



Normal & Precocious Puberty

Objectives:

- How is Hypothalamic – Pituitary – Gonadal Axis regulated?
- How is puberty assessed children?
- How to approach a child a puberty disorder?

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Special thanks to team 437 & Faisal alsaif

 Notes

 Important

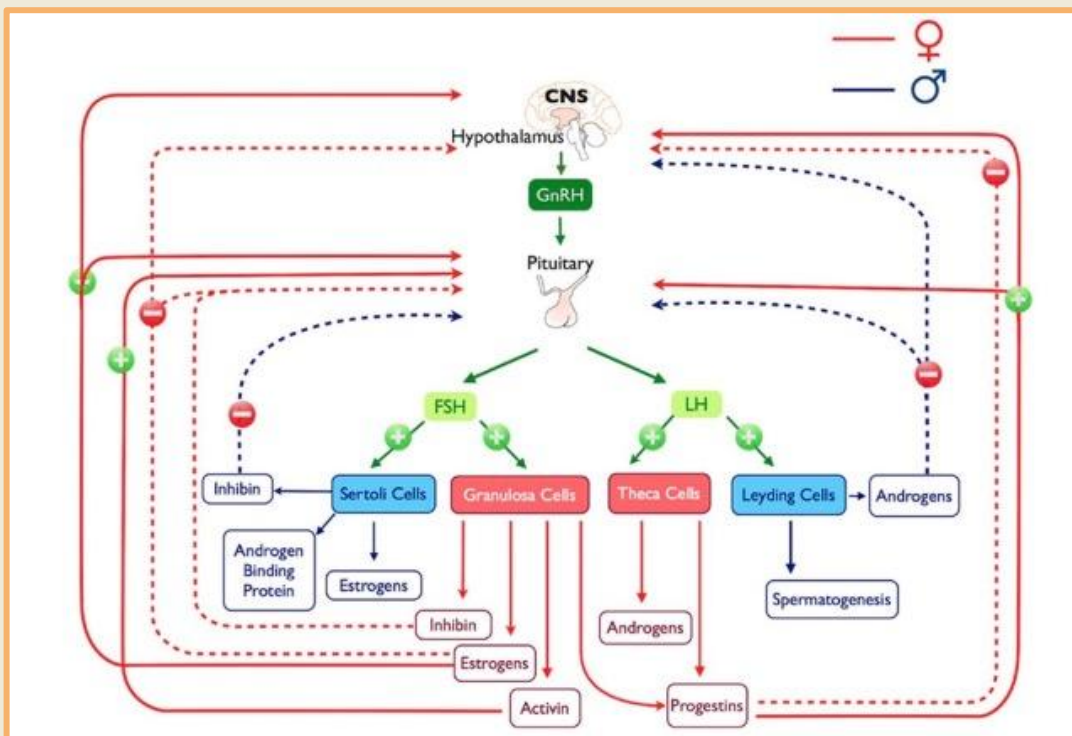
 Book

Puberty

Definition:

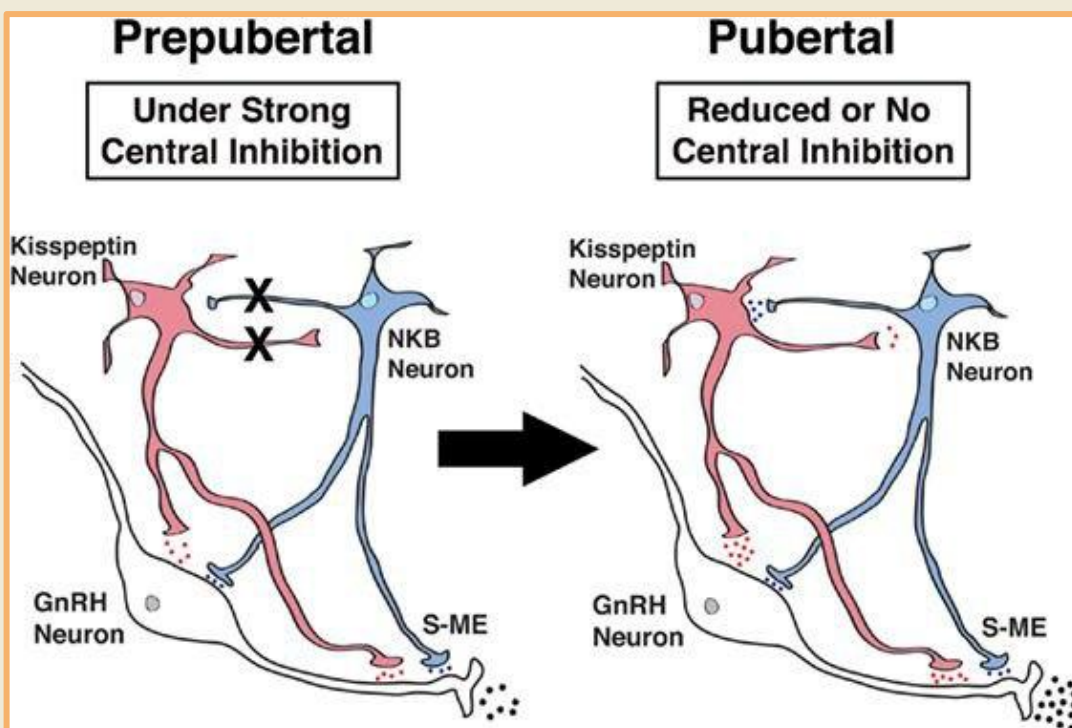
PUBERTY is the developmental stage during which a child becomes a young adult, characterized by the maturation of gametogenesis, secretion of gonadal hormones, and development of secondary sexual characteristics and reproductive functions.

