cm
  MPH (boys) = (father's height + mother's height + 13)/2 cm

TABLE. NORMAL GROWTH RATE IN CHILDREN

Age	Growth velocity (cm/year)
<6 months	16 to 17
6 to 12 months	8
1 to 2 years	10 to 14
2 to 3 years	8
3 to 4 years	7
4 to 10 years	5 to 6
Pubertal acceleration	8 to 12 (girls), 9 to 14 (boys)

- Tanner stage of puberty
- asymmetric testicular enlargement in boys (which may indicate the presence of a Leydig cell or germ cell tumour)
- neurological signs and symptoms suggesting an intracranial lesion (e.g. headache, change in appetite and weight, visual deficits)
- limb length discrepancy, scoliosis or frequent fractures (suggesting polyostotic fibrous dysplasia in McCune–Albright syndrome)
- café-au-lait spots (in a child with precocious puberty this should raise the suspicion of McCune–Albright syndrome or neurofibromatosis type 1)
- neurofibromas, axillary freckling (suggesting neurofibromatosis type 1).

Investigations

Recommended initial investigations for children with suspected precocious puberty include:

- bone age (x-ray of left hand and wrist). Bone age more than two standard deviations greater than mean for the child's chronological age suggests true precocious puberty
- oestradiol or testosterone level (depending on sex and signs of oestrogenisation or virilisation), sex hormone binding globulin level (to calculate free testosterone level)
- LH and FSH levels
- thyroid-stimulating hormone and free thyroxine levels if hypothyroidism is suspected.

A suggested strategy for GPs is to assess bone age and, if it is advanced, to undertake the blood tests. These blood tests should be perfomed early in the morning (around 8 am).

Specialist referral

If results of any of the above tests are abnormal for chronological age or there is a high level of concern then the child should be referred to a paediatric endocrinologist for further investigation. All children with precocious puberty and neurological or abdominal symptoms should be referred to a paediatric endocrinologist as soon as possible.

Depending on the presentation, further investigations may include:

- measurement of DHEAS, 17-hydroxyprogesterone, prolactin, human chorionic gonadotrophin and alpha-fetoprotein levels
- assessment of other hormones, depending on individual cases
- pelvic ultrasonography in girls to assess the size of the uterus and endometrial thickness and to rule out ovarian pathology. A uterine volume greater than 2 mL or uterine length greater than 34 mm, or a pear-shaped uterus with thickened endometrium suggests progressive central precocious puberty
- testicular ultrasonography in boys if a testicular mass is suspected on clinical examination
- adrenal ultrasonography if adrenal androgen levels are elevated or there is contrasexual peripheral precocity
- MRI of the brain with pituitary slices in cases of central precocious puberty in girls younger than 6 years and all boys, even in the absence of neurological signs
- liver ultrasonography if alfa-fetoprotein levels are elevated or a tumour is suspected
- leuprorelin (GnRH) stimulation test to determine whether the child has central or peripheral precocious puberty
- a short synacthen test in children with exaggerated adrenarche to exclude congenital adrenal hyperplasia.

GPs could perform any of these tests at their discretion, depending on the child's signs and symptoms.

Treatment

Treatment of precocious puberty involves treatment of any underlying pathology that will affect the child's health. In addition, treatment should be considered to preserve final adult height and prevent distress from early pubertal changes.

In children with idiopathic, neurogenic or secondary activation of central precocious puberty who are at risk of short stature, treatment with a GnRH agonist such as leuprorelin can allow height to catch up with bone age. In these children, treatment is indicated for girls with a chronological or bone age less than 12 to 12.5 years and boys with a bone age of 13 to 13.5 years, under the supervision of a paediatric endocrinologist. The constant stimulation of the GnRH agonist downregulates LH and FSH, stopping the normal pulsatile release that is seen in puberty.

Other options to treat girls with precocious puberty and menarche who are tall and expected to attain midparental height or have a developmental disability include medroxyprogesterone (10 mg daily

or an intramuscular depot injection) or an oral contraceptive pill taken continuously. These treatments may be indicated for cessation of menses in girls with psychosocial difficulties, cerebral palsy or emotional immaturity.

Children who have McCune–Albright syndrome may be treated under the supervision of a paediatric endocrinologist with aromatase inhibitors, such as letrozole in girls or anastrozole in boys. Familial male-limited precocious puberty can be treated with anastrozole along with an antiandrogen such as bicalutamide.

Follow up

All children with precocious puberty or benign variants should have regular (every three months) assessment of pubertal status and growth. Treatment should be adjusted as required to adequately suppress pubertal progression and to attain midparental height.

Delayed puberty

When puberty fails to occur spontaneously then secondary sexual characteristics other than adrenarche will not develop. Absence of breast development by the age of 13 years or menarche by 16 years in girls or a testicular volume less than 3 mL by 14 years in boys warrants investigation for delayed puberty.

Causes of delayed puberty include constitutional delay of puberty, hypogonadotrophic hypogonadism (with a hypothalamic or pituitary cause) and hypergonadotrophic hypogonadism (caused by testicular or ovarian failure), as summarised in Box 3.

The most common cause is constitutional delay of puberty, but this is a diagnosis of exclusion and may be difficult to differentiate from hypogonadotrophic hypogonadism. A family history of a 'late bloomer' may support the diagnosis of constitutional delay.

LH and FSH levels are low in young people with hypogonadotrophic hypogonadism and high in those with hypergonadotrophic hypogonadism. In both cases, oestrogen or testosterone levels are low.

