PUBERTY AND ITS COMPLICATIONS

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DEFINITION

A phase of development between childhood and complete, functional maturation of the reproductive glands and external genitalia (adulthood)

For females, the normal age of onset : 8-13 years (average 11 years)

For males, the normal age of onset : 9-14 years (average 13 years)

This period is characterized by ;

. the maturation of the Hypothalamic-pituitary-gonadal axis as it is tightly regulated by a negative feedback mechanism

. Appearance of secondary sexual characteristic

. Acceleration of growth

. Capacity for fertilization

. Psychosocial changes

PHASES OF PUBERTY

The age of pubertal onset may vary, but the order of changes that occur in each person is consistent.

- Adrenarche: activation of adrenal androgen production (axillary and pubic hair, body odor, and acne)
- Gonadarche: activation of reproductive glands by the pituitary hormones FSH and LH
- Thelarche: onset of breast development
- Pubarche: onset of pubic hair growth
- Menarche: onset of menstrual bleeding

PHYSIOLOGY

•Unknown initial trigger → ↑ activators and/or ↓ inhibitors of GnRH secretion →**pulsatile GnRH** secretion→ ↑**FSH** and ↑**LH** secreted by the anterior pituitary gland→ stimulation of the Leydig cells and Sertoli cells in the testicles, and the theca and granulosa cells in the ovary.

PUBERTY IN FEMALES

Normal age of onset: 8–13 years (average 11 years) Normal order of changes: adrenarche(The initial endocrine change in puberty) → gonadarche

→ thelarche (age of onset 8–11 years and the first physical sign of puberty) → growth spurt (age of onset 11.5–16.5 years) → pubarche (mean age of onset 12 years) → menarche (age of onset 10–16 years, mean age: 13 years)

Influential factors of puberty :

- General health (nutritional state, bodyweight)
- Genetics
- Social environment(e.g., family stress)