ADOLESCENCE is used widely as a generally synonymous term for puberty, but the term often is used to convey an added connotation of cognitive, psychological, and social change

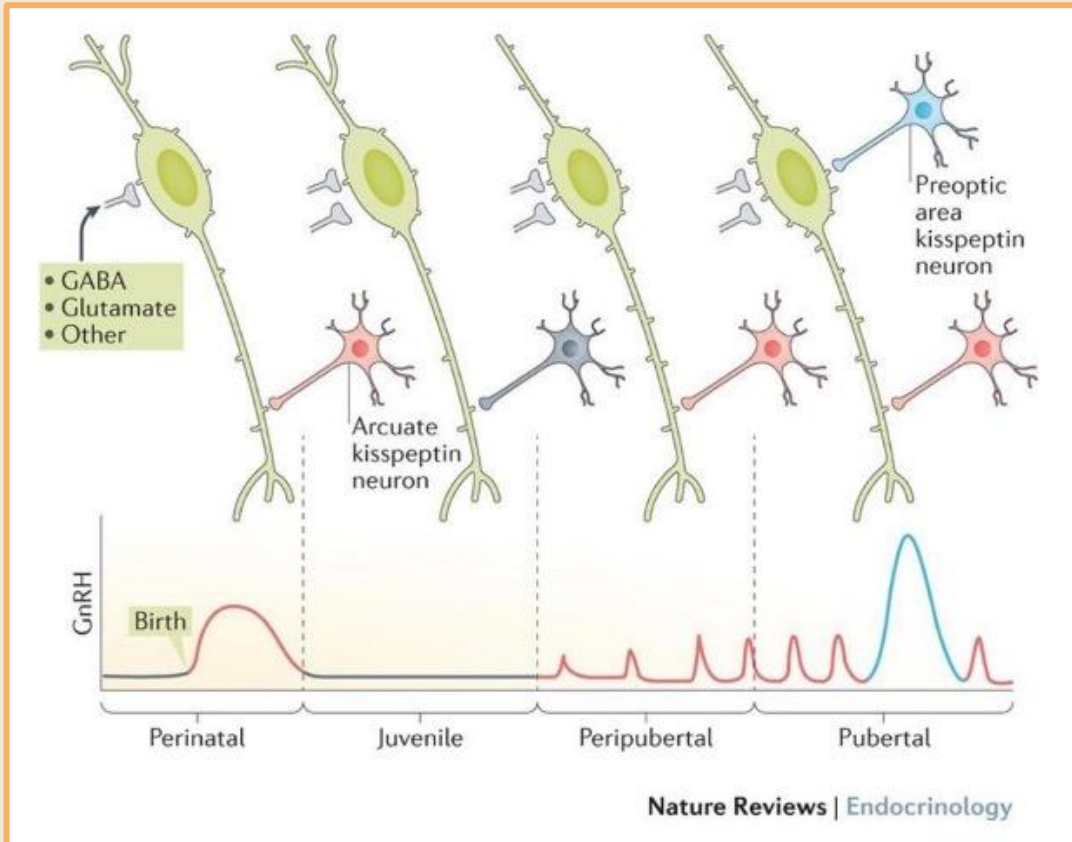


what triggers puberty? mutation in kisspeptin peptide or neurokinin B impact the time of puberty

KNDY neurons in hypothalamus → kisspeptin peptide → triggers release of GnRH



Puberty

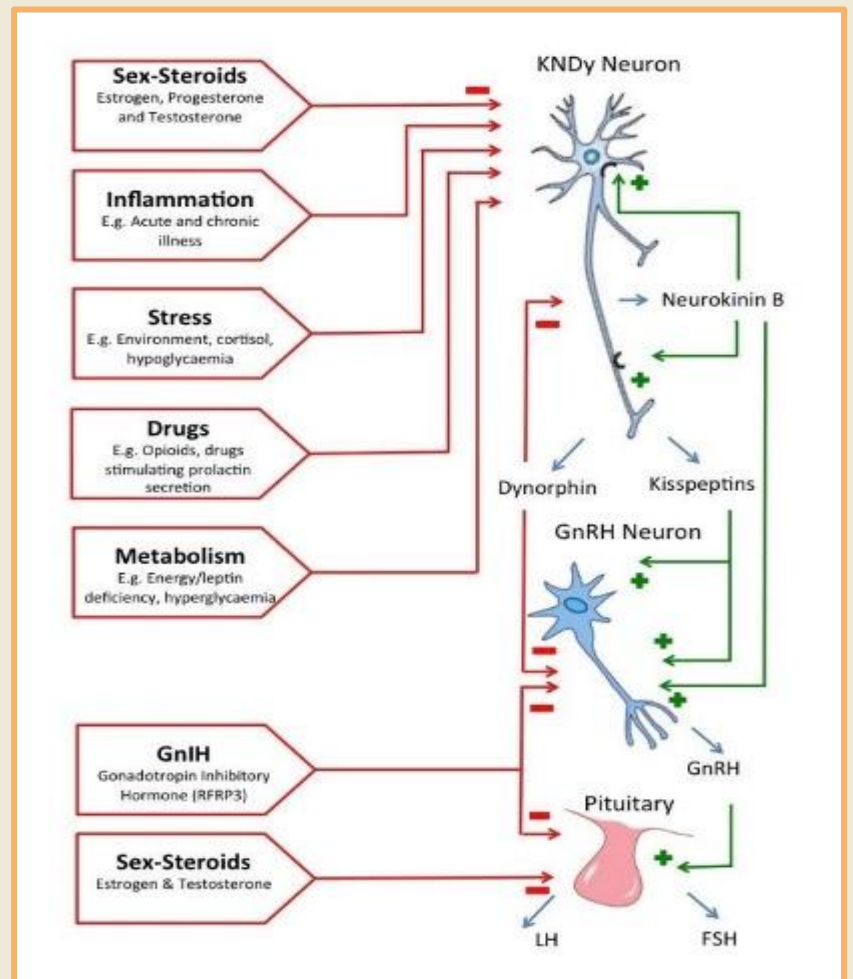


The level of infants sex hormones 6- 9 months of age is the same as adult but they don't develop puberty because of 2 theories: 1- It's not pulsatile 2- The receptors

