PUBERTY & ADOLESCENCE

* The gonads are functionally quiescent from birth until PUBERTY.
Thereafter, the Hypothalamic-Pituitary-Gonadal Axis is activated causing Gonadotrophic hormones (pituitary) to act on the Gonads resulting in

'Gonadal maturation & its effects':
1. Gametogenesis
2. ↑ in Gonadal Sex Hormones
3. Enlargement of Accessory sex organs
4. Development of secondary sexual characters.

* PUBERTY refers to the stage of Gonadal development & maturation (gametogenic & endocrine fn.) to the point where Reproduction becomes possible for the first time.

Girls	Boys
b/w 8 - 13 yrs (avg 12 yrs)	b/w 9 - 14 yrs (avg 14 yrs)

* ADOLESCENCE refers to the period of Sudden spurt of physical growth b/w childhood & adulthood
Range - 3 to 5 years.

ONSET OF PUBERTY - MECHANISM (Neuro - Hormonal)

* The activation of PULSATILE release of GnRH from Hypothalamus is the endocrine hallmark of the onset of Puberty

GnRH travels to the Anterior Pituitary via Hypothalamo - Hypophyseal Portal Circulation & stimulates Gonadotrope cells of Ant. Pituitary to release Gonadotropins < FSH, LH → Gonadal Maturation.

* The GnRH releasing Hypothalamic Neurons are located in the ARCUATE NUCLEUS (mainly) (Mediobasal Hypothalamus) which is adjacent to 3rd Ventricle & Medial Eminence.

These neurons are stimulated by neurons expressing
- kisspeptin
- neurokinin B
- dynorphin

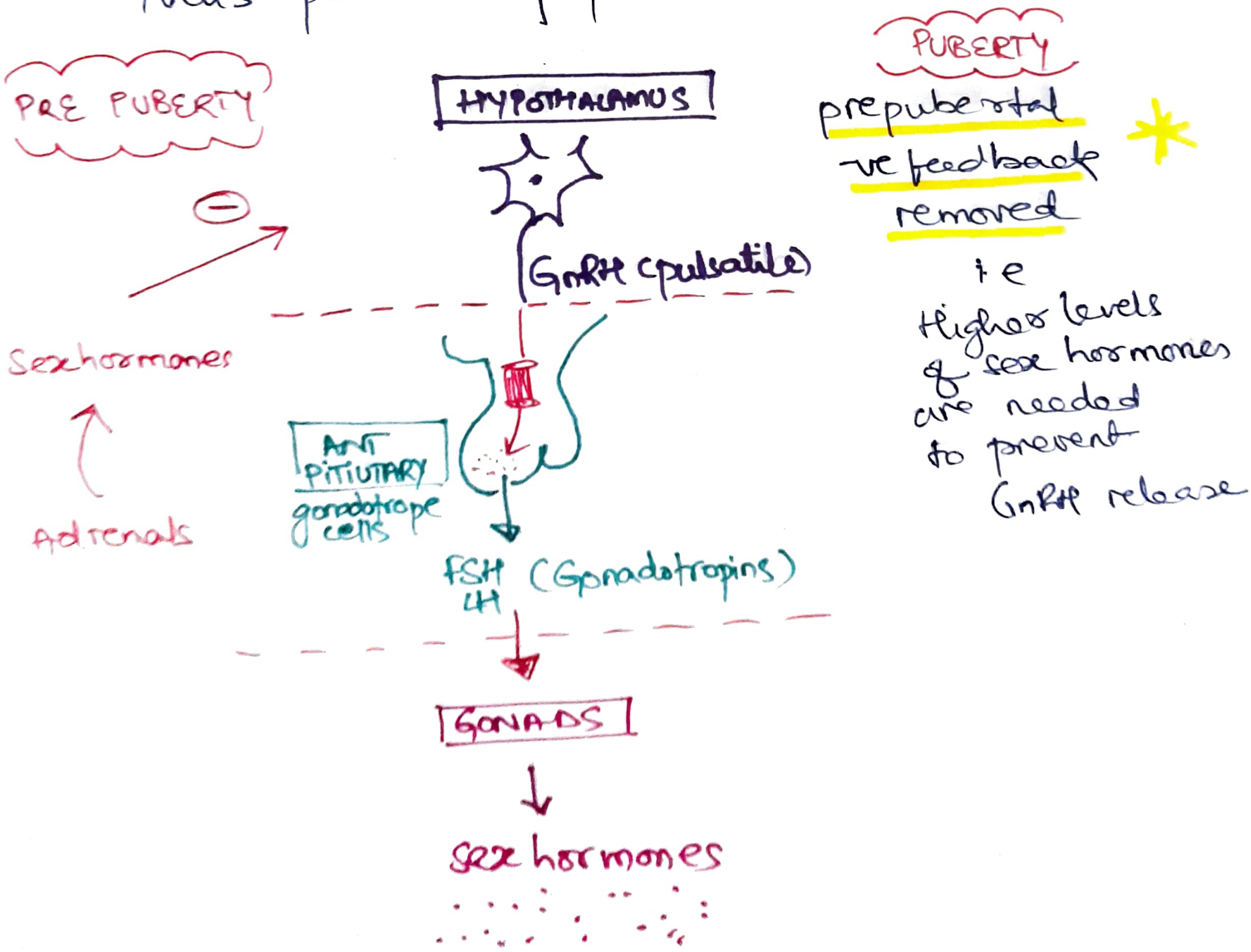
& glial cells,
- tanycytes
- astrocytes
- ependymal cells