PHYSICAL CHANGES DURING PUBERTY

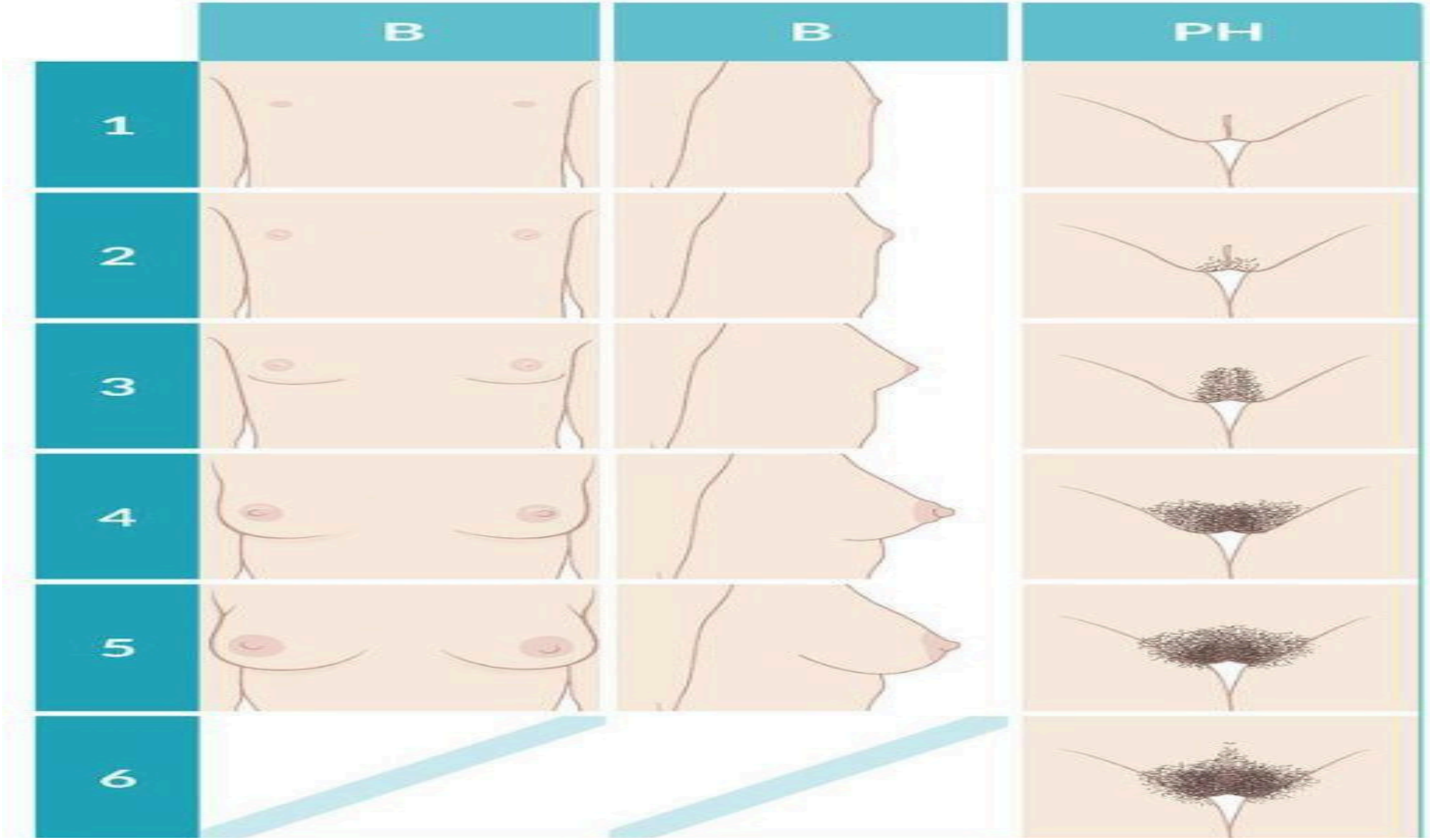
Tanner stage

A sexual maturity rating (SMR) scale used to assess the development of secondary sexual characteristics

Tanner Stages	Breast development (girls)
B1	• Prepubertal appearance and size • Occasional elevation of the nipple
B2	• Enlarged mammary glands form a breast bud • Slight increase in areolar diameter, nipple protrusion
B3	• Further enlargement of mammary glands • Breast bud extends beyond the areolar diameter
B4	• Nipple and areola form a secondary mound which projects above the breast tissue
B5	• Adult breast • Areola with projection of papilla only

	Pubic hair development (boys and girls)
Ph1	• Usually no pubic hair, vellus hair possible
Ph2	• Sparse, lightly pigmented hair (straight or curled) on the labia/base of the penis
Ph3	• Dark, coarse, curly hair spreading over the pubic symphysis
Ph4	• Adult pubic hair that does not extend to the inner thighs
Ph5	• Adult pubic hair that extends to the inner thighs with horizontal upper border
Ph6	• Further growth of pubic hair along linea alba in the direction of the umbilicus

PHYSICAL CHANGES DURING PUBERTY



OTHER MORPHOLOGICAL CHANGES DURING PUBERTY

- **Growthspurt**
  - Linear growth during adolescence is approx. 5 cm/year from 4 years of age to puberty Varies between the sexes, generally occurs between ages 13–15 years (in girls, it can begin two years earlier).
  - Includes↑ growth in trunk and limbs
  - Assessed using growth velocity charts
  - It generally lasts 2 years, girls complete it atage 15and boys atage 17.

- **Bone growth**
  - Accelerated during puberty Determined by:testosterone ,estrogen ,IGF 1,calcitriol, and GH

  •Order of growth:↑ length →↑ width →↑ mineralcontent →↑ density

OTHER MORPHOLOGICAL CHANGES DURING PUBERTY

- **Body weight and composition during adolescence**
  - Boys: initial ↓ bodyfat (earlypuberty) → ↑ leanbody mass (late puberty)
  - Girls: gradual increase in body fat
  - Affected bynutritional status

- **Dermatological changes**
  - Acne vulgaris,hyperhidrosis, and hair problems (e.g.,seborrheic dermatitis)

    •Activation of the adrenal cortex→pubertal hormonal fluctuation → ↑sebum secretion and excessive sweating →skin and hair changes