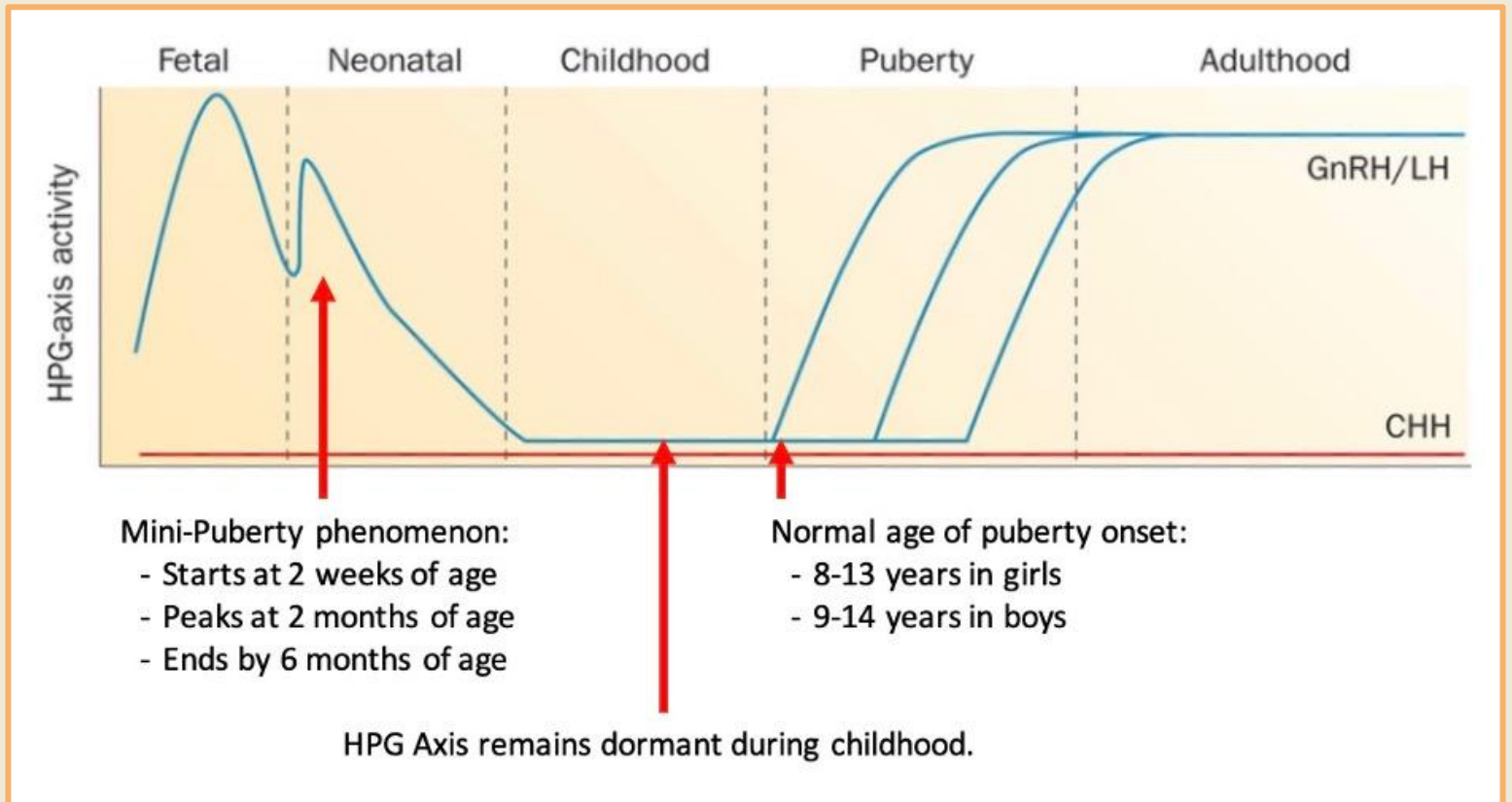
Note that in Klinefelter syndrome has gonadal failure and if you give testosterone in first 3-6 months of life they will have better IQ

what triggers puberty? Nobody knows
 put according to research there are neurons that signal through GnRH neurons. The KNDy neuron
 puberty start with Kiss

“kisspeptin”



Puberty Pattern



Puberty typically occurs between the ages of 8 and 13 in girls, and 9 and 14 in boys.

if before or after this duration evaluate the patient

Over the last 20 years, the mean age at which puberty starts in girls has lowered. However, the age at which menarche occurs has remained stable. (Race, ethnicity, family history, and obesity affects it)

Puberty follows a **well-defined sequence** of changes that may be assigned stages (Tanner staging).

Puberty Description

Term	Signs	Result of
gonadarche	Testicular enlargement	Testicular activation by FSH/LH
Adrenarche	Body odor, skin oiliness, pubic hair, Axillary hair, and acne	Adrenal gland activation by ??
Thelarche	Breast development	Ovary activation by FSH/LH
Pubarche	Pubic hair growth	Adrenal, ovarian or testicular androgens
Menarche	First menses	Ovarian activation by FSH/LH
spermarche	Appearance of sperms in morning void	Testicular activation by FSH/LH

