433 Teams

OBSTETRICS & GYNECOLOGY

Puberty and disorders of pubertal development

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Objectives

Puberty & Disorders of Pubertal development

- ✓ **Describe the endocrinological-Hypothalamus-Pituitary- gonadal axis and target organ in normal Puberty.**
- ✓ **Describe the different stages of somatic and psychological changes of puberty.**
- ✓ **Define puberty abnormalities (Precocious and delayed puberty).**
- ✓ **List types of female precocious puberty.**
- ✓ **Mention the investigations used to evaluate precocious and delayed puberty.**
- ✓ **List treatment options of precocious and delayed puberty**

Puberty

- It is the transitional period of development during which an individual mature from childhood to sexual & reproductive maturity.

Major characteristics of this period :

1-Maturation of the 1ry sexual characteristics :
Hypothalamic Pituitary Ovarian Axis
2-Development of 2ry sexual characteristics :
- ✓ Sexual hair
- ✓ Breasts
- ✓ Genitalia

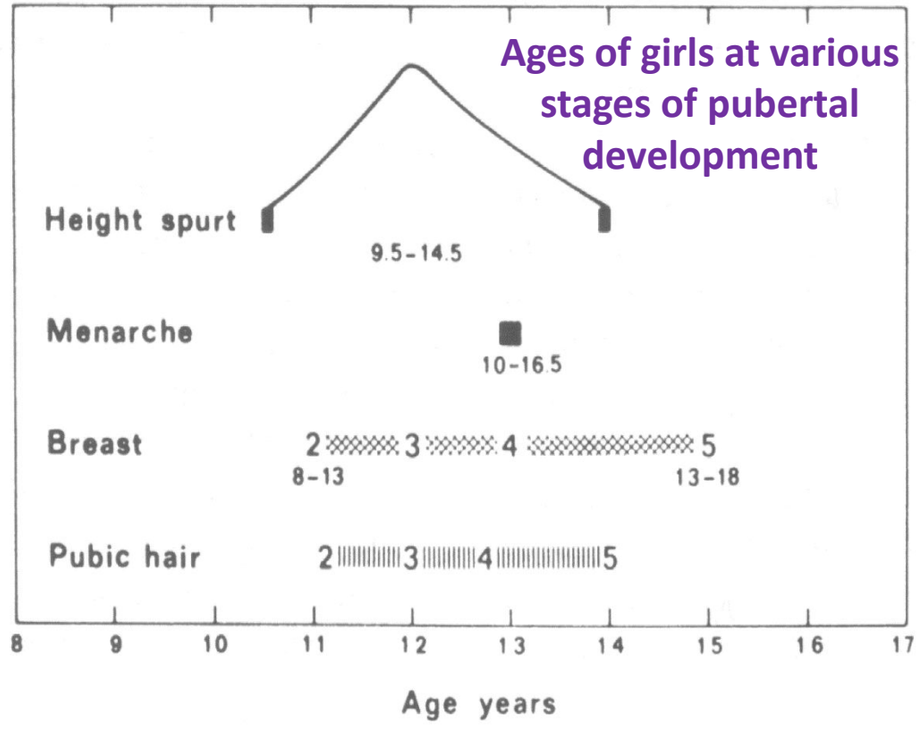
3-Dramatic growth spurt
4-Phycological changes ⇨ mental & emotional maturity

Onset of puberty :

- ✓ Females 8-13Y
- ✓ Males 9-14Y

Somatic changes of puberty :

1-Breast development	mean 10.6 Y
2-Pubic & axillary hair	11.2Y
3-Maximal growth velocity	12Y
onset of growth spurt	9.6Y
4-Menarche	12.7Y



Does menarche mark the attainment of reproductive maturity?

- No, the reproductive system continues to mature for around 3-4 years
- Number of ovulatory cycles ↑ from 10% to 90%
- Duration of menstrual cycle ↓

What is the time from onset to completion of puberty?