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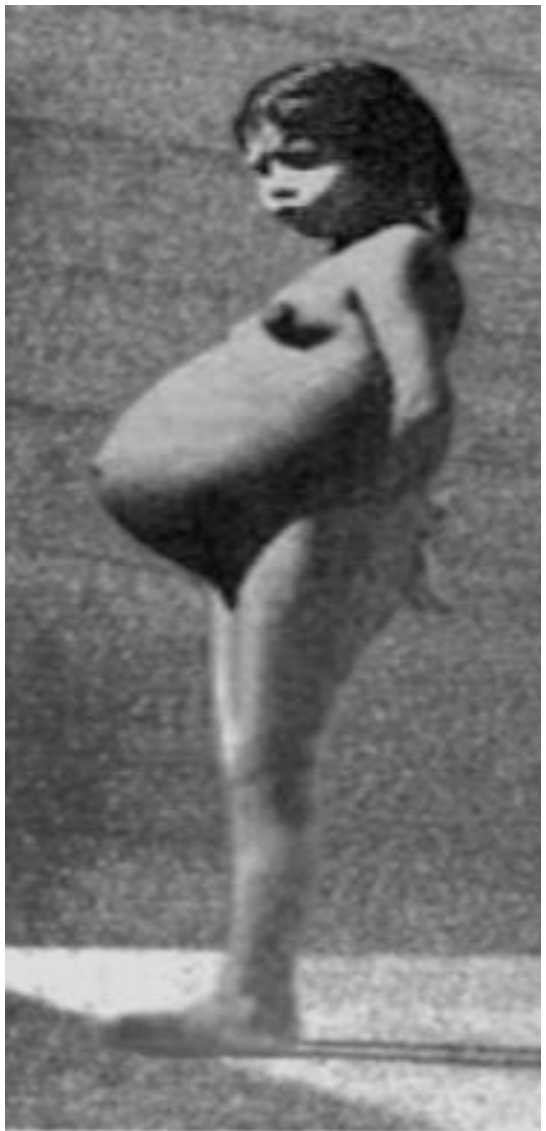
