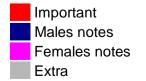


#5 Puberty in males and females

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



Revised by هشام الغفيلي & خولة العماري

Resources: 435 male's & female's slides +Kaplan physiology Lecture notes

Editing file: Here

Puberty Introduction

Definition of puberty: two definitions

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



Onset of puberty:

- Occurs between 8 and 14yrs in girls Q
- Occurs between 9 and 14yrs in boys

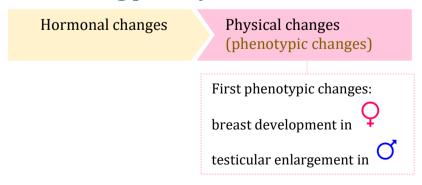
Terms & Events:مصطلحات مهمه جدا

Thelarche	Pubarche	Menarche	Adrenarche	Gonadarche
Development of breast in female only. While The development of breast in male is called Gynecomastia	Development of axillary & pubic hair.	The first menstrual period	The onset of increased secretion of androgens, responsible for development of pubic and axillary hair, body odor and acne.	maturation of gonadal function

Is there any relation between Thelarche & pubarche? NO ,because thelarche occur due to increase of estrogen , while pubarche occur due to increase androgen..

arche is a Greek word means "beginning"

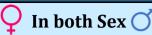
Changes occur during puberty:



NOTE: (Hormonal changes precedes physical changes)



Hormonal Changes



- In young children . LH and FSH levels are insufficient to initiate gonadal function.
- Puberty is associated with activation of the HPG axis
- At the puberty (Between 9-12 yrs ithin) there is †Stimulation of hypothalamo-pituitarygonadal axis:

†pulsatile secretion of GnRH(LHRH) leads to حطوا تحت بولستايل 20 خط

↑pulsatile secretion Gonadotropins (FSH &LH),

Then stimulate the gonads to

1 Secretion of the sexual steroids (estrogenes & androgens"testosterone")

Initiate Gonadal **development** & appearance of the **secondary sex** characteristics

#Keep in mind: if the hormone secreted continuously (not in pulses) the target tissue won't respond, so pulsatile secretion is very imp. LH is the main hormone that initiate puberty without LH puberty won't take place(increase frequency & amplitude of LH شي مهم مهم مهم مهم مهم لازم تعرفونه pulses is necessary to initiate puberty)

- Another event of puberty is the appearance of large **nocturnal pulses** of **LH** during REM sleep (One of the earliest events of puberty precedes phenotypic changes by several years) عد ترب البرغ كل لِلهُ تعدث زياد
- A significant event early in puberty is an **increased sensitivity of the GnRH receptors** in the anterior pituitary. من يزيد افراز الجي إن ارتش عند البلوغ وش معنى بهذي الفتره بالذاات ؟؟الجواب مازل غامض بس لاحظوا انه عند قرب البلوغ بتزيد حساسية الرسيبترز له ي

Extragonadal Hormonal Changes During Puberty: ایش الهورمونك الاخری الی بتزید قتره البلوغ

- ↑adrenal steroid(androgen)
- ↑GH secretion from anterior pituitary increases→elevation of IGF-I→↑somatic growth.
- 1TSH (thyroid stimulating hormone) secretion from anterior pituitary increases in both sexes:
 - increases metabolic rate
 - promotes tissue growth

In boys LH and FSH release increases ~10 yrs. of age Spermatogenesis increase androgen secretion adrenals also secrete androgen Sertoli cells also secrete some estrogen The roles of androgen in boys' puberty?

androgens initiate growth of sex accessory structures1 (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

In girls \subseteq



- 1) Surge of LH release initiates 1st ovarian cycle (usually not sufficient to cause ovulation mcq). يىنى اول
- 2) Estrogen increases due to growing follicles.

The roles of estrogen & androgen in girl's puberty?

- **Estrogen** induces the **secondary sex characteristics**: growth of pelvis, deposit of subcutaneous fat, growth of internal reproductive organs, external genitalia & breast development.
- androgen release by adrenal glands increases (but not as much as in male) → growth of pubic hair, lowering of voice, growth of bone, increased secretion from sebaceous glands (glands secrete oil waxy matter).