- ✓ Average 4.2 Y
- ✓ Range 1.5-6 Y

Mechanism controlling FSH & LH secretion in infants :

1-the main mechanism is the level of sex steroids

▲Peak FSH & LH (Estrogen ↓) ⇨⇨ 1-2 years

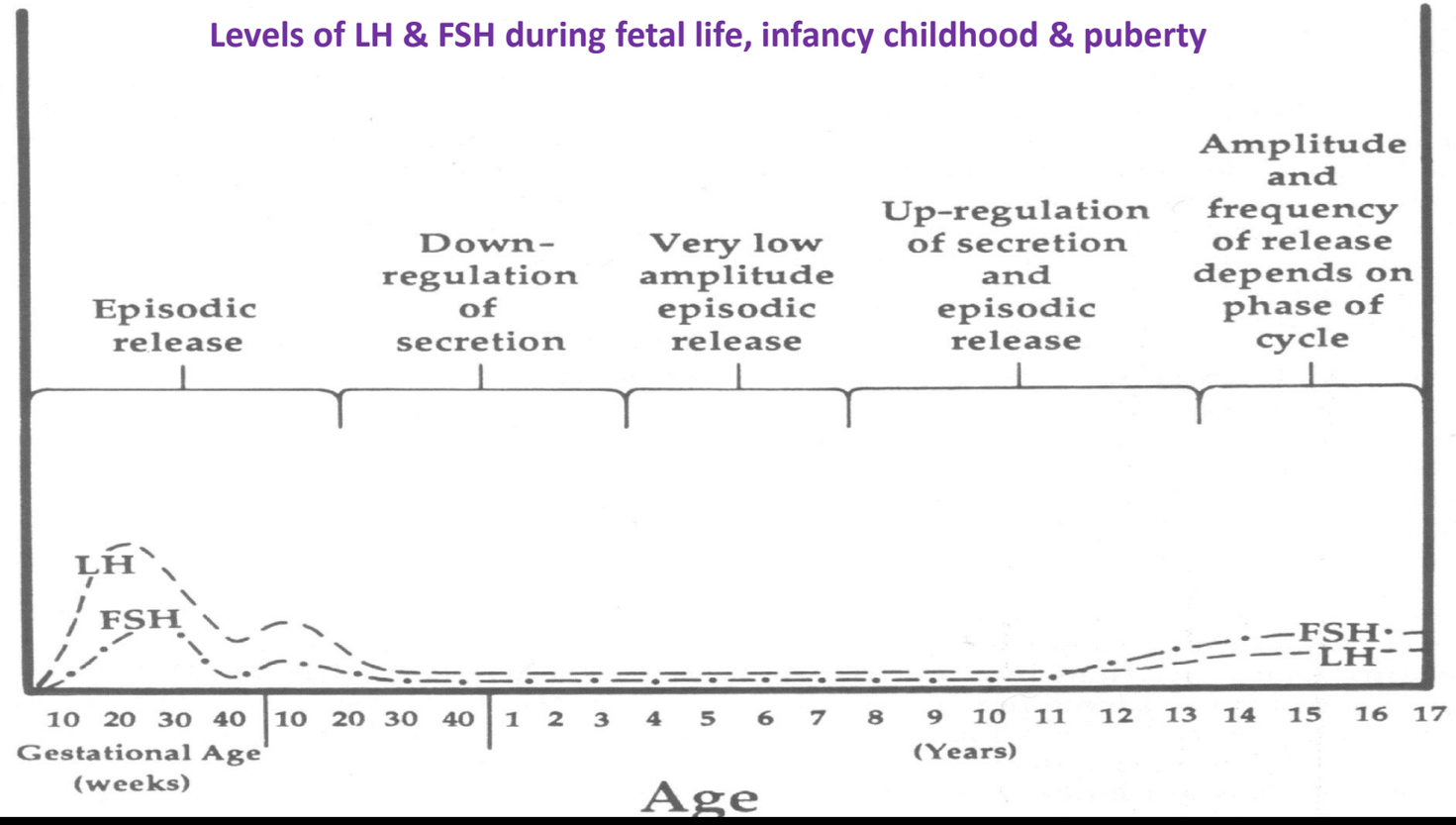
2- The intrinsic CNS inhibitory mechanism

