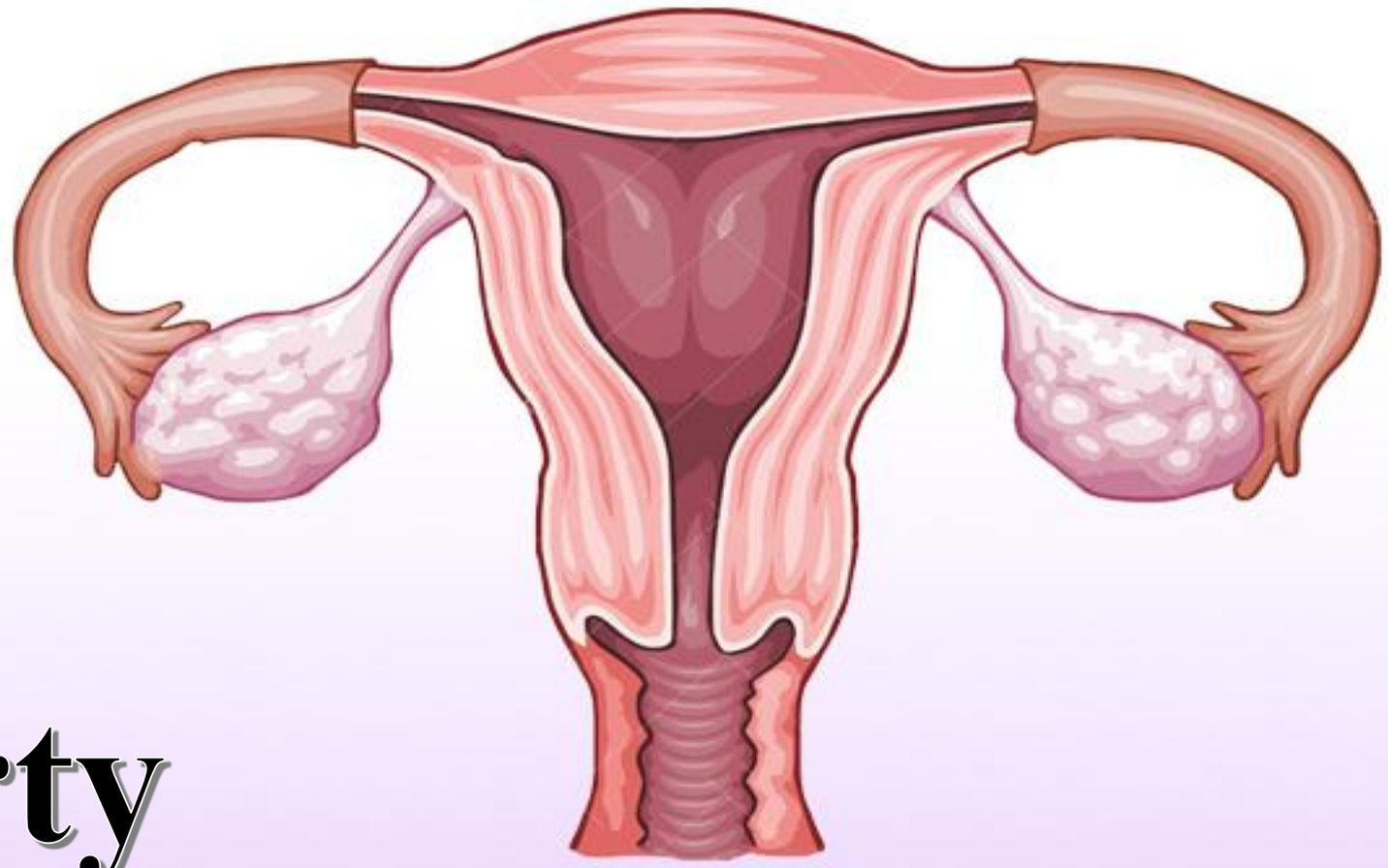
Physiology team



L3-Puberty

Sources:

✓ **male slides**

Objectives

- Define Puberty
- Recognize the physiology of puberty related to changes in hypothalamic-pituitary-gonadal axis
- Describe the physical changes that occur at puberty in males and females
- Describe the pathophysiological conditions associated with puberty

Definition of puberty: A stage of human development when sexual maturation and growth are completed and result in ability to reproduce (Physiological transition from childhood to reproductive maturity)

Accelerated somatic growth

Maturation of primary sexual characteristics (gonads and genitals)	Appearance of secondary sexual characteristics (pubic and axillary hair, female breast development, male voice changes,...)	Menstruation and spermatogenesis begin (important!) **in girls:** between 8 and 14yrs **in boys:** between 9 and 14yrs

Puberty - terms & events

Thelarche	Development of breast in female
Puberache	Development of axillary & pubic hair
Menarche	The **first** menstrual period
Adrenarche	the onset of an increase in the secretion of androgens; responsible for the development of pubic/axillary hair, body odour and acne.
Gonadarche	Maturation of gonadal function.