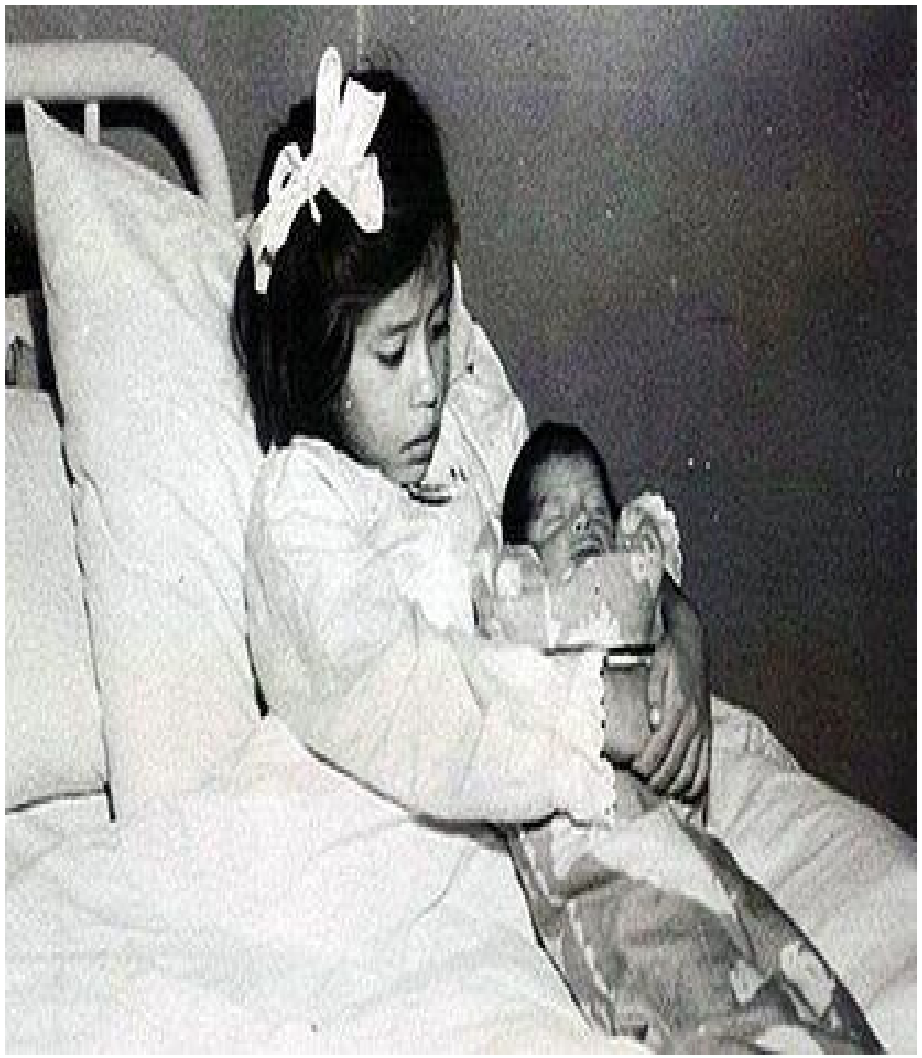
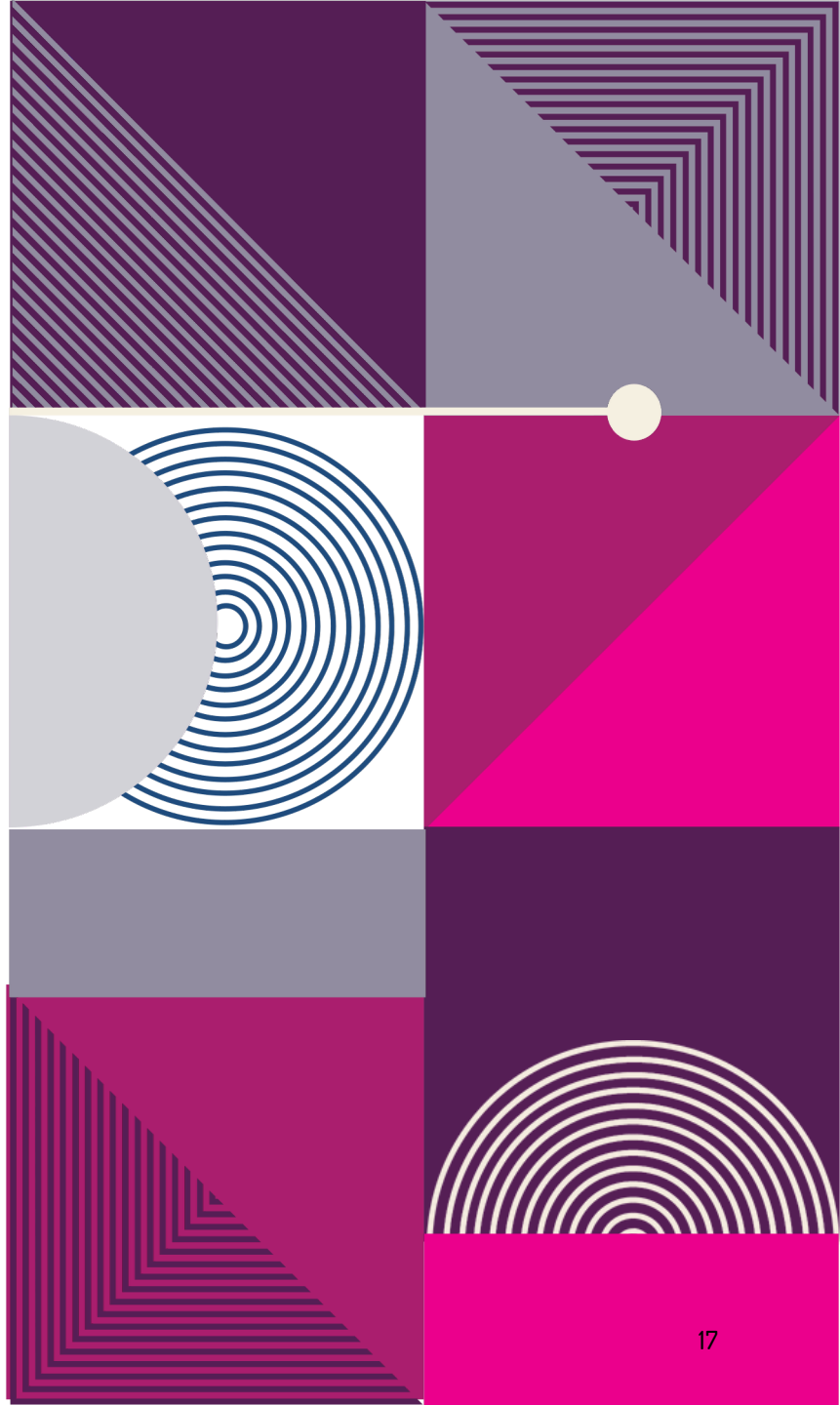




