The reproductive system, delayed puberty, precocious puberty

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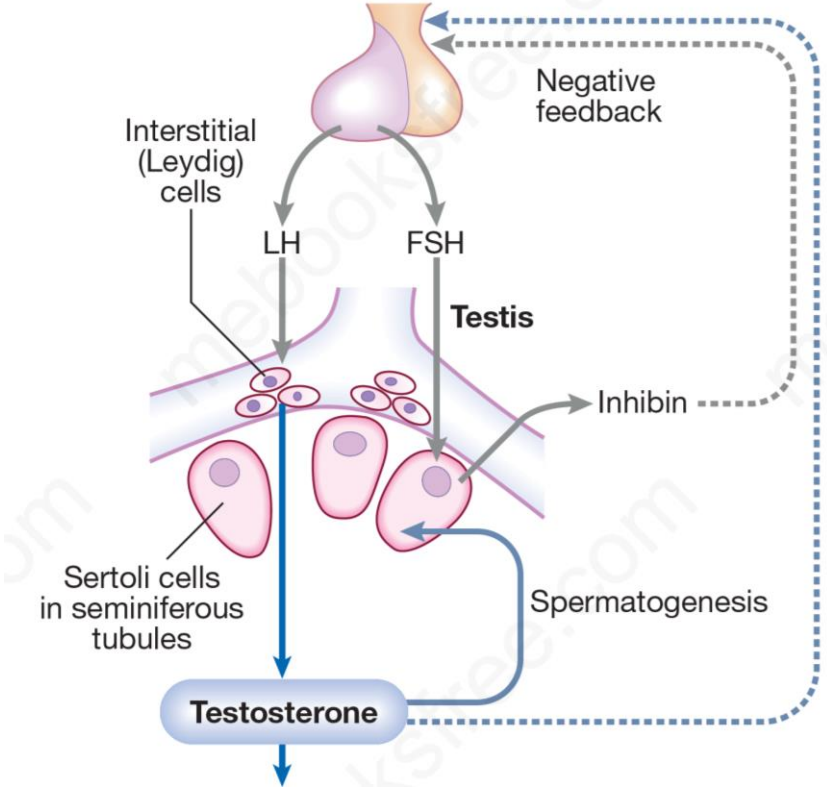