بيجيكم سؤال باختبار الاسبوع الجاي من اين يفرز الاستروجين في المرأه؟؟

From the granulosa cells & theca INTERNA(Not theca EXTRANA, theca externa act as capsule & later will secrete proteolytic enzymes)

Accessory Sex Organs. The internal organs of the male reproductive system are called accessory organs. They include the vas deferens, seminal vesicles, prostate gland, and bulbourethral (Cowper's)

Physical Changes

In boys

In girls \subseteq



1)Testicular enlargement (12-13 yrs) is the first sign (often the First signs go unnoticed)

- Puberty begins when Testis volume reaches (1,6-6 ml)MCQ
- There is Growth of the testes, largely because of an increased number of seminiferous سألناهم العام القبل الماضي سبب كبر حجم التيستيس tubules
- Leydig cell proliferation in the testes, and increased synthesis and secretion of testosterone. As plasma levels of testosterone increase. There are:
 - growth of the sex accessory organs² such as the prostate. VERY IMP
 - facial, pubic, and axillary hair appears and there is growth of the penis, lowering of the voice, and initiation of spermatogenesis (spermarche).

لاحظوا اهمية التيستيكيولر انلارجمنت بالبلوغ لو ماحصل ماراح يزيد التيستيستيرون فبلتالي نمو الاعضاء الثانوية وظهور اعراض البلوغ الاخرى لن

2) Penile and scrotal enlargement occur approx 1 yr after testicular enlargement. Pubic hair appears at same time.

3) There is a pronounced linear growth spurt

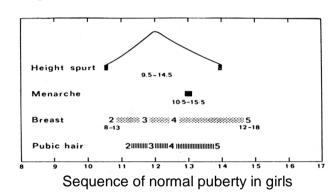
In males, the growth spurt develops near the end of puberty.

1)Breast enlargement (Thelarche) usually first **sign**.breast budding³ occur before breast development.

2) Growth of pubic hair is the second sign (dependent on increased secretion of adrenal androgens [العام الماضي سألناهم ايش العلامه الثانيه للبلوغ ومعظمهم اخطؤوا وكتبوا نمو الثدي (adrenarche)

3) Growth spurt⁴ peaks before menarche, Growth spurt and closure of the epiphyses: typically begin and end earlier in girls than in boys MCO. In females, the growth spurt begins early in puberty and is near completion by menarche.

4) Menarche usually 2-3 yrs after breast development, menarche usually is the last sign (last physical changes)



Tanner Scale

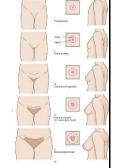
- defines physical measurements of development based on external primary and secondary sex characteristics, such as the size of the breasts, genitals, testicular volume and development of pubic hair.
- Tanner Scale 5 stages from childhood to full maturity (P1(prepuberty) P5(full puberty)).
- Reflect 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

Pubertal Stages (Tanner) Male: helpful image

- **P1** Prepubertal, testicular volume < 1.5 ml [9 yrs and younger]
- Testicular volume between 1.6 and 6 ml; skin on scrotum thins. Few pubic hairs [9-11 yrs]
- P3 Testicular volume between 6 and 12 ml, Lenghtening of penis. Further growth of testes and scrotum [11-12.5 yrs]
- P4 Testicular volume between 12 and 20 ml; scrotum enlarges further and darkens. Incresed pubic/ axillary hair [12.5-14 yrs]
- P5 Testicular volume greater than 20 ml. Genitalia adult in size and shape. Completed pubic/axillary hair growth [14+ yrs]

Pubertal Stages (Tanner) Female: helpful image

- P1 Prepubertal
- P2 Early development of subareolar breast bud +/small amounts of pubic and axillary hair
- P3 Increase in size of palpable breast tissue and areolae, increased pubic/axillary hair
- P4 Breast tissue and areolae protrude above breast level. Further increased pubic/axillary hair growth
- P5 Mature adult breast. Complete pubic/axillary hair growth



Female's & male's doctors said, the(tanner stages) is extra & they won't ask us about it, that's why I highlighted it in grey

² Accessory Sex Organs. The internal organs of the male reproductive system are called accessory organs. They include the vas deferens, seminal vesicles, prostate gland, and bulbourethral (Cowper's) glands.