Kallman syndrome, where the olfactory nerves and hypothalamic nerves fail to migrate correctly, is associated with a reduced sense of smell and is a cause of hypogonadotrophic hypogonadism. Stress, weight loss, eating disorders, excessive exercise and chronic disease affect the hypothalamic–pituitary–gonadal axis and can also delay puberty or delay menarche in girls.

Prolactinomas present with delayed puberty, galactorrhoea, primary or secondary amenorrhoea and headaches. Polycystic ovary syndrome is associated with hyperprolactinaemia and is another common cause of delayed menarche. It can also present with premature adrenarche and often has a strong family history. Antipsychotics and certain other medications are known to increase prolactin levels, which suppress gonadotrophin release.

Pubertal arrest may be the first sign of a tumour involving the pituitary or hypothalamus; other possible symptoms include slowed growth, weight gain, polyuria and polydipsia.

Diagnosis of delayed puberty

Clinical assessment

Clinical assessment for young people with suspected delayed puberty is recommended to cover:

- history of puberty, including timing, in parents
- growth, including midparental height
- neurological symptoms suggesting an intracranial lesion (an indication for urgent referral to specialist)
- midline defects such as cleft palate or lip, which may be associated with pituitary insufficiency
- visual impairment (optic atrophy due to septo-optic dysplasia)
- anorexia or bulimia nervosa, stress, inflammatory bowel disease, coeliac disease, thyroid disease, other chronic illnesses, polycystic ovary syndrome and use of drugs such as antipsychotics
- dysmorphic features that correspond to an identified syndrome
- past history of chemotherapy or radiotherapy
- Tanner stage of puberty (note that some patients may present with

3. CAUSES OF DELAYED PUBERTY

Constitutional delay in puberty
(a diagnosis of exclusion)

Hypogonadotrophic hypogonadism (low gonadotrophins)

- Genetic
- Intracranial tumours (e.g. craniopharyngioma)
- Post-traumatic brain injury
- Cranial irradiation
- Multiple pituitary hormone deficiency
- Isolated gonadotrophin deficiency
- Genetic disorders (e.g. Prader–Willi, Laurence–Moon, Bardet–Biedl and Kallmann syndromes)
- Chronic disease (e.g. inflammatory bowel disease, cystic fibrosis, renal failure, thalassaemia)
- Hypothyroidism
- Cushing syndrome
- Hyperprolactinaemia (e.g. prolactinoma, polycystic ovary syndrome, antipsychotic therapy)
- Undernutrition, anorexia, bulimia
- Obesity
- Excessive exercise, stress

Hypergonadotrophic hypogonadism (high gonadotrophins)

- Genetic disorders (e.g. Klinefelter, Turner and Noonan syndromes, XX male, Albright hereditary osteodystrophy)
- Primary testicular cause in boys
  - gonadal dysgenesis
  - androgen biosynthetic defects
  - anorchia/cryptorchidism
  - chemotherapy
- Primary ovarian failure in girls
  - gonadal dysgenesis
  - chemotherapy, radiation
  - oophorectomy
  - autoimmune oophoritis
  - aromatase deficiency
  - disorder of steroidogenesis

pubertal arrest, having started puberty but not progressing appropriately)
- in males, examination to rule out undescended testes and measure stretched penile length.

It is important to rule out disorders of sexual development (e.g. lipoid congenital adrenal hyperplasia, 17α-hydroxylase deficiency, aromatase deficiency, 5α-reductase deficiency and androgen insensitivity).

Investigations

Recommended investigations for young people with delayed puberty include:
- measurement of LH, FSH, oestradiol or testosterone levels
- karyotyping for Turner syndrome, Klinefelter syndrome or a disorder of sexual development
- evaluation of other hormones, including thyroid function tests and measurement of prolactin, cortisol and adrenocorticotrophic hormone (ACTH) levels
- tests to exclude chronic diseases such as coeliac disease and inflammatory bowel disease
- pelvic ultrasonography to assess the size of the uterus and confirm the presence of ovaries or testes
- bone age
- if neurological signs are present, urgent MRI of the brain with pituitary slices and referral to a specialist.

Treatment

The treatment of young people with delayed puberty involves treatment of the underlying cause and induction and maintenance of puberty. Testosterone therapy in boys and oestrogen and progesterone therapy in girls should be given under the supervision of a paediatric endocrinologist.

Conclusion

Puberty involves physical body changes and maturation of reproductive function. Pulsatile secretion of GnRH from the hypothalamus is required for normal puberty to start. Accurate assessment of sexual maturity using visual Tanner staging and breast palpation in girls and measurement of testicular volume in boys are essential to determine whether puberty has commenced.

Early onset of puberty is mostly benign in girls but is more likely to be pathological in boys. If gonadotrophin and/or sex steroid levels or bone age are abnormal for chronological age then the child should be referred immediately to a paediatric endocrinologist. Precocious puberty before the age of 8 years in girls and 9 years in boys can be due to either central gonadotrophin-dependent or peripheral gonadotrophin-independent pathways.

Delayed puberty, beginning after ages 13 years in girls and 14 years in boys, is most commonly due to constitutional delay. Other causes include hypogonadotrophic hypogonadism and primary gonadal failure.

Depending on the presentation, either reassurance and ongoing monitoring or urgent investigations and referral to a specialist for further management may be warranted. MT

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COMPETING INTERESTS: None.