Puberty Assessment

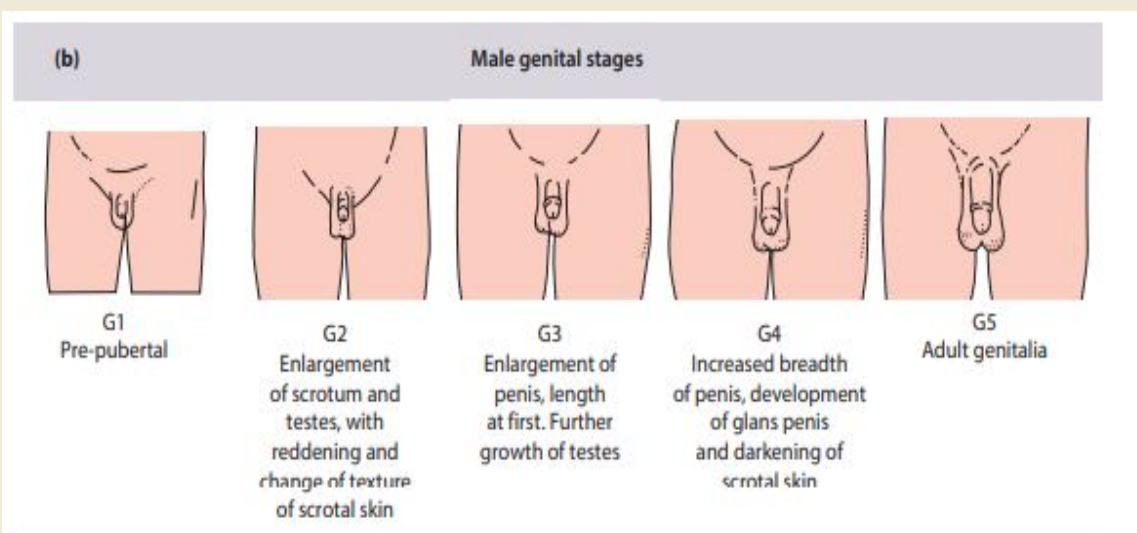
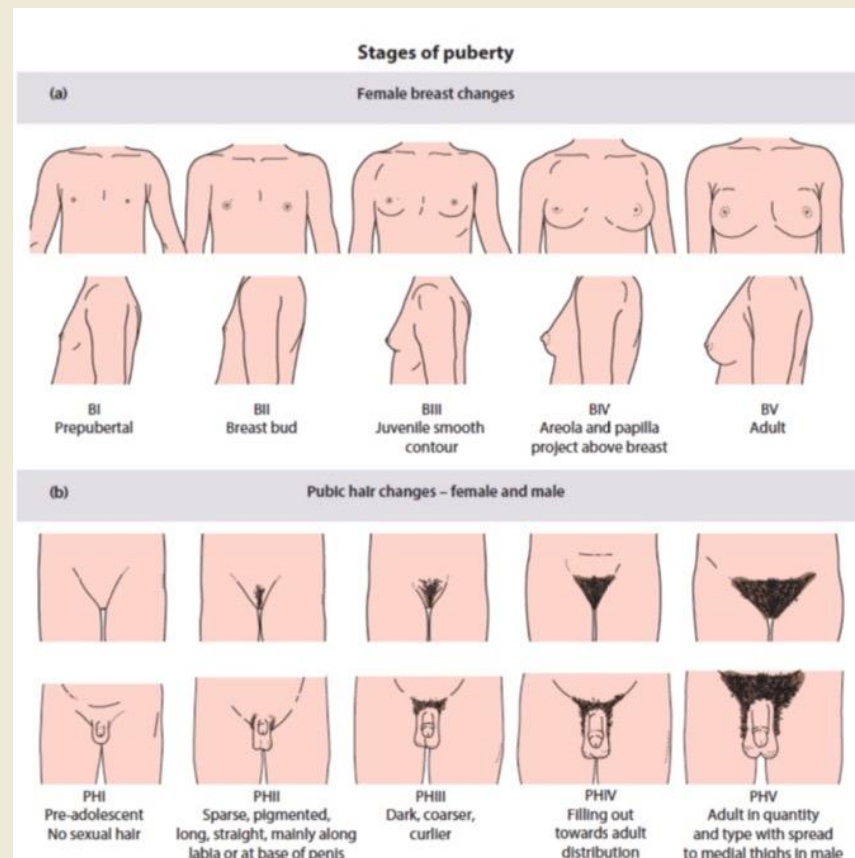
Tanner staging:

Stages are classified by:

- pubic hair
- testes (for males)
- breasts (for females)

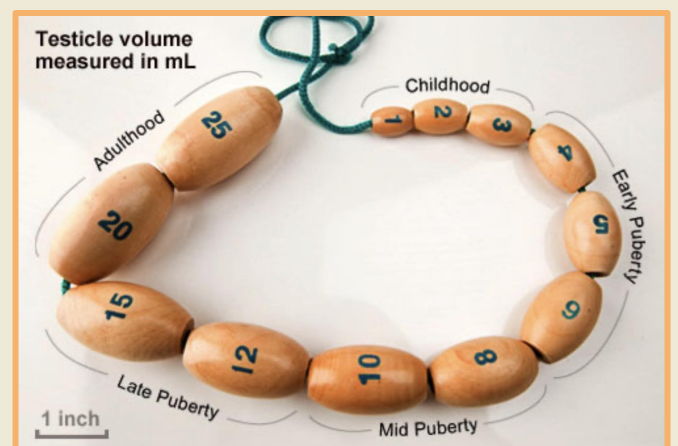
Breast budding in girls (Tanner II) indicates onset of puberty