Facial, axillary and body hair growth

Scalp balding & Skin sebum production

Penis and scrotal development

Prostate development and function

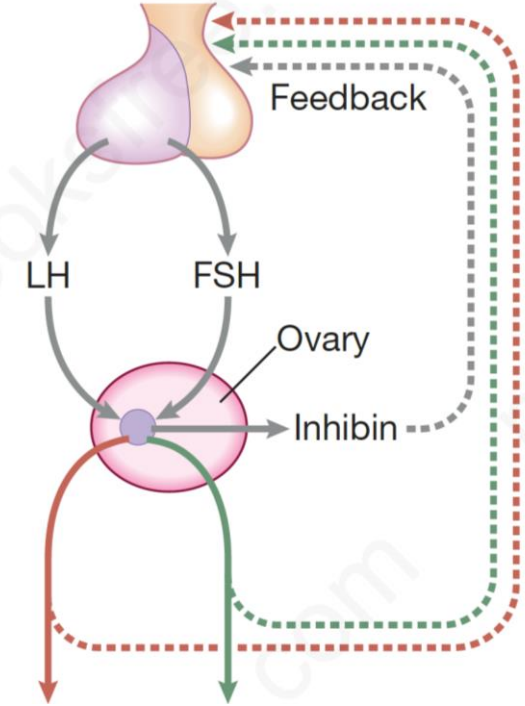
Laryngeal enlargement

Muscle power

Bone metabolism/epiphyseal closure

Libido

Aggression



- Oestradiol

Endometrial proliferation

Genital development and lubrication

Breast proliferation

Bone epiphyseal closure and mineral content

Brain

Body fat distribution

Skin sebum

- Progesterone

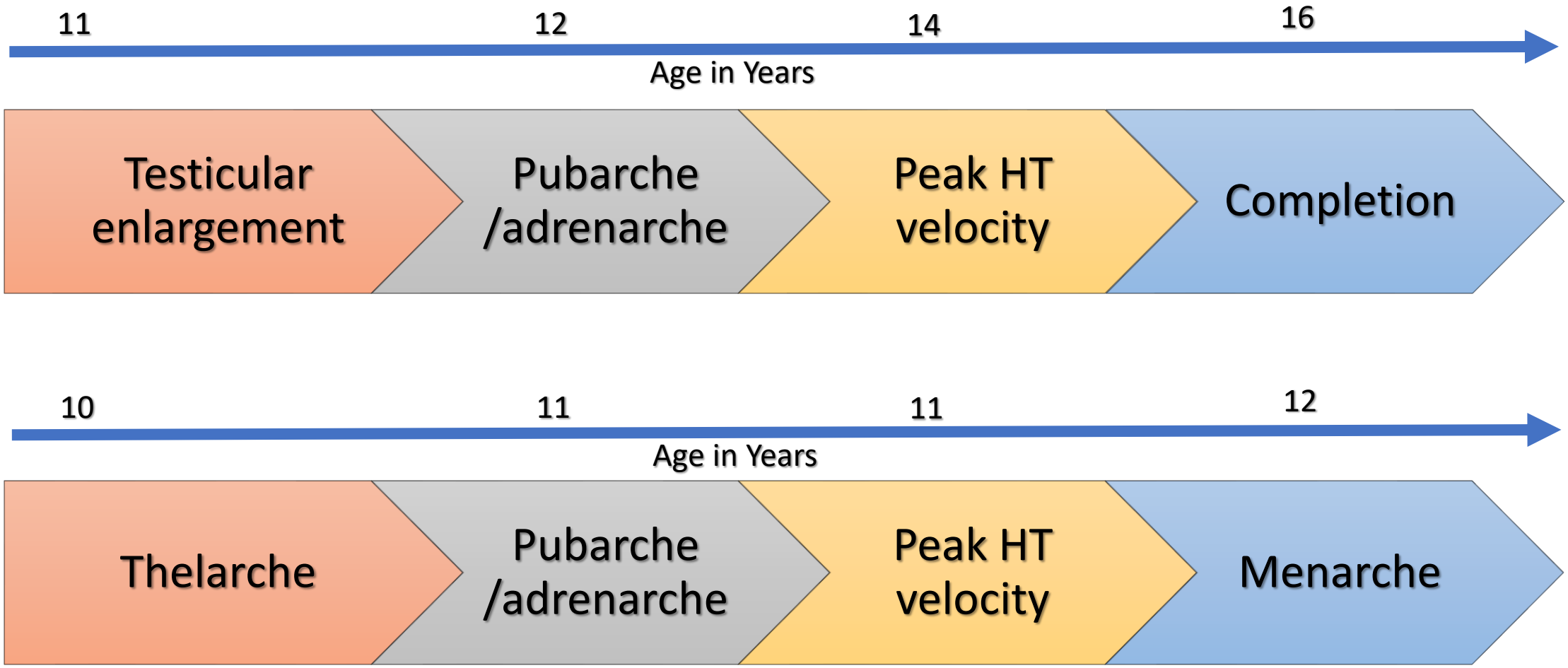
Endometrial secretory change

Increased myometrial contractility

Thermogenesis

Breast swelling

Terminology



Delayed puberty

- Delayed puberty is defined clinically by the absence or incomplete development of secondary sexual characteristics by an age 2 to 3 standard deviations above the mean age of onset of puberty

- The absence of breast development by age 12 to 13 years in girls or absence of testicular enlargement by age 13 to 14 years in boys.
- However, there are clear racial and ethnic variations in the timing of puberty, such as earlier onset of puberty in African American girls compared with their White counterparts.

Epidemiology and etiology

- By definition, delayed puberty occurs in approximately 5 % of apparently healthy individuals in a given population.
  - Constitutional delay of growth and puberty (CDGP) – 53 percent of subjects (63 percent of males and 30 percent of females)
  - Functional hypogonadotropic hypogonadism – 19 percent
  - Other causes of hypogonadotropic hypogonadism (eg, isolated gonadotropin-releasing hormone [GnRH] deficiency, including Kallmann syndrome, or a central nervous system tumor) – 12 percent
  - Primary hypogonadism – 13 percent
  - Unclassified – 3 percent

Clinical assessment

- Previous or current medical disorders,
- Social circumstances
- Family history
- Body proportions, (eunuchoidism)
- Sense of smell
- Pubertal stage
- The presence or absence of testes in the scrotum
- Current weight and height may be plotted on centile charts, along with parental heights and previous growth measurements in childhood.

Constitutional delay of puberty

- This is the most common cause of delayed puberty but is a much more frequent explanation for lack of pubertal development in boys than in girls.
- Short stature: Affected children are healthy and have usually been more than 2 SD below the mean height for their age throughout childhood.
- Delayed bone age: bone age is lower than chronological age.
- Tend to have a familial pattern of involvement (parents, or siblings)
- Constitutional delay of puberty should be considered as a normal variant, as puberty will commence spontaneously. However, affected children can experience significant psychological distress.

Hypogonadotrophic hypogonadism (low or normal FSH/LH)

Structural hypothalamic/pituitary disease.