Precocious

Puberty



What is Precocious Puberty ?

•Precocious puberty: refers to the development of any sign of secondary sexualmaturationatan age 2.5 standard deviations earlier than the expected age of pubertal onset.

•In North America, these ages are 8 years for girls and 9 years for boys.

•The incidence of precocious puberty is 1 in 10,000 children in North America,

and it is approximately five times more common in girls.

•In 75% of cases of precocious puberty in girls, the cause is idiopathic

CLASSIFICATION

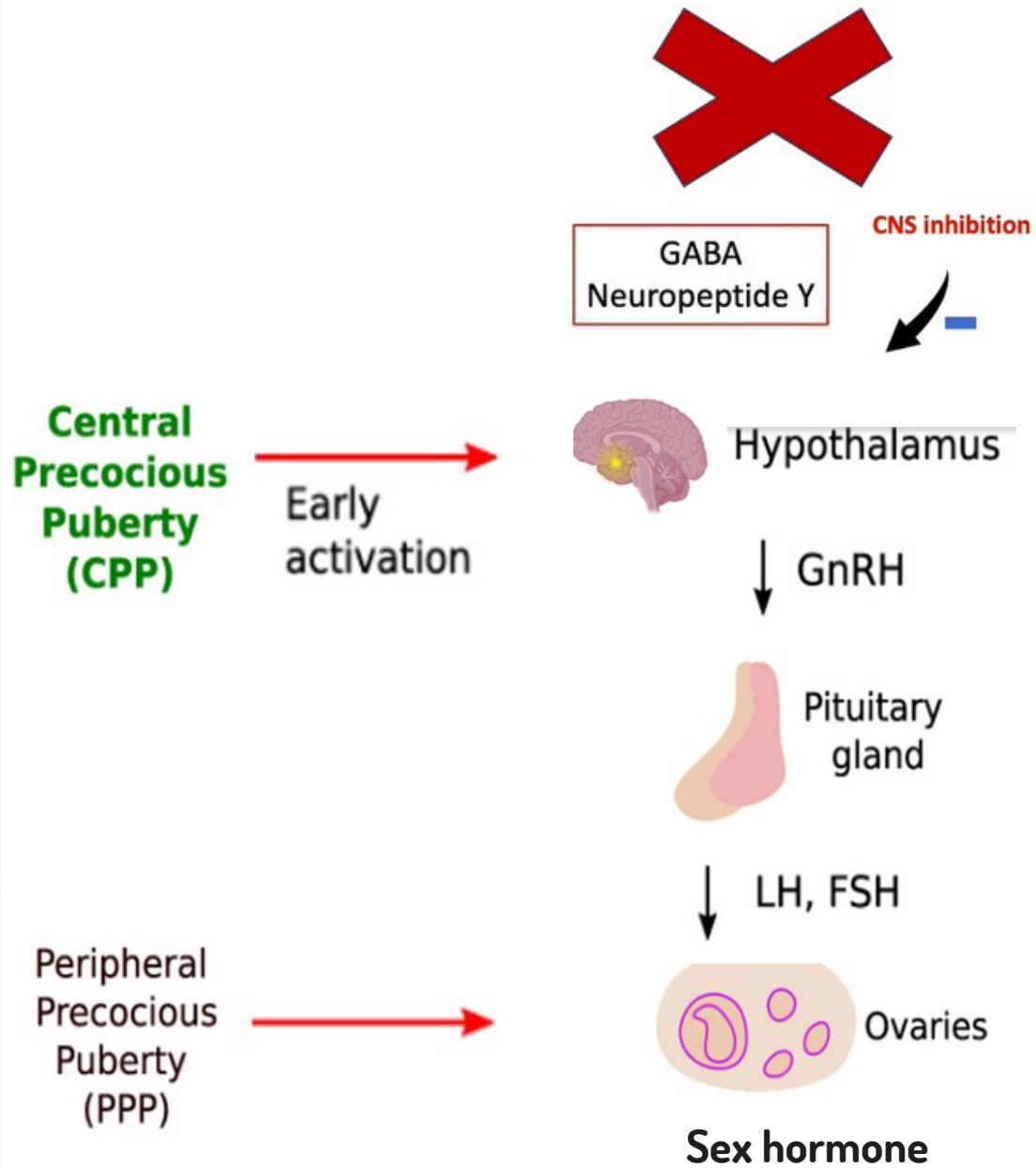
1) Central (True) precocious puberty

(gonadotropin-dependent)

2) Peripheral (Pseudo) precocious puberty

(gonadotropin-independent)

3) Benign / non-progressive pubertal variants



Excitatory Neurotransmitters in the brain ↑

Glutamate

Kisspeptin

Early activation of GnRH neuron

- Id io pathic CNS lesion
- Genetics (**MRF3 , KISS1)**
- **Others**

Sex Steroid increased

- **Exogenous steroids**
- McCune-Albright syndrome
- Congenital adrenal hyperplasia
- **O the rs**

Sexual Development : e2 ,Androgen
reproductive Development : FSH,LH

Aspect	Central Precocious Puberty (CPP)	Peripheral Precocious Puberty (PPP)
Definition	Elevated **GnRH** levels	Excess secretion of **sex hormones** from gonads, adrenal glands, or exogenous sources.
hormones	LH -increse FSH- increse Estrogen –increase **Sexual Development(+)** **reproductive Development(+)**	LH –decrease FSH- decrease Estrogen –increase **Sexual Development(+)** **reproductive Development(-)**

CENTRAL PRECOCIOUS PUBERTY (CPP)

Etiology

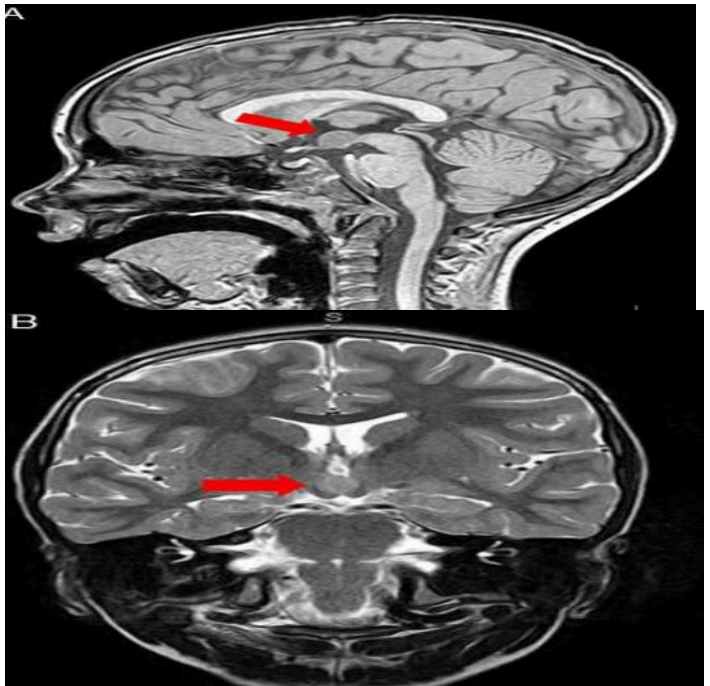
- **Idiopathic** most common)
- **CNS lesions** : Intracranial tumors (e.g., hypothalamic hamartoma, glioma, craniopharyngioma,) ,Hydrocephalus
- **Trauma**
- **Infections** (e.g., encephalitis, meningitis)
- **Radiation**
- **Genetics** (**MRF3 , KISS1)**
- **internationally adopted children**
- **Familial precocious puberty**
- **Syndromes** (Neurofibromatosis type 1, Sturge Weber syndrome)