▲Gradually develops with continued growth & maturation of the CNS

⇨⇨ Minimum FSH & LH level ⇨⇨ 6-8 years

▲The principal CNS inhibitor of GnRH is GABA

Levels of LH & FSH during fetal life, infancy childhood & puberty

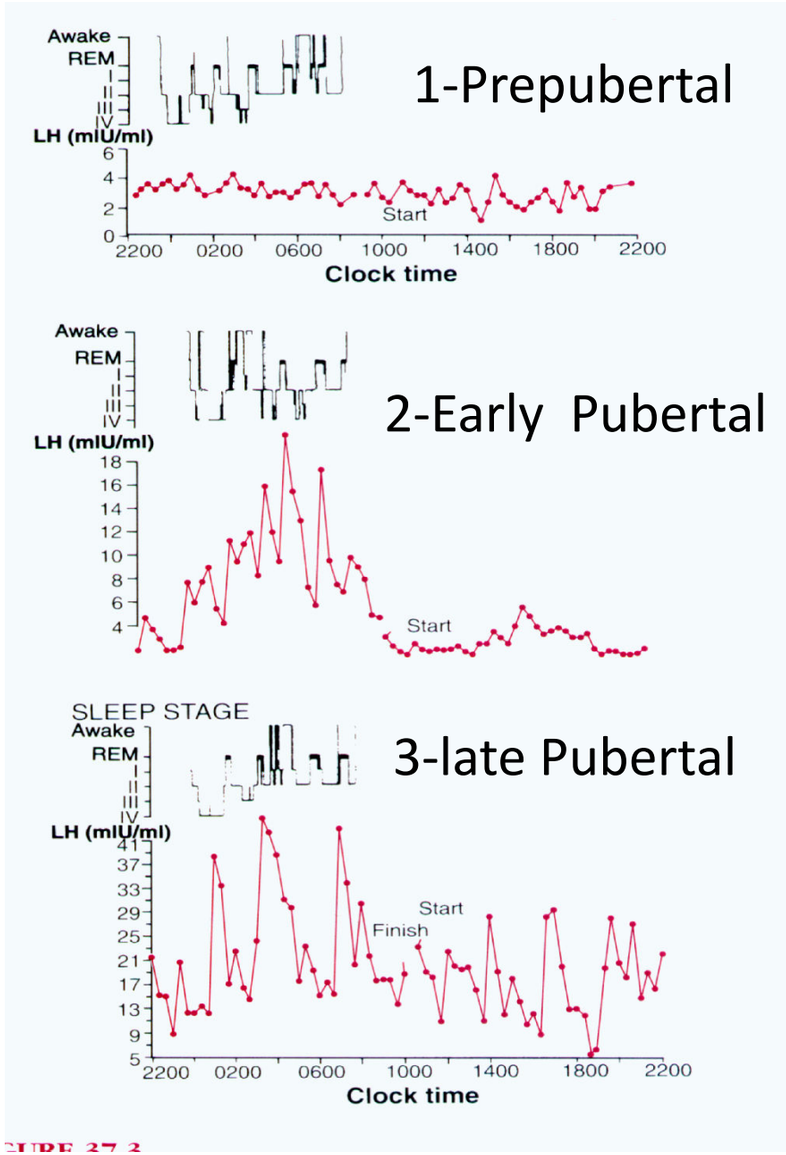


Maturation of the HPO axis

The sequence of maturation :