Note that there's no stage 0 it starts with 1



Orchidometer: Measures testicular volume in mL

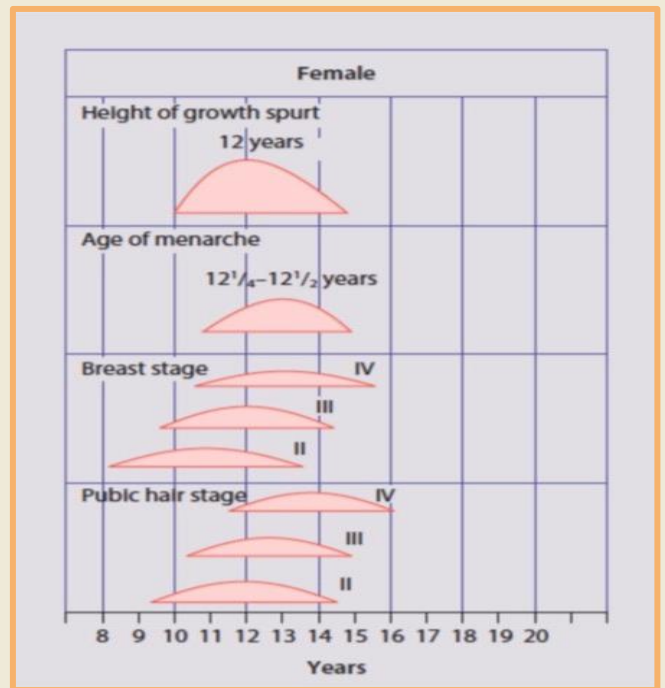
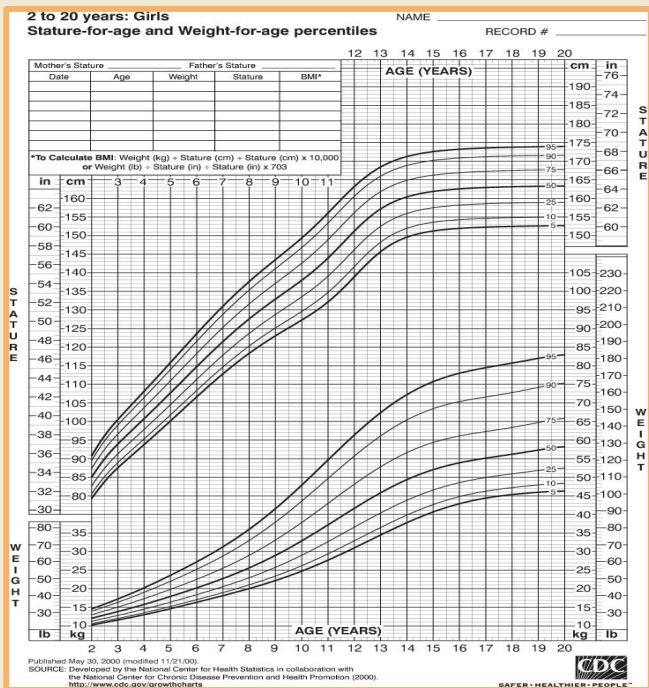
< 3 mL = childhood, 4 mL indicates the onset of puberty



Puberty Assessment

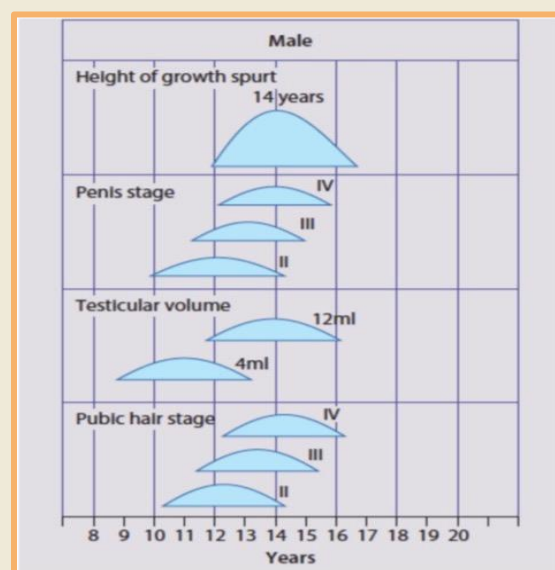
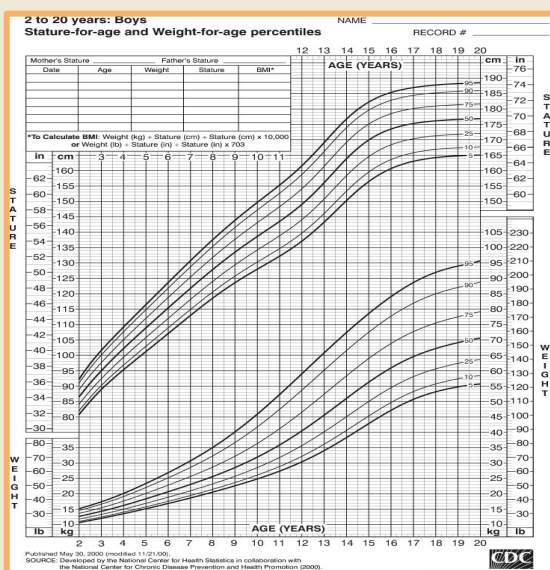
Females:

- 1- Breast development**—a palpable breast disc is the first sign, usually starting between 8.5 and 12.5 years
- 2- Pubic hair growth and rapid height growth** – occur almost **immediately** after breast development
- 3- Menarche**- occurs on average 2.5 years after the start of puberty and signals that growth is coming to an end, with only around 5-cm height gain remaining. Thus, **early puberty and menarche it will most likely affect their height.**



Males:

- 1- Testicular enlargement** to over 4-mL volume – the first clinical sign of puberty
- 2- Pubic hair growth** – follows testicular enlargement, usually between 10-years and 14-years of age
- 3- Rapid height growth** – when the testicular volume is 12 mL to 15 mL, after a delay of around 18 months
- 4- The growth spurt in males occurs later and is of greater magnitude than in females,** accounting for the greater final average height of males than females.



Delayed puberty

✳️ Absence of pubertal signs by the age of 14 in boys, and the age of 13 in girls

Delayed puberty is **common in boys** and usually due to constitutional delay in growth and puberty. Relative insensitivity of the testes, in girls pubertal delay is uncommon and a cause should be sought.