IMPORTANT

Hormonal changes in puberty:

gradual activation of the GnRH (LHRH)

↓

increases frequency and amplitude of LH pulses.

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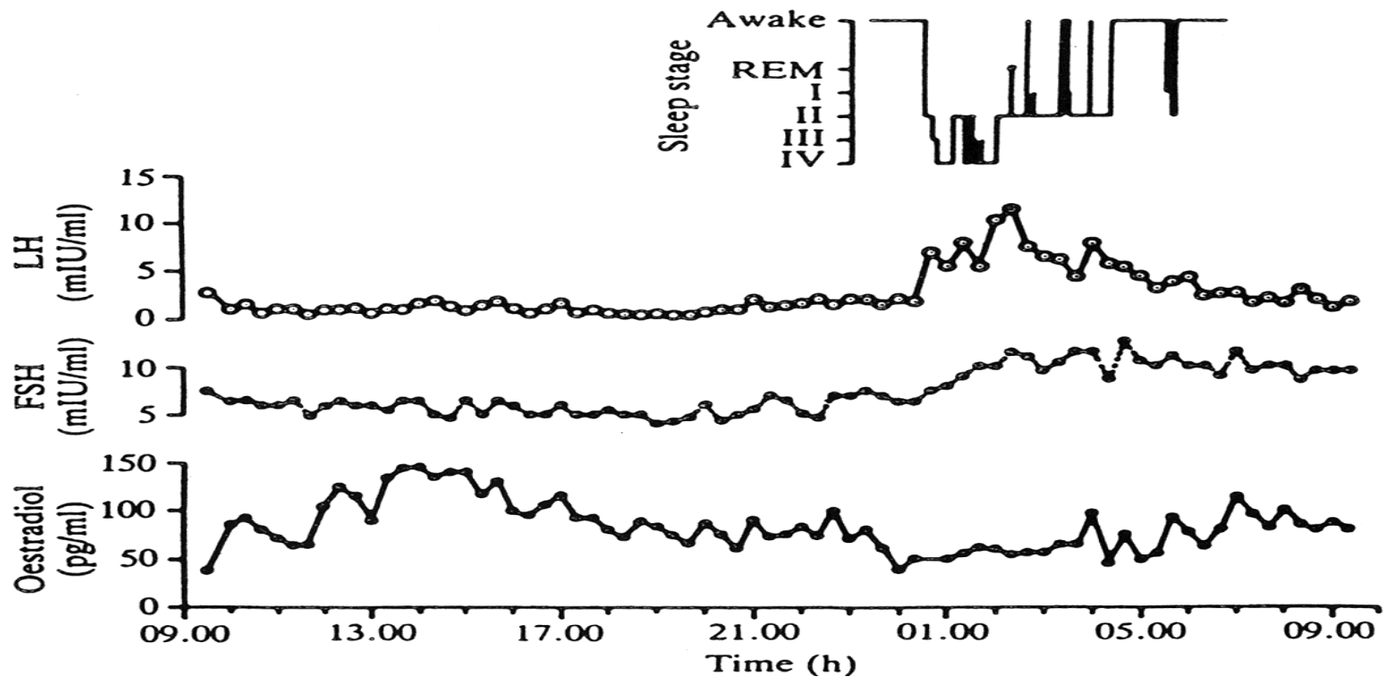
gonadotropins stimulate secretion of sexual steroids (estrogenes and androgenes)

↓

extragonadal hormonal changes (elevation of IGF-I, and adrenal steroids)