- ✓ At the onset of puberty GnRH pulses(↑) occur during daytime & sleep ⇨ LH pulses
- ✓ The frequency of LH pulses ↑ with further maturation
- ✓ LH pulses appear during day time & ↑ in amplitude
- ✓ As menarche approaches ⇨ the pulses are detected all the time (no diurnal variation)
- ✓ Similar changes occur in FSH pulses
- ✓ LH/FSH ratio ↑

*Plasma LH conc measured every 20 min for 24 hrs



Initiation of puberty

✓ Factors responsible for the initiation of puberty :

***UNKNOWN

✓ Frisch theory :

A critical body fat & body weight are required for the initiation of menarche

✓ Supported by :

1-Highly competitive athletic training

⇨ delayed puberty

2-Delayed menarche in malnutrition

3-Overweight girls have early menarche

4-Pt with anorexia nervosa revert to pre-pubertal pattern of gonadotropin secretion as body weight ↓

Initiation of puberty

Against the theory :

- Changes in body composition occurs simultaneously with
- gonadortopin increase & does not precede it

*Leptin :

- An adipose derived protein may play a role in the initiation of puberty

- Gonadostat begins to loose its sensitivity to the –ve
-feedback by estrogen ⇨ reactivation of GnRH pulsatility ⇨ puberty

- CNS inhibitory mechanism (on the hypothalamus) wane ⇨↑ GnRH ⇨↑ FSH & LH ⇨↑ estrogen (gonadarche)

- ↑ sensitivity of the pituitary to GnRH

- ↑ sensitivity of the ovary to LH & FSH ⇨ ↑ esrtogen secretion

Adrenarche

- ✓ The maturational ↑ in adrenal androgen secretion
- ✓ **DHEA , DHEAS, AND**
  - ⇨ development of pubic & axillary hair
  - ⇨ adult type body odor
  - ⇨ acne
  - ⇨ oily skin & hair
- ✓ **DHEAS** -----First detected at 7 Y
  -----Maximum at 15 Y
- ✓ The mechanism of initiation is unknown
- ✓ Adrenal androgens ⇨↑ bone age & linear growth
- ✓ Premature adrenarche ⇨ ↓ adult height
- ✓ Adrenarche & gonadarche are not associated

Gonadarche

- ✓ The onset of pubertal gonadal activity due to reactivation of HPO axis ⇨ ↑ estrogen.
- ✓ The process of ovarian follicular growth & atresia is initiated in utero. It continues from birth to puberty. It is independent of gonadotropin secretion & results in only minimal estrogen secretion.
- ✓ Reactivation of HPO axis ⇨ ↑ gonadotropin pulses ⇨ sustained follicular development to antral stage ⇨ significant estrogen production.
- ✓ There is direct relationship between follicular size & estrogen secretion.

Menarche

✓ When there is sufficient gonadotropin stimulation of the ovaries ⇨ follicular growth (~16mm) ⇨ ↑ estrogen ⇨

proliferation of the endometrium untill ⇨ it outgrows the estrogen capacity to maintain it or ⇨ the follicle undergo

atresia ⇨ ↓ estrogen ⇨ menstruation (MENARCHE)

✓ Anovulatory cycles occur during the first 6-18 months

"endometrium is not exposed to progestrone" ⇨ irregular unpredictable menstrual flow

Ovulatory menstrual cycles

- ✓ Requires further maturation of the HPO axis ⇨ development of the +ve feedback mechanism ⇨ LH surge ⇨ ovulation & corpus luteum formation ⇨ progestron production

- ✓ Early ovulatory cycles have short or inadequate luteal phase ⇨ HPO axis has not achieved full maturity