Approach to delayed puberty

Constitutional delay of growth and puberty	Hypogonadotropic hypogonadism	Hypergonadotropic Hypogonadism
<p>In an otherwise healthy child.</p> <p>Family Hx of delayed puberty in a parent</p> <p>Short stature, delayed bone age.</p> <p>Spontaneous recovery at Bone age 12-13</p> <p>FSH/LH and sex steroids in prepubertal range</p> <p>A retrospective diagnosis.</p> <p>most common</p> <p>An affected child will have delayed sexual changes compared with his/her peers, and bone age would show moderate delay. The legs will be long in comparison to the back. Eventually, the target height will be reached as growth in affected children will continue for longer than in their peers.</p>	<p>Difficult to differentiate from CDGP</p> <p>If congenital, could be associated with, cryptorchidism and/or micropenis in boys.</p> <p>Due to Pituitary/ Hypothalamic pathologies</p> <p>No spontaneous recovery</p> <p>FSH/LH and sex steroids in prepubertal range</p> <p>DDx: Pituitary hypoplasia (associated with other pituitary deficiencies, septo-optic dysplasia, CHARGE)</p> <p>Isolated Gonadotropin Deficiency [Kallmann syndrome] (associated with anosmia/hyposmia).</p> <p>Secondary (Trauma, Tumor, Radiation, Autoimmune, undernutrition, excessive exercising, hypothyroidism, hyperprolactinemia, Cushing's)</p>	<p>Difficult to differentiate from Hypogonadotropic hypogonadism in prepubertal age range.</p> <p>If congenital, could be associated with Ambiguous genitalia, cryptorchidism and/or micropenis in boys.</p> <p>Due to a gonadal pathology FSH/LH are extremely elevated in pubertal age range.</p> <p>DDx: Gonadal failure (congenital dysgenesis, Turner Syndrome, Klinefelter syndrome)</p> <p>Secondary: Trauma, Tumor, infection, radiation, Autoimmune, galactosemia.</p>

Delayed puberty

Investigations:

- ❖ Bone age
- ❖ FSH, LH levels
- ❖ Testosterone (boys), estradiol (girls)
- ❖ TSH, FT4 and prolactin
- ❖ Karyotype
- ❖ LHRH stimulation test in consultation with endocrinology
- ❖ MRI Pituitary + Olfactory pulp, gonadal imaging

management: extra from abu wardah

- Following reassurance that puberty will occur, treatment is usually not required.
- Oral oxandrolone can be used in young males: weakly androgenic anabolic steroid will induce some catch-up growth but not secondary sexual characteristics.
- In older boys, low-dose intramuscular testosterone will accelerate growth as well as inducing secondary sexual characteristics.
- In girls, as the ovaries are sensitive to gonadotropins, delayed puberty is less common and organic cause should be excluded.
- Karyotyping should be performed to identify Turner syndrome, and thyroid and sex steroid hormones should be measured.
- Females may be treated with oestradiol for several months to induce puberty.

- The aims of management are to:
 - identify and treat any underlying pathology
 - ensure normal psychological adaptation to puberty and adulthood
 - accelerate growth and induce puberty if necessary.



Case history 12.4

Constitutional delay in growth and puberty

A 14-year-old boy is concerned that he is short. He is well, but gets teased at school about his height. His mother had menarche at 13 years of age and his father recalls that he was still growing when he left school at the age of 16 years. Examination reveals a generally well boy, with stage 1 pubic hair and testicular volumes of 4 ml bilaterally. His bone age is delayed by 20 months. So, his short stature is secondary to a lack of height acceleration during puberty. As his mood has been significantly affected by his delayed puberty, he is treated with testosterone for 6 months with good effect on his growth rate and confidence. He then continues to make pubertal progress independently and reaches a final adult height of 166 cm (2nd to 9th centile) (see Fig. 12.9c).

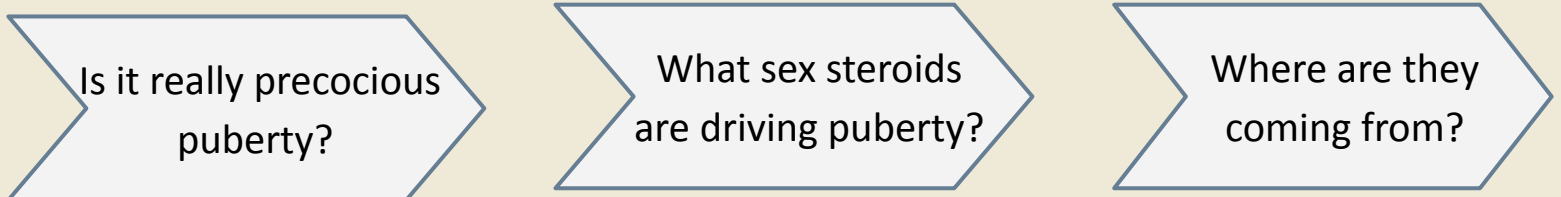
Precocious puberty

Definition:

Appearance of pubertal signs **before age 8 in girls**

Appearance of pubertal signs **before age 9 in boys**

Approach:



- Avoid pitfalls (hairy body, obesity, uterovaginal injuries)
- Gather additional information (Height velocity and bone age)

→ Inappropriate timing:

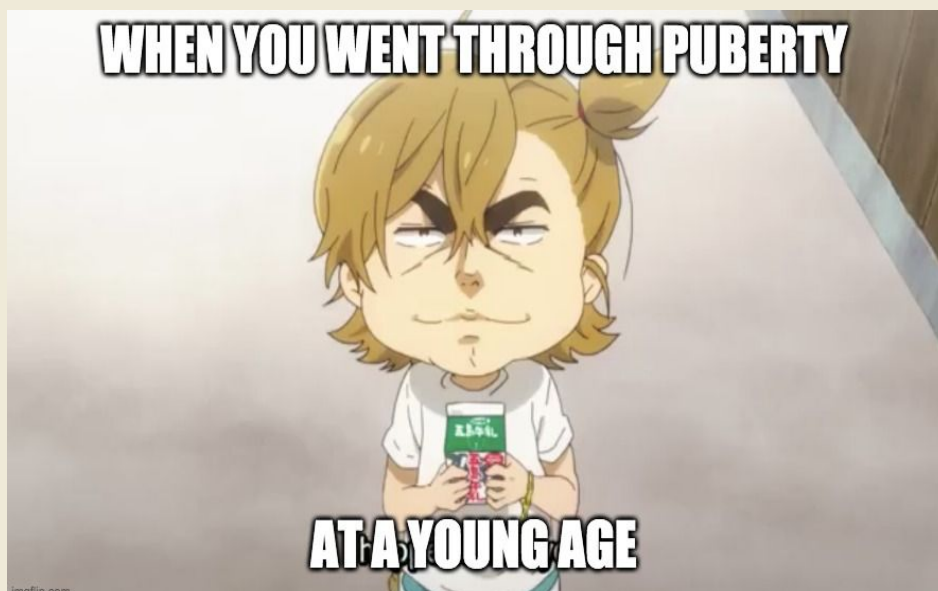
<8 y in girls

< 9 in boys

→ Inappropriate tempo (The progression):