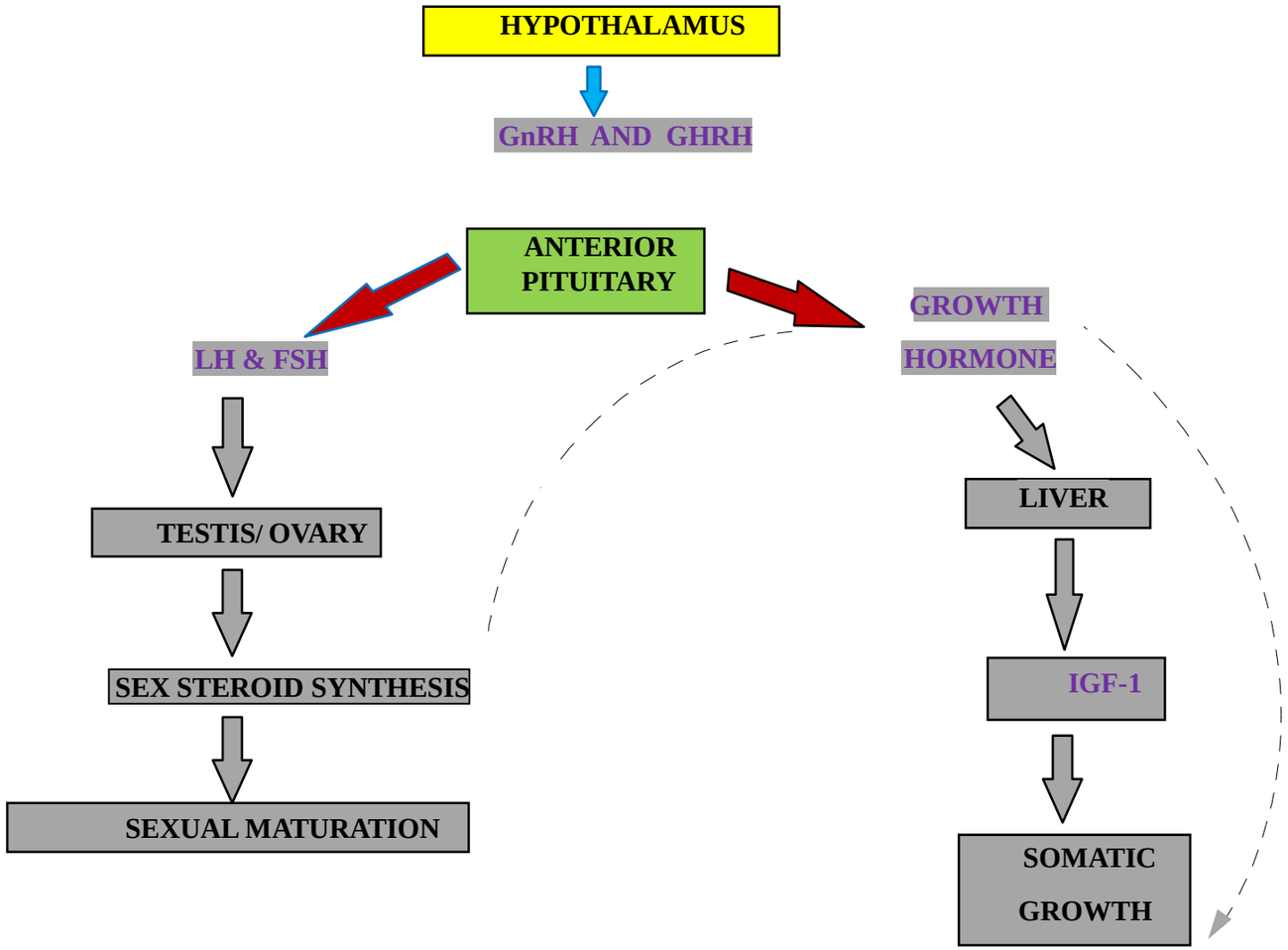


- Hormonal changes produce physical changes (Next slide)
- Nocturnal GnRH pulsatility (LH secretion) precedes phenotypic changes by several years
- First phenotypic changes: breast development / testicular enlargement
- in young children, LH and FSH levels are insufficient to initiate gonadal function
- During puberty , blood levels of LH, FSH increase.
- amplitude of pulses increases, especially during sleep
- high levels of LH, FSH initiate gonadal development

Physical changes:

- 5 stages from childhood to full maturity
- Tanner Scale (P1 – P5)
- Reflect progression in changes of the external genitalia and of sexual hair
- Secondary sexual characteristics
- Mean age 10.5yrs in girls
- Mean age 11.5 – 12yrs in boys