Physical events of puberty

I-Maturation of the genital organs

Prepubertal

1-UTERUS

-Ratio of corpus : cx ⇨ 1:2

-Tubular shape

-Length --- 2-3 cm

-Volume ----- 0.4-1.6

-Endometrium ⇨ single layer of cuboidal cells

2-OVARIES

-Volume -----0.2-1.6 ml

-Non functional

Pubertal ---adult

1-UTERUS

-Ratio of corpus :cx ⇨2:1

-Pear shape

-Length ----5-8

-Volume ----- 3-15 ---

-Endometrium ⇨ ↑ thickness

2-OVARIES

-Volume ------2.8-15 ml

-Multicystic

Maturation of the genital organs

Prepubertal

3-VAGINA

-Reddish in color

-Thin atrophic columnar epithelium

PH ---neutral

Length—2.5-3.5

Pubertal ---adult

3-VAGINA

-Thickening of the epithelium

Cornification of the superficial layer ⇨⇨ stratified squamous Epithelium

-Dulling of the reddish color

-PH ----acidic 3.8-4.2

-Secretion of clear whitish discharge ⇨ in the months before menarche

-Length ---7.5 cm

Maturation of the genital organs

External genitalia :

Under the effect of estrogens ⇨

1-Labia majora & minora ↑ in size & thickness

Rugation & change in color of the labia majora

2-The hymen thickens

3-Clitoris enlarge

4-Vestibular glands begin secretion

Under the effect of adrenal androgens & ovarian androgens ⇨ growth of pubic & axillary hair

II-breast development
thelarche

- ✓ The first visible change of puberty
- ✓ Thelarche is induced by estrogen
- ✓ Starts at 10.6 completed in ~ 3 years
- ✓ Effects of estrogen on the breast
  - 1-Ductal proliferation
  - 2-Site spicific adipose deposition
  - 3- Enlargement of the areola & nipple
- ✓ Breast development may be unilateral for several months
- ✓ Other hormones that play a role in breast development ⇨ prolactin, glucocoricoids & insulin.
- ✓ In normal girls the stage of breast development is consonant with the stage of pubic hair development.