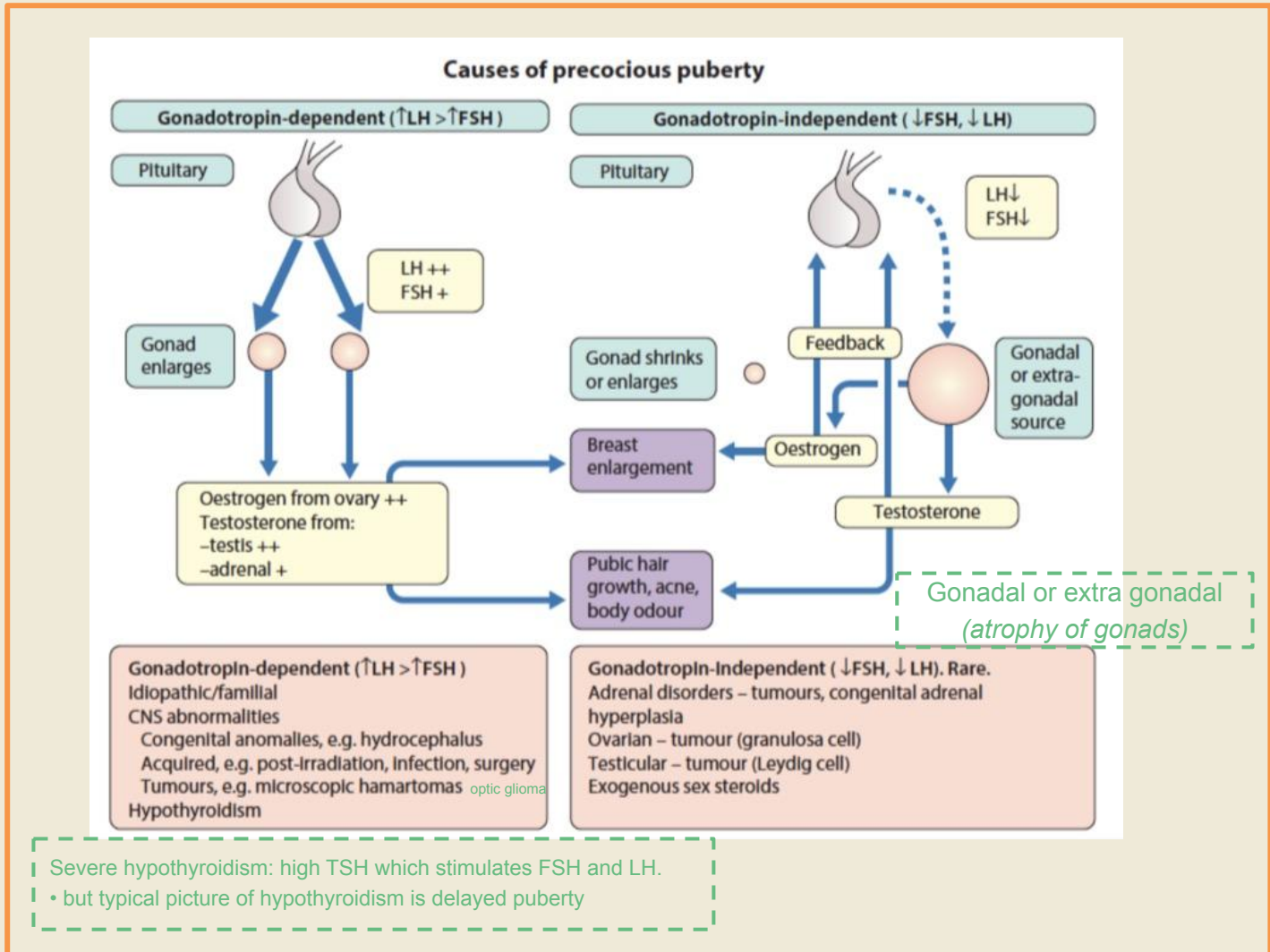
The normal progression from stage 1 - 5 take 3 - 5 years, So if a girl start breast budding while she is 9 and move to stage 4 breast while she is 10 we call this precocious puberty

Think about normal pubertal variations (Premature thelarche and premature adrenarche)



Precocious puberty

Assessment:



Management: extra from abu wardah

The management of precocious puberty is directed towards:

- detection and treatment of any underlying pathology, e.g. using MRI scan to identify an intracranial tumour, particularly in boys.
- reducing the rate of skeletal maturation, which is assessed by bone age. An early growth spurt may result in early cessation of growth and a reduction in adult height.
- addressing psychological/behavioural difficulties associated with early progression through puberty.
- delaying the onset of menarche in girls. It is possible to delay gonadotropin-dependent puberty using **gonadotropin-releasing hormone analogues**. treatment of choice in central PP



Case history 12.3

Gonadotropin-dependent precocious puberty in a boy

This 6-year-old boy presented with precocious puberty (Fig. 12.18a,b). He was noted to have multiple café-au-lait spots consistent with a diagnosis of neurofibromatosis type 1. An MRI scan showed a mass in the hypothalamus, which proved to be an optic glioma. He was treated with radiotherapy, although full remission was not possible to achieve. The site of injection of gonadotropin releasing hormone analogue treatment to suppress his sexual development is covered by the plaster.



Figure 12.18 (a) Multiple café-au-lait spots. Neurofibromatosis type 1 was diagnosed. (b) Genitalia showing stage 3 genitalia and pubic hair with 12-ml testicles bilaterally. He also had adult body odour. (From: Wales JKH, Rogol AD, Wit JM: Pediatric endocrinology and growth. London, 2003, Saunders, with permission.)