CENTRAL PRECOCIOUS PUBERTY(CPP)

HYPOTHALAMIC HAMARTOMA

Definition:

is a benign (noncancerous) tumor-like growth in hypothalamus.
The ectopic neural cells in the lesion serve as an **accessory GnRH pulse generator**.
It presents with precocious puberty in infancy **as early as 12 months of age**
The most common brain lesion causing CPP is hypothalamic hamartoma



Clinical features

The most characteristic association is **gelastic seizures**(focal or partial seizures with bouts of uncontrolled laughing or giggling) which are usually refractory to medications.
The other associated features include cognitive, behavioral, and psychiatric symptoms

PERIPHERAL PRECOCIOUS PUBERTY

Etiology :

↑ **Androgen:** Congenital adrenal hyperplasia ,Virilizing ovarian and adrenal tumors

- ↑ **estrogen production:** McCune-Albright syndrome, HCG-secreting germ cell tumors (e.g., dysgerminomas) , Ovarian tumor (e.g. granulosa cell tumor)

- **Exogenous steroids**

- **Primary hypothyroidism.**

BENIGN / NON-PROGRESSIVE PUBERTAL VARIANTS

Premature Thelarche:

premature unilateral or bilateral development of the breast tissue in girls between the age of 12 to 24 months.

PrematureAdrenarche :

• It presents with pubic or axillary hair, body odor, or acne before the age of 8 years

PrematureMenarche:

Isolated premature menarche is the onset of vaginal bleeding in girls less than 7 years of age., Sexual abuse, vaginal foreign body, and infections of the vulva and vagina need to be ruled out.

EVALUATION

❖ 1) history

- **Age of onset of pubertal signs.**
- Rate of **progression** (rapid = more concerning).
- **Family history** of early puberty.
- **Growth history** – Any growth spurts?
- Any relevant history of **head trauma, brain infections**
- **Neurological symptoms** – Headaches, visual disturbances → Possible CNS involvement.
- **Medication history** – Use of exogenous hormones, steroids, or endocrine disruptor

❖ 2) PHYSICAL EXAMINATION

Café-au-lait spots → Suggests **McCune-Albright Syndrome, Neurofibromatosis type 1**

• Acne and oily skin → Suggests androgen excess from adrenal or gonadal sources.

• Hyperpigmentation → May indicate adrenal disorders (e.g., congenital adrenal hyperplasia).

• Hirsutism (excess facial/body hair in girls) → Suggests androgen excess (ovarian/adrenal tumor or CAH

EVALUATION

❖ 3) imaging

- **wrist x ray bone age** it is an initial screening test. If the bone age is advanced **(greater than two standard deviations)** than the chronologic age, further testing should follow.

- **MRI** is to be performed in all cases of CPP
- **Pelvic ultrasonography** , in cases of PPP, detects ovarian tumors or cysts in females

❖ 4)Labs

TEST	Findings in **CPP**	Findings in **PPP**
LH& F SH	**High**	**Low** or normal
Estrogen	High	High
GnRH stimulation test TSH	**↑LH**	**↓LH**
,T4	Normal	**↑**TSH , **↓**T4 In **1°** hyp ot hyrod ism
DHE A-S	Normal	High in CAH

the gold standard, if CPP is suspected

Management

PERIPHERAL PRECOCIOUS PUBERTY

- Treatment is directed towards **eliminating the source of sex steroids.**
- **Surgery** is indicated in gonadal and adrenal tumors.
- **In classic congenital adrenal hyperplasia (CAH)** is treated with **glucocorticoids**.
- **In McCune-Albright syndrome**, some benefit occurs with:

✓ blocking the estrogen synthesis using **aromatase inhibitors** (anastrozole, letrozole)

✓ **selective estrogen selective receptor modulator** (tamoxifen)

- The optimal treatment for **familial male-limited precocious puberty is not well established**, but the preferred treatment is a combination of an **androgen antagonist** (spironolactone) and **an aromatase inhibitor** (anastrozole, testolactone)

Central Precocious Puberty (CPP)

- **Continuous GnRH agonist** (e.g., leuprolide, buserelin, goserelin)
- Follow-up is recommended every 4–6 months to assess progression.
- Manage underlying caus