jointly to release GnRH in a pulsatile manner

I.

- During early childhood, the hypothalamus is highly sensitive to NEGATIVE FEEDBACK INHIBITORY EFFECT of small amounts of circulating sex hormones (from)
  - adrenal cortex
  - prepubertal testes

- At PUBERTY, the hypothalamic cells mature and their sensitivity for "circulating sex hormones / negative feedback" decreases, thus permitting pulsatile GnRH release.



II.

1-2 years prior to Puberty, an event called **ADRENARCHE** occurs.

GIRLS - 8-10 yrs
BOYS - 10-12 yrs

(i.e before Gonadotropin release & Gonadal sex hormone production)

Increased Adrenal Androgen, (without rise of Cortisol & ACTH) brings about

(1) increase in Gonadal Sex Hormones
∴ cause - maturation of Reproductive System/organs

These Adrenal Androgens also cause:

(2)
* Growth of pubic & axillary hair of both sexes
* Growth of muscle mass & strength
* ↑ sebum production - oily skin
  - mild acne
* Body Odour
* Libido / sexual attraction

* Anterior Pituitary releases a peptide AASH ADRENAL ANDROGEN STIMULATING HORMONE → Acts on ZONA RETICULARIS OF ADRENAL CORTEX by channelling more PREGNENOLONE to the Androgenic Pathway → ↑ Androgens ⋮ ↑ circulating sex hormones ∴ act alongside reduced sensitivity of Hypothalamus

III. **Pineal Gland** maybe involved in Puberty Control.

- grows till 7yrs
- ✗
- begins to involute in 2nd decade

located in the groove b/w SUPERIOR COLLICULI, ~~adjacent~~ attatched to 3rd V by a hollow stalk

Parenchymal cells of Pineal Gland → MELATONIN into (↑ ∝ light exposure) CSF Blood

MELATONIN has a GONADOTROPIN inhibitory EFFECT.

In the 2nd decade, as Melatonin ↓ ∴ involution of PG, this inhibitory effect on Gonadotropins are removed.

IV. **LEPTIN** - protein hormone produced by Fatty tissue - Adipose/Fat cells under OB Gene influence

↓

facilitates GnRH release

Critical body weight is required for LEPTIN release and pubertal onset.

Thus there is a link b/w nourishment status & pubertal onset.

SEQUENCE OF EVENTS DURING PUBERTY

occur over a period of 3 to 5 YRS

2-5 YRS

2-4 YRS

MODIFIED TANNER METHOD

FEMALE	AGE	STAGE	AGE	MALE
* PRE ADOLESCENT (ADRENARCHE) Adrenal Androgens ↑ ✓ initiation of skeletal growth	upto 7½ YRS	1	7½ YRS	* PRE ADOLESCENT (ADRENARCHE) Adrenal Androgens ↑
* TELARCHE Breast Buds Appear	10½ YRS	2	12 YRS	Genital development begins ∵ * TESTICULAR ENLARGEMENT (∵ growth of Seminif. Tubules)
* PUBARCHE Axillary & Pubic hair appear * Breast enlarges * Sudden ↑ height (peak height velocity)	2YRS	3	14 YRS	* Axillary & Pubic hair appears * PENIS ENLARGEMENT * SPERMARCHE Sperm appears in morning urine sample
* MENARCHE menstruation Starts * Breast areola elavates & projects	13 YRS (11-15 YRS)	INTERVAL 4	15 YRS	* Sudden ↑ height (Height Spurt) * further growth of testis, penis, genitalia
* ✓ Adult Genitalia * ✓ Secondary Sex characters	14 YRS	5	16½ YRS	* Adult Genitalia ✓ * Secondary Sex characters ✓