Precocious puberty

The child with precocious puberty and café-au-lait macules (CALMS):



Dr: It's important for you to differentiate between the two

McCune- Albright Syndrome	Neurofibromatosis -1
Caused by auto activation of the gonadotropin receptor	Caused by optic gliomas adjacent to the pituitary gland
Gonadotropin independent precocious puberty (Suppressed FSH/LH)	Gonadotropin Dependent (Elevated FSH /LH)
CALMs respect midline and have rough borders	CALMs cross midline and have smooth borders.
Associated with fibrous dysplasia	Associated with Axillary freckling Plexiform Neurofibromas and Lisch nodules (Hamartomas).
Caused by somatic GNAS mutations	Caused by germline NF1 mutations (autosomal dominant)

Investigations

- ❖ Bone age
- ❖ FSH, LH levels
- ❖ Testosterone (boys), estradiol (girls)
- ❖ Adrenal androgens for boys and girls.
- ❖ TSH, FT4 and prolactin
- ❖ LHRH stimulation test in consultation with endocrinology
- ❖ MRI Pituitary (if gonadotropin dependent)
- ❖ Gonadal/ Abdominal imaging to r/o tumors (if gonadotropin independent)

★ Precocious puberty in girls is common and usually due to the premature onset of normal puberty. Precocious puberty in boys is rare and a pathological cause must be excluded.

Extra

Premature thelarche

- ❖ This usually affects girls between 6 months and 2 years of age.
- ❖ The breast enlargement may be asymmetrical and fluctuate in size, rarely progressing beyond stage 3 of puberty.
- ❖ It is differentiated from gonadotropin dependent precocious puberty by the absence of other features of puberty or significant acceleration in growth.
- ❖ It is non-progressive and self-limiting.
- ❖ Investigations are not usually required.
- ❖ High maternal levels of prolactin can cause newborn babies to be born with breast buds and even to lactate. These self-resolve in days.



Case history 12.2

Premature thelarche

This 18-month-old female developed enlargement of both breasts (Fig. 12.16). There were no other features of puberty and she was growing normally. Her bone age was only mildly advanced (21 months). Her subsequent growth rate was normal. A diagnosis of premature thelarche was made.



Figure 12.16 Premature breast development in an 18-month-old girl. The absence of a growth spurt and axillary and pubic hair differentiates it from gonadotrophin dependent precocious puberty. It is self-limiting and usually resolves. (From: Wales JKH, Rogol AD, Wit JM: Pediatric endocrinology and growth. London, 2003, Saunders, with permission.)

Extra

Premature pubarche (adrenarche)

- ❖ occurs when pubic hair develops before 8-years of age in females and before 9-years in males
- ❖ but with no other signs of sexual development.
- ❖ It is most commonly caused by an accentuation of the normal maturation of androgen production by the adrenal gland between the age of 6 years and 8 years.
- ❖ It is more common in Asian and Black children.
- ❖ There may be a slight increase in growth rate and bone age (by 12–15 months).
- ❖ It is usually self-limiting.
- ❖ A more aggressive course of virilization would suggest nonclassical congenital adrenal hyperplasia or an adrenal tumor (peripheral PP). Obtaining levels of androgens in the blood and measuring bone age help.
- ❖ differentiate premature pubarche from peripheral PP causes.
- ★ Girls who develop premature pubarche are at an increased risk of developing polycystic ovarian syndrome later in life

case related to this topic:

An 8-year-old boy is brought to the pediatrician by his parents because they noticed that he has developed pubic hair. Upon examination, the pediatrician notes dark sparse hair at the base of the phallus. His testes are 3 ml bilaterally. His height is in the mid-parental range with no accelerated growth rate. His bone age was mildly advanced (9 years).

Questions

1- John, a 3-year-old boy, is referred to paediatric outpatients because of concern about the development of pubic and axillary hair. His testes are 1.5 ml in size (prepubertal). His blood pressure is 100/75 mmHg. Gonadotropin levels are normal for a prepubertal boy (undetectable) but his bone age is 5 years.

What is the most likely cause of his early pubertal development?

Select one answer only.

- A. Adrenal tumour
- B. Brain tumour
- C. Idiopathic precocious puberty
- D. Prader-Willi syndrome
- E. Testicular tumour

2- Chelsea, a 7-year-old girl, is brought by her mother to the paediatric clinic. Her mother is concerned about Chelsea's early development of puberty. Chelsea has started to develop breasts and, more recently, some pubic hair. On examination she has breast development stage 3 and pubic hair development stage 2. She has not started her periods, but has had a growth spurt recently. An ultrasound of her pelvis shows multicystic ovaries and enlarging uterus.

What is the most likely cause of her early pubertal development?

Select one answer only.

- A. Brain tumour
- B. Congenital adrenal hyperplasia
- C. Idiopathic precocious puberty
- D. Ovarian tumour
- E. Turner syndrome

3- Sophia, an 18-month-old girl, is brought to outpatients by her mother, who is very worried as she has developed breasts. She is otherwise well and has been growing normally. On examination she has breast development stage 3 (BIII) but no pubic or axillary hair. Her bone age is 20 months.

What is the most likely cause of her early pubertal development?

Select one answer only.

- A. Brain tumour
- B. Congenital adrenal hyperplasia
- C. Idiopathic precocious puberty
- D. Premature thelarche
- E. Premature pubarche

Answers

1- A. Adrenal tumour

Premature sexual development in boys is uncommon and usually has an organic (rather than constitutional or familial) cause. With his prepubertal testes, hypertension and normal gonadotropin levels, the abnormality is likely to be in his adrenal glands.

2- C. Idiopathic precocious puberty

Precocious puberty in females is usually due to premature onset of normal puberty. The sequence of puberty in this child is normal and there is also been an associated growth spurt, which makes an idiopathic cause for the precocious puberty more likely.

3- D. Premature thelarche

Sophia has breast development and no other signs of puberty. She has premature thelarche.