Functional gonadotrophin deficiency:

- Chronic systemic illness (e.g. asthma, malabsorption, coeliac disease, cystic fibrosis, renal failure)
- Psychological stress
- Anorexia nervosa
- Excessive physical exercise
- Hyperprolactinaemia
- Other endocrine disease (e.g. Cushing's syndrome, primary hypothyroidism)

Isolated gonadotrophin deficiency (Kallmann's syndrome)

Hypogonadotrophic hypogonadism

- Isolated gonadotrophin deficiency is usually due to a genetic abnormality that affects the synthesis of either GnRH or gonadotrophins.
- The most common form is Kallmann's syndrome, in which there is primary GnRH deficiency and, in most affected individuals, agenesis or hypoplasia of the olfactory bulbs, resulting in anosmia or hyposmia.
- If isolated gonadotrophin deficiency is left untreated, the epiphyses fail to fuse, resulting in tall stature with disproportionately long arms and legs relative to trunk height (eunuchoid habitus).
- Cryptorchidism (undescended testes) and gynaecomastia are commonly observed in all forms of hypogonadotrophic hypogonadism.

Hypergonadotrophic hypogonadism (high FSH/LH)

Acquired gonadal damage

- Chemotherapy/radiotherapy to gonads
- Trauma/surgery to gonads
- Autoimmune gonadal failure
- Mumps orchitis
- Tuberculosis
- Haemochromatosis

Developmental/congenital gonadal disorders

- Steroid biosynthetic defects
- Anorchidism/cryptorchidism in males
- Klinefelter's syndrome (47XXY, male phenotype)
- Turner's syndrome (45XO, female phenotype)

Investigations

- FSH, LH, testosterone (male), estradiol (female).
- General: CBC, LFT, RFT, celiac screen.
- TFT, PRL
- Bone age by LT hand and wrist X-ray
- Karyotype
- Sellar MRI
- Evaluation of iron overload

Management

- Low dose of conjugated estrogen (oral or trans dermally) up titrated slowly over 6-12 month, then cycle induction with progestin.
- Low dose Testosterone (IM or trans dermally) uptitrated slowly.
- Gonadotrophin (FSH, LH or HCG) in case of fertility issue.
- GnRH SC pump may be used in Kalman's syndrome.

Precocious puberty

- Precocious puberty is traditionally defined as the onset of secondary sexual characteristics before the age of eight years in girls and nine years in boys.
- These limits are chosen to be 2 to 2.5 standard deviations (SD) below the mean age of onset of puberty.
- More common in girls than boys.

Central precocious puberty

- CPP (also known as gonadotropin-dependent precocious puberty or true precocious puberty) is caused by early maturation of the hypothalamic-pituitary-gonadal axis.
- CPP is characterized by sequential maturation of breasts and pubic hair in girls and of testicular and penile enlargement and pubic hair in boys.
- In these patients, the sexual characteristics are appropriate for the child's gender (isosexual). Advanced bone age

Idiopathic

Commonest

Secondary to CNS lesions

(eg, hypothalamic hamartomas, other CNS tumors and lesions, cranial radiation)

Peripheral precocity

- Peripheral precocity (also known as peripheral precocious puberty, gonadotropin-independent precocious puberty) is caused by excess secretion of sex hormones (estrogens or androgens) from the gonads or adrenal glands, exogenous sources of sex steroids, or ectopic production of gonadotropin from a germ-cell tumor (eg, human chorionic gonadotropin [hCG]).
- Iso or contra sexual, advanced bone age

Benign or nonprogressive pubertal variants

- Benign clinical pubertal variants include
- isolated breast development in girls (premature thelarche) or
- isolated androgen-mediated sexual characteristics (such as pubic and/or axillary hair, acne, and apocrine odor) in boys or girls (premature adrenarche, which results from early activation of the hypothalamic-pituitary-adrenal axis, as confirmed by mildly elevated levels of dehydroepiandrosterone sulfate [DHEAS] for age).

- Both of these conditions can be a variant of normal puberty.
- Normal or slightly advanced bone age

Clinical evaluation

- History: (associated diseases, progressed features of puberty, growth velocity)
- Clinical examination: (stage of puberty, testicular size, height, syndromes)

Investigations

- Bone age: advanced in pathological.
- Basal LH concentrations >0.2 to 0.3 mIU/L and/or stimulated LH concentration post-GnRH or GnRH agonist of >3.3 to 5.0 mIU/L Dx central precocious puberty.
- Testosterone, estradiol, DHEA-S, 17-OH progesterone.
- Brain MRI, abdominal CT/MRI, pelvic US, testicular US

Treatment

- Aim: reduce psychosocial stresses, avoid premature epiphysial closure.
- GnRH agonist for CPP
- Treat the underlying cause in PP.