Tanner staging
of breast development

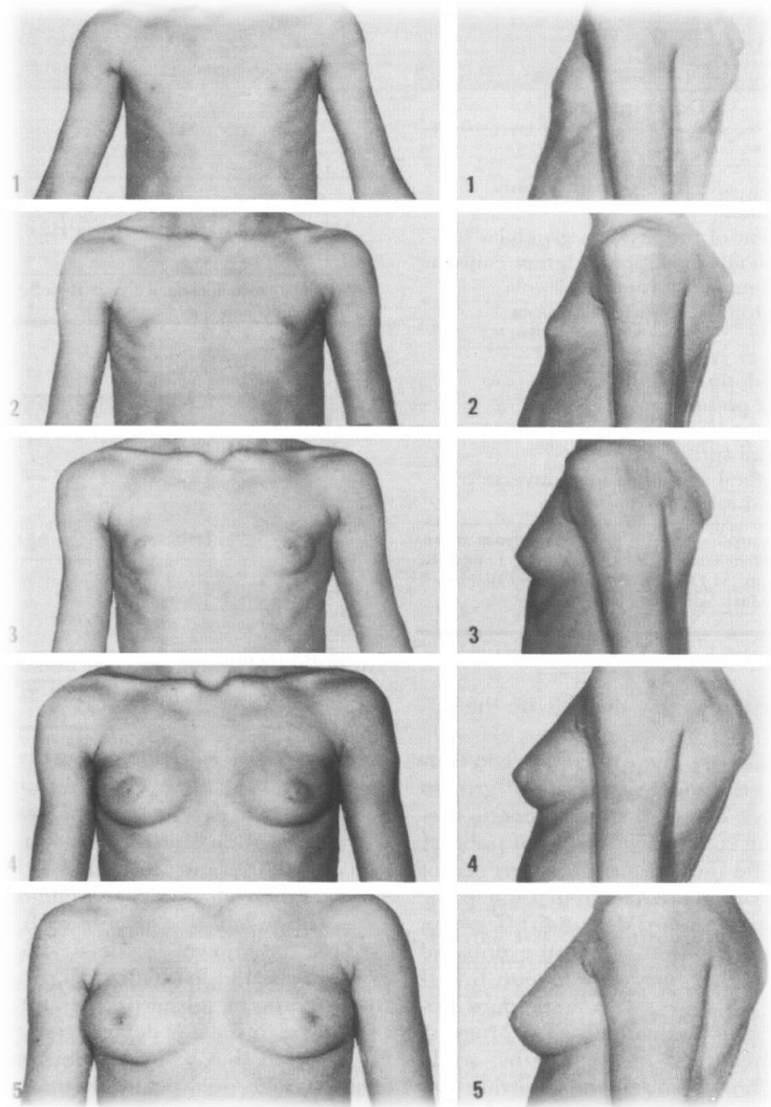
Stage 1 : Prepubertal

Stage 2 : Breast bud

Stage 3 :Enlargement of breast & areola

Stage 4 :Areola &nipple form a mound atop breast tissue

Stage 5 :Adult configuration areola &beast having smooth contour



Tanner staging
of pubic hair development

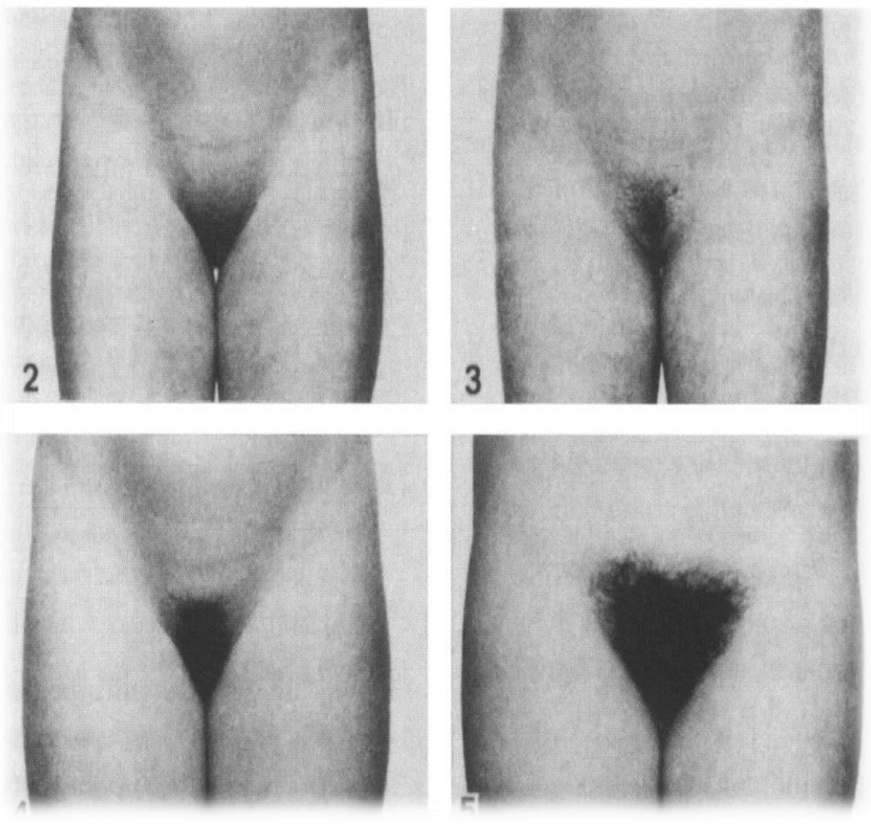
Stage 1 : No pubic hair

Stage 2 : Sparse downy hair on the medial aspect of the labia majora

Stage 3 : Darkening, coarsening & curling of hair which extends upwards & laterally