SECONDARY SEX CHARACTERS

FEMALE		MALE
STRUCTURAL		STRUCTURAL
Narrow shoulders Broad hips Arms diverge Thighs converge	BODY CONFIGURATION	Broad shoulders Narrow hips
Smooth, light	SKIN	thick, dark, oily
	HAIR	
fine, scanty	BODY	rough, dark abundant
-	FACE	Beard, moustache
Thick growth Frontal hairline rounded	SCALP	recedes in lateral frontal regions
+	AXILLARY	+
limited by horizontal upper line - flat topped (concave) ▽	PUBIC	grows towards umbilicus (convex) △ triangle ē Apex up
Soft	MUSCLES	↑ bulk, strength
female distribution of fat .. deposition in Breast, Hips → curves contours	FAT (%)	proportion of body fat is less ē less %fat
Broader Wide outlet (Wide subpubic angle)	PELVIS	Narrow Bones sturdy Subpubic angle pointed
- Clitoris size ↑. labia - majora enlarges - minora - Well developed Breasts - Uterus growth ↑ vagina	GENITALIA & ACCESSORY SEX ORGANS (adult type)	- penis scrotum ↑ size, pigmented - scrotal skin thickens Rugal folds appear - Prostate, seminal vesicles bulbourethral glands enlarge & secretion begins

FEMALE		MALE
FUNCTIONAL		**FUNCTIONAL**
No change (soft shrill) High pitch	Voice	Larynx enlarges vocal cords lengthen & thicken Voice - loud low pitched (bass) deep (voice breaks)
Lower	BMR	5 -10% Higher
Lower	RBC count Hb conc	Higher
PSYCHOLOGICAL		**PSYCHOLOGICAL**
- more emotional - shy - affectionate - maternal instinct - sexually attracted to males		- more aggressive - extrovert - competitive - interested in opposite sex

HORMONES:

① Gonadotropins (FSH, LH) (from Ant. Pit) - Birth to pre adolescent → slow rise → not ↓ checks of Gonadal Hormones E/P
- at puberty levels suddenly rise

② Gonadal Sex Hormones - 7 to 10yrs - slow increase
Early teenage yrs - rapid rise
Estrogen in ♀
Testosterone in ♂

③ Thyroxine ↑

④ GROWTH HORMONE -

birth to prepubertal age - intermittent secretion (peaks every 24 hrs)

at puberty - basal level doesn't rise but ↑ in frequency of peaks amplitude

⇓

generalised growth spurt of adolescence

DISORDERS OF PUBERTY

related to time of ONSET

gonads ⓝ
no endocrine prob
delayed pub.
↓
1° amenorrhoea Eunuchoid form

EARLY ONSET PRECOCIOUS PUBERTY

onset of puberty
♀ < 8yrs Breast buds
♂ < 9yrs Testicular enlargement

mc in girls

TRUE PRECOCIOUS PUBERTY

- early devlpt of 2° sex chr.
  +
- early start of gametogenesis
- early but ⓝ pubertal gonadotropin secretion from Ant. Pit
  ∴ no other endocrine disorder
- proceeds iso sexually

PSEUDO PRECOCIOUS PUBERTY

- early devlpt of 2° sex ch but no gametogenesis
- ∵ abnormal exposure to sex hormones to immature child
- there maybe signs of virilization in ♀
- ⓝ sequence of pubesty altered

LATE ONSET DELAYED OR ABSENT PUBERTY

♀ 2° sex characters have not appeared by 13 yrs
↓
menarche not occurred by 17 yrs

♂ Testicular Enlargement & development not occurred by 20 yrs

mc in boys

Features:

1) lack of pubertal development
2) short stature
3) associated features of endocrine abn.
4) low gonadotropin levels

CAUSES:

(1) Constitutional / Physiological delay
(2) PANHYPOPITUITARISM (no gonadotropins released)
(3) 1° GONADAL failure
XXY, XO
(4) Deficiency ← enzymes of steroid synth. / receptors in target tissue

CAUSES OF PRECOCIOUS PUBERTY

TRUE

1) Constitutional / Idiopathic

2) Conditions disturbing neural pathway for feedback ⊖ of GnRH release from hypothalamus
   a) Cerebral disorders involving Ventral hypoth. near infundibulum
      tumours, infection, developmental abn.
   b) Pineal gland tumours