SUMMARY

Aspect	Central Precocious Puberty (CPP)	Peripheral Precocious Puberty (PPP)
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hormones	LH -increse FSH- increse Estrogen –increase **Sexual Development(+)** **reproductive Development(+)**	LH –decrease FSH- decrease Estrogen –increase **Sexual Development(+) reproductive Development(-)**
Etiology	• **Idiopathic** (most common) • **CNS lesions** : Intracranial tumors (e.g**., hypothalamic hamartoma,**glioma, c rani op har yngi om a) • **Trauma** • **Infections** (e.g., encephalitis, meningitis) • H ydroc e pha lu s • R adi ati on • **Genetics** MRF3 , KISS1 • **internationally adopted children** • **Familial precocious puberty** • **Syndromes** Neurofibromatosis type 1, Sturge Weber syndrome,	❖ **↑Androgen:** • Congenital adrenal hyperplasia Virilizing ovarian and • adrenocortical tumors ❖ **↑ estrogen production:** • HCG-secreting germ cell tumors (e.g., dysgerminomas) • Ovarian tumor (e.g. granulosa cell tumor) • **McCune-Albright syndrome** ❖ **HCG-secreting tumors:** • Dysgerminoma Malignant embryonal • cell carcinoma Choriocarcinoma • ❖ **Exogenous steroids** ❖ **Primary hypothyroidism.** ❖ Familial male-limited precocious puberty (**testotoxicosis**)
Management	❖ countinuous GnRH agonist	• excessive hormonal production from a tumor in the body: surgical • removal Precocious puberty caused by CAH: glucocorticoids replacement Ovarian cysts: no intervention is necessary (spontaneous resolution is c om mo n) • McCune Albright syndrome: blocking estrogen synthesis using aromatase • inhibitorsot estrogen selective receptor modulator (tamoxifen)

DELAYEDPUBERTY

WHAT IS DELAYED PUBERTY?

•Puberty that happens late is called delayed puberty.

means a child's physical signs of sexual maturity don't appear by age 12 in girls or age14 in boys.This includes breast or testicle growth, pubic hair, and voice changes.

CAUSES OF PUBERTY DELAY

- The causes of delayed onset of puberty can be divided into:
- Pathological delay(Primary & Secondary Hypogonadism)
- Physiological delay (Constitutional delay)

PRIMARY HYPOGONADISM (HYPER GONADOTROPIC HYPOGONADISM)

- Decrease or absence of sex hormones due to dysfunction in the gonads, despite high gonadotrophins.
- Cells cannot respond to FSH and LH or cells cannot produce hormones.
- The result is a decrease or absence of estrogen and progesterone in females and testosterone in males so NO negative feedback on the hypothalamus, leads to overproduction of LH and FSH.

CAUSES OF PRIMARY HYPOGONADISM :

- Congenital: Turner syndrome, and Klinefelter syndrome.
- Acquired:followingchemo-or radiotherapy for childhood cancer, or trauma to the gonads.

SECONDARYHYPOGONADISM (HYPOGONADOTROPIC HYPOGONADISM)

1.Defined as Hypothalamus & pituitary dysfunction. So Inability to produce GnRH, LH & FSH,orSuppression from other hormones like prolactin &and thyroid hormones.

CAUSES OF SECONDARY HYPOGONADISM

- **Acquired:**

radiotherapy, chemotherapy, trauma. • Congenital: Kallmann syndrome and Panhypopituitarism

- **General:**

anorexia nervosa,excessive exercise,stress(all this increases cortisol production which decreases sensitivity pituitary to the GnRH), Malnutrition, Obesity.

