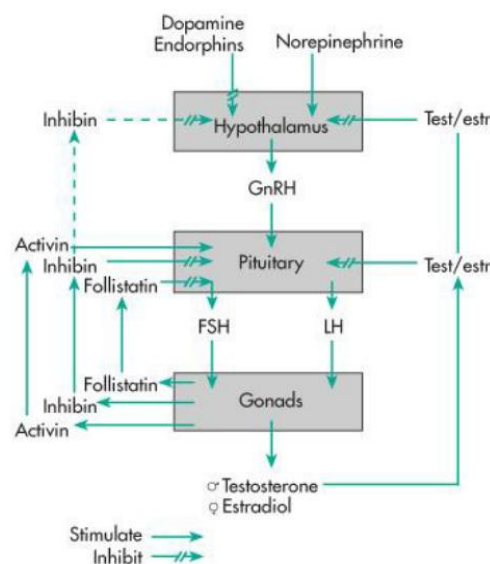




- Hypothalamic-Pituitary-Gonadal axis (see the figure):

- When a person reaches puberty, the secretion of GnRH from hypothalamus will change from being continuous to pulsatile secretion during REM-stage of sleep. This will stimulate the anterior pituitary gland to secrete gonadotropins (e.g. FSH and LH).
- **Hormones controlling pulsatile secretion of GnRH from hypothalamus are:**
 - ✓ Positive effects on GnRH secretion: glutamate and leptin.
 - ✓ Negative effect on GnRH secretion: GABA, melatonin and NPY.



- Gonadotropins in turn, enhance the production of sex hormones from gonads (testes in males; ovaries in females).
- **In males:** LH stimulate leydig cells of the testes to produce testosterone while FSH stimulates the process of spermatogenesis.
- **In females:** FSH is needed for follicular growth in ovaries while LH is needed to induce ovulation (at day 14 of a 28-day menstrual cycle).
- Sex steroids (testosterone in males; estradiol in females) will express a negative feedback on the level of hypothalamus and anterior pituitary gland.

- Puberty: it is defined as a stage of growth and human development in which a person becomes capable or reproducing. The following are the major events which occur during puberty:

- Growth spurt.
- Maturation of genitals and gonads.
- Appearance of secondary sexual characteristics (e.g. axillary/pubic hair; development of breasts in females; deep voice in males with increased muscle bulk... etc).
- Menstruation (in females) and spermatogenesis (in males).

- Puberty is noticed to be:

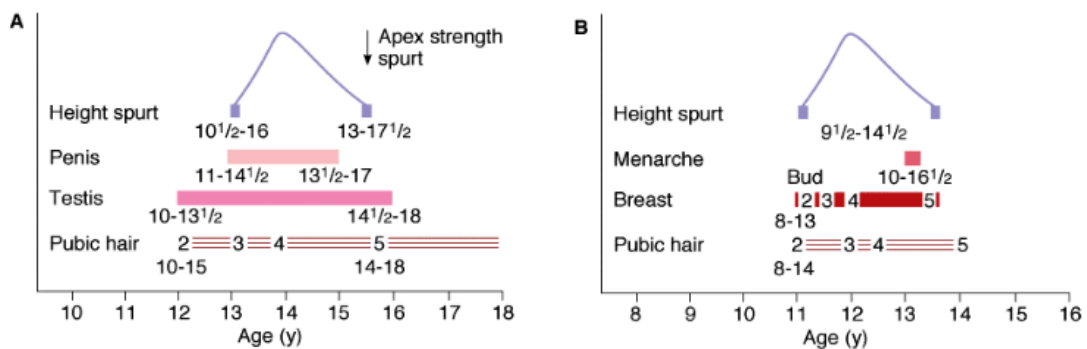
- Earlier in obese females.
- Delayed in patients who suffer from chronic medical condition or those with malnutrition.
- Genetic factors may also play a role.

- Important terminologies:

Thelarche	Indicates the onset of breast development in females
Pubarche	Refers to the appearance of pubic/axillary hair in both males and females
Menarche	Indicates the onset of the menstrual cycle. Notice that the menstrual cycle is anovulatory (no eggs are produced) in the first 2-3 years.

- Sequence of sexual development (the following graphs are important for OSPE exam; YOU HAVE TO MEMORIZE THEM):

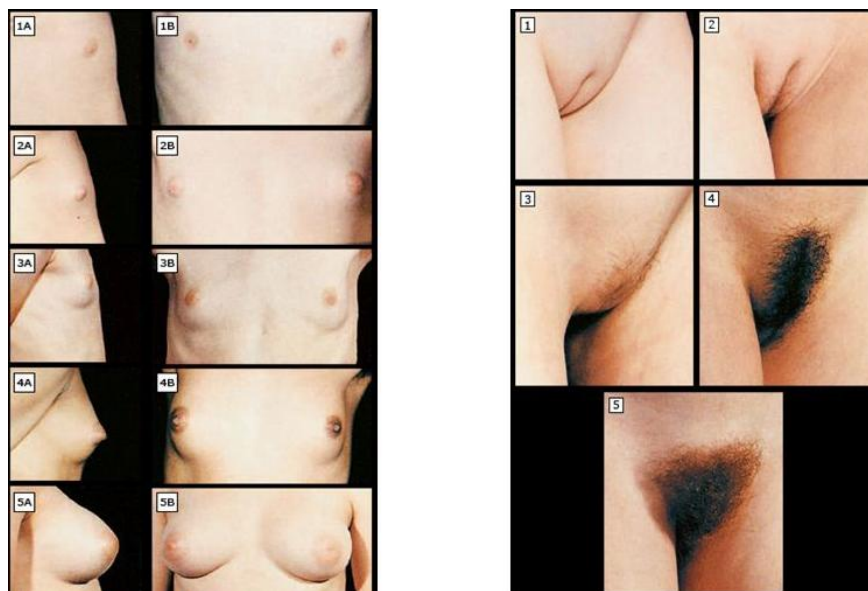
- **In males:** puberty is between 10-16 years of age. The first events is represented by enlargement of testes (> 2.5 cm or volume of 3 ml) followed by appearance of pubic hair and then elongation of the penis. Epiphyseal closure is delayed in males and this explains why they are taller than females.
- **In females:** puberty is between 9-14 years of age. The first events is represented by breast budding (thelarche) followed by appearance of pubic hair and then axillary hair and finally the menstrual cycle (after 2.5 ± 1 years from thelarche). Estrogen causes earlier epiphyseal closure in females resulting in their shorter stature.