Girls		Boys	
• **Breast enlargement usually first sign (Thelarche)** • Menarche usually 2-3 yrs after breast development • Growth spurt peaks before menarche • Pubic and axillary hair growth: sign of adrenal androgen secretion • Starts at similar stage of apocrine gland sweat production and associated with adult body odour		• LH and FSH release increases ~10 yrs. of age • spermatogenesis; androgen secretion • androgens initiate growth of sex accessory structures (e.g. prostate), male secondary sex characteristics (facial hair, growth of larynx) • androgens causes retention of minerals in body to support bone and muscle growth • Sertoli cells also secrete some estrogen	
P1	Prepubertal	**P1**	Prepubertal, testicular volume **< 1.5 ml** [9 yrs and younger]
P2	Early development of subareolar breast bud +/- small amounts of pubic and axillary hair	**P2**	Testicular volume between 1.6 and 6 ml; skin on scrotum thins. Few pubic hairs [9-11 yrs]
P3	Increase in size of palpable breast tissue and areolae, increased pubic/axillary hair	**P3**	Testicular volume between 6 and 12 ml, Lenghtening of penis. Further growth of testes and scrotum [11-12.5 yrs]
P4	Breast tissue and areolae protrude above breast level. Further increased in pubic/axillary hair growth	**P4**	Testicular volume between 12 and 20 ml; scrotum enlarges further and darkens. Incresed pubic/ axillary hair [12.5-14 yrs]
P5	Mature adult breast. Complete pubic/axillary hair growth	**P5**	Testicular volume greater than **20 ml.** Genitalia adult in size and shape. Completed pubic/axillary hair growth [14+ yrs]



- GH secretion from anterior pituitary also increases
- TSH (thyroid stimulating hormone) secretion from anterior pituitary increases in both sexes:
  - increases metabolic rate
  - promotes tissue growth

Timing of puberty:

- Trend toward earlier puberty exists within Western Europe and USA
- Puberty usually completed **within 3 - 4 yrs of onset**
- Examination of lifestyle changes may give clues regarding mechanisms inducing onset

Influencing factors for puberty timing

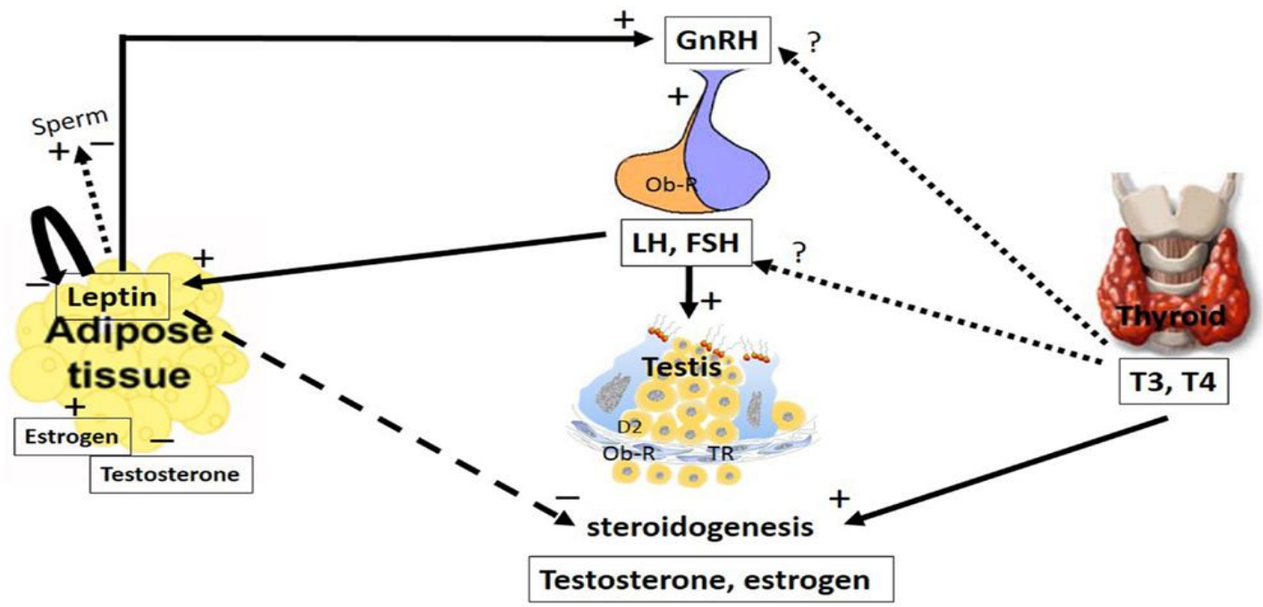
1. Genetics: 50-80% of variation in pubertal timing
2. Enviromental factors:

Nutritional status:

- Critical body weight must be attained before activation of the reproductive system.
- earlier puberty due to improvement of nutrition, living conditions, healthcare.
- evidence supporting hypothesis:
  - **obese girls go through early menarche**
  - malnutrition is associated with delayed menarche
  - primary amenorrhea is common in lean female athletes

3. Leptin: regulates appetite and metabolism through hypothalmus. Permissive role in regulating the timing of puberty.

Relation between leptin and puberty : Leptin binds to specific hypothalmus receptors and increase the secreation of GnRH and therefore releasing of LH + FSH



Disorders of puberty

Early of precocious puberty

- Precocious onset of puberty is defined as occurring younger than 2 yrs before the average age

Girls < 8 years old

Boys < 9 years old

- More common in females*
- Uncommon in males
- May be associated with a growth spurt

Delayed puberty

1. Initial physical changes of puberty are not present
   - by age 13 years in girls (or primary amenorrhea at 15.5-16y)
   - by age 14 years in boys

1. Pubertal development is inappropriate
   - The interval between first signs of puberty and menarche in girls or completion of genital growth in boys is **more 5 years**

Gonadotropin-dependent precocious puberty	**Gonadotropin-independent precocious puberty**	**Gonadal failure (Hypergonadotropin hypogonadism)**	**Gonadal deficiency (Congenital hypogonadotropin hypogonadism)**
1. Premature activation of the (HPG) axis 2. Intra-cranial lesions (tumours, hydrocephalus, CNS malformations) 3. Gonadotropin secreting tumours – v. rare	• Precocious pseudopuberty* • No spermatogenesis or ovarian development • FSH & LH suppressed • Congenital adrenal hyperplasia (CAH) • Sex steroid secreting tumors (adrenal or ovarian)	1. Turner's Syndrome (Congenital) 2. Post-malignancy chemo / radiotherapy / surgery (Acquired) 3. Polyglandular autoimmune syndromes	1. Hypothalamic/pituitary lesions (tumours, post-radiotherapy) 2. Rare gene mutations inactivating FSH/LH or their receptors

Precocious pseudopuberty: abnormality in the ovary to produce estrogen without the presence of LH. •

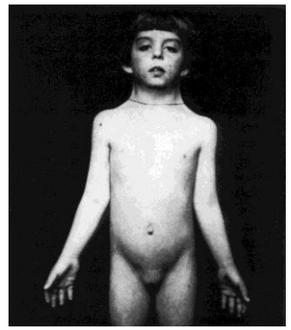
Gonadotropin: LH & FSH. •

* When the Q mention that the patient is female → precocious puberty .

IMPORTANT

Turner syndrome

- **Karyotype 45,X (45,X/46,XX**, structural abnormalities of X chromosome)
- Short stature (final height 144-146 cm), Gonadal dysgenesis, Skeletal abnormalities, Cardiac and kidney malformation, Dysmorphic face
- No mental defect
- Impairment of cognitive function
- Therapy: growth hormone, sex hormone substitution
- It is rare and more common in female than male .



MCQs

1. What is the first secondary sexual characteristic does appear for female?
   a. Thelarche
   b. Puberrache
   c. Menarche
   d. Gonadarche
2. During development of the testis in male, the testicular size ranges between?
   a. 6-12 ml
   b. 12-20 ml
   c. 6-20 ml
   d. 1.5-20 ml

3. A 6-year old female came to the hospital with vaginal bleeding. The GP noticed large breast and growth of pubic hair. He arranged for some hormonal assays.

- Estrogen: High
- LH & FSH: normal

What is the cause of her precocious puberty?

   a. Intracranial lesion
   b. Premature activation of HPG axis
   c. Precocious pseudopuberty
   d. Turner's syndrome

4. A female experienced an early menarche. Which of the following could cause such a manifestation?
   a. Active-lifestyle (athlete)
   b. Chemotherapy
   c. Obesity
   d. Turner's syndrome

5. When spermatogenesis usually begins?
   a. 8-14yrs
   b. 8-12yrs
   c. 9-12yr
   d. 9-14yrs

1-A 2-D 3-C 4-C 5-D

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Reproductive Block