- **Tumors:**

prolactinoma, craniopharyngioma

KALLMANN SYNDROME

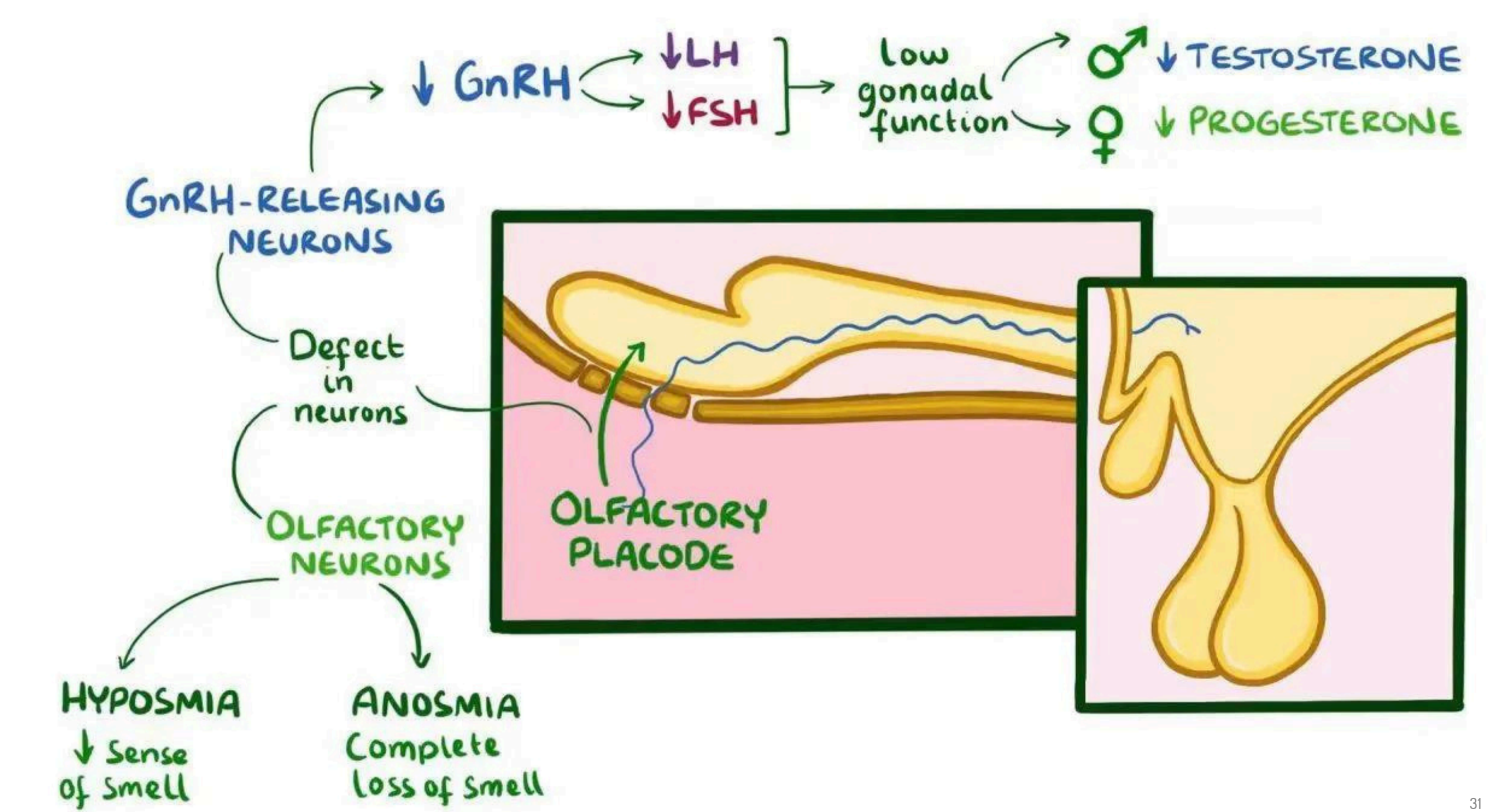
(Hypogonadotropic hypogonadism and anosmia) Normal height

NORMAL EXTERNAL AND INTERNAL GENITAL ORGANS

(infantile)

Result from a mutation of the KAL gene on the X chromosome or from autosomal mutations that prevent the embryologic migration of GnRH neurons in to the hypothalamus.

- **Diagnosis:**
- **Hormoneslevel: ↓ GnRH ↓ LH ↓ FSH ↓ ESTROGEN ↓ PROGESTERON** normal level ofother pituitary gland
- **Genetic test**
- **Smelltest**
- **Normal pituitary and hypothalamuson MRI**
- **Treatment: HRT.**


↓ GnRH
↓LH
↓FSH
Low gonadal function
↓ TESTOSTERONE
↓ PROGESTERONE
GnRH-RELEASING NEURONS
Defect in neurons
OLFACTORY NEURONS
OLFACTORY PLACODE
HYPOSMIA
↓ Sense of smell
ANOSMIA
Complete loss of smell

CRANIOPHARYNGIOMA

- A benign tumor arising from a remnant Rathke pouch (embryological origin for anterior pituitary gland)
- Most common childhood supratentorial tumor

- The tumor arises in the suprasellar region and can extend into the intrasellar region.

- (Compression symptoms):
- Compression of the pituitary gland due to intrasellar extension→hypopituitarism (Hypogonadotropic hypogonadism, Failure to thrive, central diabetes insipidus)

PROLACTINOMA

- BenignTumor(Adenoma)of the pituitary gland that secretes excess prolactin hormo
- Signs & Symptoms:
- Amenorrhea,Galactorrhea ,Gynecomastia, decrease Libido, infertility.
- Complications:
- 1.Loss of vision &headache (if left untreated aprolactinoma may grow large enough to compress your optic nerve).
- 2.Osteoporosis & fractures (low level of estrogen Will decrease bone density).

DIAGNOSIS AND TREATMENT OF PR O LACT I NEM I A

- **Diagnosis:**
- CT & MRI
- Prolactin serum level >100 ng/mL
- **Treatment:**
- Pharmacotherapy: dopamine agonists (cabergoline)
- Surgery
- Radiation

CONSTITUTIONALDELAY

• Temporary delay puberty (puberty onset and progression can be normal, itonly happens later in age).

•Caused by immature pulsatile release of gonadotrophin-releasing hormone.

• Slow rate of maturation, not pathological.

• Do not cause infertility.

• Typically, genetic components (run in the family).

• Do not require treatment.

DIAGNOSIS OF DELAYED PUBERTY

•Comparing the individualized sexual development with Tanner scale •Detailed medical history (underlying medical illness and family history)

• Radiologicalimage

• Hormone test (Type of Hypogonadism) • Karyotype (to examine chromosomes, identify genetic problems)

اللّهمّ إنّا نستطعمك لأهل غزّة فأطعمهم

من جوع وارزقهم من حيث لا يحتسبوا

رزقًا حلالًا طيّبًا مباركًا فيه

THANK YOU