- **Tanner staging of puberty:**

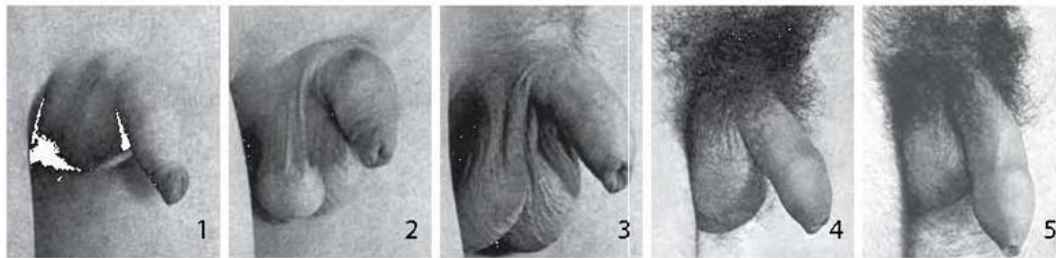
• **Females (breast development and pubic hair):**

Stage	Events
Stage-I	This is the pre-pubertal stage in which there is no breast or pubic hair development
Stage-II	Breast budding with enlargement of areola + sparse, long, downy pubic hair
Stage-III	Further enlargement of breast + pubic hair becomes darker and coarser
Stage-IV	Areola is elevated above the contour of the breast + pubic hair becomes of adult-type but medial aspects of thighs are still not involved
Stage-V	Adult breast with areola at level of breast contour + adult pubic hair covering medial aspects of thighs



• **Males (genitalia and pubic hair):**

Stage-I	This is a pre-pubertal stage in which there are no changes in genitalia or pubic hair
Stage-II	Testicular enlargement + sparse, long, downy pubic hair
Stage-III	Further testicular enlargement and penile elongation + pubic hair becomes darker and coarser
Stage-IV	Increased penile girth + pubic hair becomes of adult-type but medial aspects of thighs are still not involved.
Stage-V	Adult size genitalia (testes volume > 20 ml) + adult pubic hair covering medial aspects of thighs



- **Adrenarche refers to the production of androgens from zona reticularis of adrenal gland cortex. Functions of adrenal hormones are the following:**

- Development of pubic/axillary hair.
- Epiphyseal growth which occurs before puberty and has to reach a certain threshold for puberty to begin.

- **Disorders of puberty:**

- **Precocious puberty** **البلوغ المبكر:**
 - ✓ Is breast development before 7 years of age in females; testicular enlargement before 9 years of age in males.
 - ✓ Categories:

Premature thelarche	<ul style="list-style-type: none"> • Breast development in first 2 years of life with no other secondary sexual characteristics. • Due to transient activation of Hypothalamic-Pituitary-Gonadal Axis (HPGA). • No treatment needed
Premature adrenarche	<ul style="list-style-type: none"> • Pubic/axillary hair development without breast development or testicular enlargement. • It is common in girls after 5 years of age. • No treatment needed.
Central precocious puberty	<ul style="list-style-type: none"> • It is premature activation of HPGA which is more common in girls. • Clinical features: <ul style="list-style-type: none"> ✓ Girls (cause is idiopathic): breast development, pubic hair and rapid growth ✓ Boys (cause is always organic and head MRI must be done to detect tumors, trauma, infection... etc): testicular enlargement, pubic hair and rapid growth • Investigations: <ul style="list-style-type: none"> ✓ ↑FSH, LH and sex steroids ✓ GnRH stimulation test: by injecting synthetic GnRH and watching for ↑LH (notice that there is flat response in peripheral precocious puberty).
Peripheral precocious puberty	<ul style="list-style-type: none"> • Peripheral production of sex steroids independent of FSH and LH. • Causes: exogenous sex steroids, gonadal tumors or adrenal tumors. • Clinical features: <ul style="list-style-type: none"> ✓ Boys: Feminization (gynecomastia) or premature onset of pubic hair. ✓ Girls: virilization or breast development • Treatment depends on the underlying cause



- **Delayed puberty:**

- ✓ It refers to no breast development by 13 years in females; no testicular enlargement by 14 years in males.

- ✓ Classification:

Hypogonadotropic hypogonadism	<ul style="list-style-type: none">• No activation of HPGA• ↓FSH, ↓LH and ↓sex steroids• Example: Kallman syndrome (isolated gonadotropin deficiency associated with anosmia)
Hypergonadotropic hypogonadism	<ul style="list-style-type: none">• There is gonadal failure• ↑FSH, ↑LH and ↓sex steroids• Examples: Klinefelter syndrome (in boys); Turner's syndrome (in girls).