³ Budding=developing of fat tissue in the breast

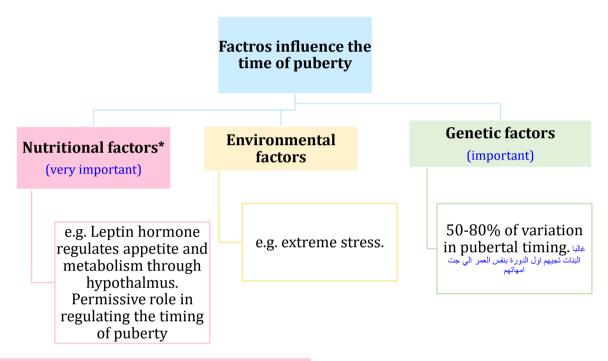
⁴ Define growth spurt: an occurrence of growing quickly and suddenly in a short period of time

Timing of Puberty & factors influencing it

Timing of Puberty:

- Trend toward earlier puberty exists within Western Europe and USA
- Puberty usually completed within 3 4 yrs of onset (IMOPRTANT) معرفون هالشي مهم :البلوغ في البنت يبدأ مبكر لكن ينتهي مبكر بعكس الولد يبدأ (IMOPRTANT) متأخر لكن يستمر لفترة أطول من البنت
- Examination of lifestyle changes may give clues regarding mechanisms inducing onset

Influencing Factors:

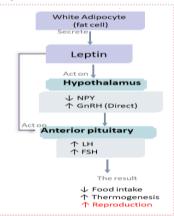


*Nutritional factor:Potential Involvement Of Leptin:

سوال الى يطرح نفسه وش علاقة التغذية بتو قيت النلو غ?؟؟؟يش السمان يبلغون ميكر بينما النحاف يتأخر عندهم البلو غ؟؟ايش علاقة الدهون بالموضو ع؟؟؟بنحاول نحل اللغز تحت:))

Leptin Cause accelerates the HPG axis:

Normally, leptin is secreted from white adipocytes during eating, then leptin goes to hypothalamus to stimulate GnRh & inhibit NPY⁵, also leptin has direct effect on AP to stimulate LH & FSH secretion. ((resulting in accelerate activation of HPG axis and initiation of early puberty))



- 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 amenorrhea⁶ is common in lean female athletes(very Imp)

⁵ NPY (neuropeptide Y) is a potent stimulator of food intake, has an inhibitory effect on GnRH secretion.

⁶ In **primary amenorrhea**, menstrual periods have never begun (by age 16)

Pubertal Disorders

Precocious(early) puberty		Delayed puberty		
Precocious onset of puberty is defined as: occurring younger than 2 years before the average age: Girls <8 years old Boys <9 years old facts about Precocious puberty: More common in females. bc fat is more in female than male Uncommon in males (usually pathological). Maybe associated with a growth spurt		When Puberty is described as delayed puberty? If the Initial physical changes of puberty are not present: • by age 13 years in girls (or primary amenorrhea at 15.5-16y) ⁷ • by age 14 years in boys OR if the Pubertal development is inappropriate: • the interval between first signs of puberty and menarche in girls is more than 5 years • the interval between first signs of puberty completion genital growth in boys is more than 5 years		
Causes Of Precocious Puberty		Causes of Delayed puberty Delayed puberty occurs when the gonad(testis &ovaries)produce little or no sex hormones, why,what r the causes?? يا ان القوناد نفسها خربانه او ماتكونت ا او ان الهور مونات الى تحفز القوناد عطلانه .		
Gonadotropindependent Precocious puberty (true / central) Could be due to: Premature activation of the (HPG) axis. Intracranial lesions ⁸ (tumours, hydrocephalus, CNS	Gonadotropin - independent Precocious puberty (Precocious pseudopuberty) Why it called pseudopuberty? - FSH & LH suppressed - No spermatogenesis or ovarian development Could be due to: Congenital adrenal hyperplasia (CAH)	Gonadal failure (Hypergonadotropic hypogonadism) Or Primary hypogonadism (the problem from gonad itself) Could be due to: Turner's Syndrome(where there's gonadal dysgenesis) Post-malignancy chemo / radiotherapy / surgery,can cause gonadal failure. Polyglandular autoimmune syndromes9	Gonadal deficiency Or Secondary hypogonadism. (This type of indicates a problem in the hypothalamus or the pituitary gland) البش الي حاصل هنا ان القوناد ماتفرز سيكس هورمون رطيب ليش؟؟ المشكلة اما تكون ان الهايبوئلمس ماتفرز جنرائش او ان البتوتري فيها مشكله فما تستجيب للجنزيش او ان المشكلة في الريسيبتورز الموجودة على القوناد فيها طفره خلتها ماتستجيب للجونادوتروين مورمون الموجودة على القوناد فيها طفره خلتها ماتستجيب للجونادوتروين Could be due to: Congenital hypogonadotropic hypogonadism. ↓LH & FSH→the gonad won't be able to produce sex hormone.	
malformations) Gonadotrophin secreting tumors *-v. rare	Sex steroid secereting tumours (adrenal or ovarian tumors)	aucommune synaromes	 Hypothalamic/pituitary lesions (tumors*, postradiotherapy)can lead to low GnRH. Rare gene mutations inactivating FSH/LH or their receptors 	