GONADOTROPIN DEPENDENT PP

3) Increase insensitivity of LH receptors to Gonadotropins ∴ activation / mutation of G proteins & couple receptors to adenylyl cyclase

GONADOTROPIN INDEPENDENT PP

PSEUDO

1) Adrenal conditions
   a) Congenital virilizing hyperplasia
   b) Androgen secreting tumors in males
   c) Estrogen secreting tumors in females

2) Gonadal conditions
   a) Leydig cell tumor of testis (males)
   b) Granulosa cell tumor of ovary (females)

MENOPAUSE

* Permanent cessation of menstruation & fertility for a duration (min) of 12 months

- Average age of menopause = 51 to 52 yrs
  but can occur as early as 40 yrs
  later as 55 yrs

- It is preceded by PERIMENOPAUSE, which begins 3-5 yrs before Menopause
  Estrogen levels begin to drop &
  it lasts for a year after menopause.
  Menstruation becomes infrequent & can stop for a while before restarting.
  Hence menopause can be inferred only in retrospect after it has lasted a year.

- Mechanism / Cause

  ~ ∵ advancing age, ovaries become unresponsive to FSH / LH (gonadotropins)

  ~ ovaries stop producing (E) & (P) in sufficient amounts.

  ~ 5th month IUL → 6-7 million follicles
  → Birth → 1-2 million follicles
  → Puberty → 4 lakh follicles
  → every month 1000 follicles undergo atresia

CHANGES IN FEMALE PHYSIOLOGY

LATE REPRODUCTIVE AGE	PERIMENOPAUSE AGE	MENOPAUSE
INHIBIN B ↓	↓	↓
FSH slight ↑	↑	↑ ≥ 40 IU LH also ↑
Estrogen (n) E_2	↓	↓ <20pg (E_1)
Progesterone slight ↓	↓	↓ ∵ Anovulation ↓P Amenorrhoea
Difficulty in concieving Menstrual irregularity (shorter cycles) ∵ short follicular phase	menopausal transition begins Inter menstrual cycle length ↑ ≥ 7 days there can be Amenorrhoea ≥ 2m	↓ Androgens ↓ Libido No menstruation for 1 yr.
	menstrual irregularity ↓ E = Vaginal dryness mood swings sleep disturbances	MC Symptom HOT FLUSHES ∵ thermoregulatory dysfunction at level of hypothalamus Thermoregulatory Centre of Hypoth. regulates the Thermoneutral zone This is narrowed in menopausal ♀

→ contd.

(1)

* HOT FLUSHES - mc Symptom of Peri Menopause & Menopause

- Begins as sudden sensation of heat on upper chest & face (∵ vasodilatation) & rapidly becomes generalised.
- Sensation lasts for 2-4 secs, then dissipates & sweating occurs
- Associated ⊂ palpitations, shivering, anxiety
- occurs several times a day but mc at night = NIGHT SWEATS
- coincides with LH secretion surge & occurs in episodes of 30-60 mins (Circhoral secretion)
- Hypothalamus has a 'Thermoregulatory Zone'
  - Whenever a change in temperature occurs within this zone, body can handle it & doesn't react (ex: ↑ BBT ∵ Ⓟ after ovultn)
  - Estrogen inhibits Neurons ⊂ secrete Kisspeptin, Neurokinin, Dynorphin & innervate the Thermoregulatory Zone.

and this helps the Zone to function normally

in Menopause,

Thermoregulatory zone is narrowed

so slight temperature variations are not going to be tolerated

↓ Estrogen.

∴ the feedback ⊖ ε keeps KNDy neurons in check are removed.

These peptides will cause Dysregulation of the thermoreg. zone of Hypothalamus

"HOT FLUSHES"

* ② Vaginal Dryness
  Senile Vaginitis / Atrophic Vaginitis / Genitourinary Menopausal Syndrome
  ∴ ↓ Estrogen

* ③ Mood Swings
* ④ Sleep disturbances
* ⑤ Menstrual irregularity → Amenorrhea
* ⑥ Osteoporosis

- menopause following Ovarectomy or Chemo-therapy
  = SURGICAL MENOPAUSE

- Management :
  ~ care
    counselling
    support
  ~ Hormone replacement therapy

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* In Males -
  Some decline in reproductive fn from 50 yrs onwards
  But Testicular fn & potency persist till 8th decade.
  No Climacteric
  No Andropause (male menopause)