*Tumors: can cause overproduction or suppression سلاح ذوحدين

⁷ Normally Menarche occur after 3 yrs of thelarce

⁸ Lead to changes in the anatomy and also will affect the pituitary gland→↑ Gonadotropic hormones

⁹ Polyglandular autoimmune syndrome (PAS) is made up of a group of autoimmune disorders of the endocrine glands. The syndrome results in failure of the glands to produce their hormones.

Turner syndrome

Cause

Karyotype 45,X (structural abnormalities of X chromosome) is a condition in which a female is partly or completely

missing an X chromosome

Clinical manifestation

- -Short stature (final height 144-146 cm)
 - -Gonadal dysgenesis
 - -Skeletal abnormalities
 - -Cardiac and kidney malformation
 - -Dysmorphic face
- -NO mental defect(no impairment of cognative function)

Therapy

growth hormone & sex hormone substitution



EXTRA reading Taken from Kaplan physiology Lecture notes PUBERTY

Reproductive Changes

- Hypothalamic pulse generator increases activity just before physical changes at puberty.
- First noted sign in a female is breast development; first by estrogen (promotes duct growth) then progesterone (promotes development of milk-producing alveolar cells).
- First noted sign in a male is enlargement of the testes (mainly FSH stimulating seminiferous tubules).
- Pubic hair development in males and females is dependent on androgen.

Growth Changes

- During puberty, androgens promote the secretion in the following anabolic sequence:

 At puberty, if T4 is normal, ↑ androgens drive ↑ growth hormone, which drives ↑ IGF-I.
- IGF-I is the major stimulus for cell division of the cartilage-synthesizing cells located in the epiphyseal plates of long bones.
- In males, the increased androgen arises from the testes (testosterone); in females, from the adrenals (adrenarche).
- Near the end of puberty, androgens promote the mineralization (fusion or closure) of the epiphyseal plates of long bones. Estrogen can also cause plate closure, even in men.
- In females, the growth spurt begins early in puberty and is near completion by menarche.
- In males, the growth spurt develops near the end of puberty

SUMMARY

Normal pubertal development						
	Boys 🔿	Qgirls				
Age of start(yrs)	(9 - 14)	(8 -14)				
Duration of puberty(yrs) (Takes 3-4 yrs)	3,2 ± 1,8 (till adult size of testis)	2,4 ± 1,1 (till menarché)				
Hormonal Changes	 At puberty:↑ pulsatile secretion of GnRh→↑ pulsatile secretion of LH&FSH→ stimulate the gonads to release sex hormone→ Initiate Gonadal development &appearance of the secondary sex characteristics Another early event of puberty: is the appearance of large nocturnal pulses of LH during REM. Extragonadal Hormonal Changes During Puberty: ↑adrenal, GH & TSH 					
	estrogen released from Sertoli cells Androgens released from spermatogenesis & adrenal gland→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.	 ↑LH which initiate 1st ovarian cycle (usually doesn't cause ovulation) Estrogen released from growing follicle induces→secondary sex characteristics: growth of pelvis, deposit of subcutaneous fat, growth of internal reproductive organs, external genitalia & breast. androgen release by adrenal glands increases (but not as much as in male)→growth of pubic hair, lowering of voice, growth of bone, increased secretion from sebaceous glands 				
Physical changes	 Testicular enlargement first sign (Due to ↑number of seminiferous tubules)→↑ Leydig cell →↑testosterone→result in: Penile ,scrotal enlargement and Pubic hair 1 yr after testicular enlargement. growth spurt 	 Breast enlargement B2 (Thelarche) usually first sign Growth of pubic hair (dependent on adrenarche) Growth spurt 10 peaks before menarche, begin and end earlier in girls than in boys Menarche 2-3 yrs after thelarche 				
influencing factors	genetic, environmental & nutritional (↑Leptin→accelrae HPG axis '↑GnRh,↓NPY,↑LH &↑FSH' →early puberty)					
Tanners scale	reflect progression in changes of the external genitalia & of sexual hair.					

¹⁰ Define growth spurt: an occurrence of growing quickly and suddenly in a short period of time

Pubertal Disorders						
Precocious Puberty: occurring of puberty younger than 2 years before the average age		Delayed puberty: if the initial physical changes of puberty doesn't present or if the pubertal development inappropriate				
Causes Of Precocious Puberty		Causes of Delayed puberty				
Gonadotropin- dependent Precocious puberty (true / central)	Gonadotropin - independent Precocious puberty (Precocious pseudopuberty)	Gonadal failure (Hyp <u>erg</u> onadotropic hy <u>po</u> gonadism)	Gonadal deficiency			
Could be due to: Premature activation of the (HPG) axis. Intracranial lesions (tumours, hydrocephalus, CNS malformations) Gonadotrophin secreting tumours –v. rare	- FSH & LH suppressed - No spermatogenesis or ovarian development Could be due to: Congenital adrenal hyperplasia (CAH) Sex steroid secereting tumours (adrenal or ovarian tumors)	Could be due to: Turner's Syndrome Post-malignancy chemo / radiotherapy / surgery, Polyglandular autoimmune syndromes	Could be due to: Congenital hypogonadotropic hypogonadism. Hypothalamic/pituitary lesions (tumors, postradiotherapy)can lead to low GnRH Rare gene mutations inactivating FSH/LH or their receptors			

MCQs

- 1. Menstruation begin in between (year):
 - a. 10.5-14
 - b. 12-15
 - c. 9-14
 - d. 8-14
- 2. spermatogenesis begin in between (year):
 - a. 10.5-14
 - b. 12-15
 - c. 9-14
 - d. 8-14
- 3. The term Thelarche means:
 - a. development of breast
 - b. development of pubic & axillary hair
 - c. the first mensitrual period
 - d. maturation of gonadal function
- 4. The primary event of puperty:
 - a. increase androgen secretion
 - b. pulsatile secretion of GnRh
 - c. none of them
- 5. Pulsatile secretion of LH&FSH stimulate the secretion of:
 - a. gonadal steroid hormones
 - b. testosterone
 - c. estradiol
 - d. all of them
- 6. Which of these hormones responsible for the appearance of the secondary sex characteristics at puberty:
 - a. sex steroid hormones
 - b. GH
 - c. TSH

7. Which one of these is A significant event early in puberty:

- a. increased sensitivity of the GnRH receptors
- b. appearance of large **nocturnal pulses** of LH during REM sleep.
- c. Increase sensitivity in GH reseptor
- d. A&B
- 8. Testicular volume between 6 and 12 ml, Lenghtening of penis. Further growth of testes and scrotum. Which stage is this:
 - a. P1
 - b. P2
 - c. P3
 - d. P4
- 9. Which one of these is a Gonadotropindependent precocious puberty:
 - a. hydrocephalus
 - b. Congenital adrenal hyperplasia
 - c. FSH & LH suppressed
 - d. no spermatogenesis or ovarian development
- 10. The cause of Gonadal failure:
 - a. Turner's Syndrome
 - b. Hypothalamic/pituitary lesions
 - c. rare gene mutation inactivating FSH/LH or their receptors

Answer key:

1 (d) | 2 (c) | 3 (a) | 4 (b) | 5 (d) | 6 (a) | 7 (d) | 8 (c) | 9 (a) | 10 (a)



Thanks to this amazing team!

عمر آل سليمان حسن الشماسي عبدالرحمن السياري روان الضويحي نوره العقيل ريم العقيل مي العقيل