Stage 4 : Hair of adult consistency limited to the mons

Stage 5 :Hair spreads to medial aspect of thighs



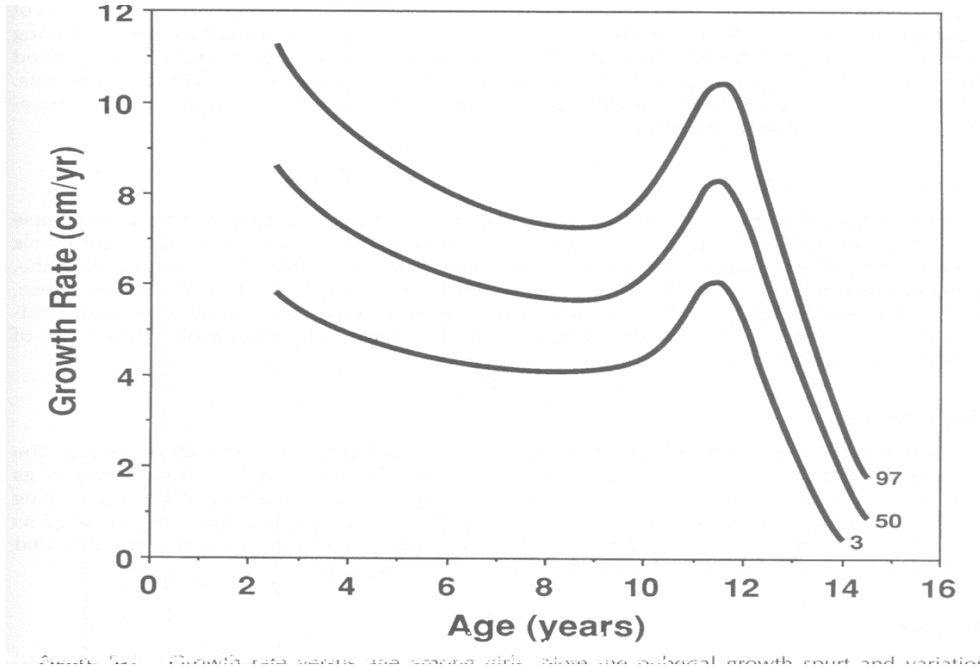
III-Growth spurt

- ✓ A global process involving :
- ↑ skeletal growth rate
- ↑ muscle mass growth of all internal organs

- ✓ Dependent on mainly on estrogen & growth hormone

  however adrenal androgens also play a role
- ✓ Estrogen has :
  - ⇨ direct anabolic effect
  - ⇨ ↑ growth hormone
  - ⇨ ↑ insulin like growth factors
- ✓ The onset of growth spurt antedates thelarche & pubarche.

*Growth rate versus age in girls



Growth spurt

- ✓ Peak Height Velocity

  -8.1 cm/year (before puberty 3-6 cm/y)

  -by the time PHV is achieved ⇨ 90% of adult height has been achieved

  -the average ↑ in height from the onset of growth spurt to cessation of growth 25 cm

  -girls who start the growth spurt early will have a shorter adult height

- ✓ Bone age is more closely correlated with pubertal events than chronological age.

Pubertal disorders

Abnormalities in the process of sexual maturation

- ✓ Precocious puberty
- ✓ Delayed puberty
- ✓ Dissencronous
(eg. Physical changes are not followed by menarche after an appropriate interval)

- ✓ Heterosexual changes
- ✓ Timing of progression of pubertal changes

Precocious puberty

✓ Early onset of puberty before 8 Y for girls 9 Y for boys.

Difficult to ascertain the early age limit because

A -15% of black girls
- 5% of white girls

} Breastdevelopment at 7 Y of age without associated early menarche

B -17.7% of black girls
-2.8 % of white girls

} Pubic hair development at 7 Y of age

✓ Most cases of PP are 2ry to idiopathic premature maturation of the HPO axis with Gn RH release

Central precocious puberty

- ✓ CPP is physiologically normal pubertal development that occur at an early age

- ✓ GnRH dependent
  ↑ GnRH pulses ⇨ ↑ gonadotropins ⇨ ↑↑ ovarian estrogen production & eventual ovulation

- ✓ It follows the pattern of pubertal changes that occur in normal puberty

- ✓ More common in girls than boys

Causes :

1-Idiopathic ----- 80-90%

2-CNS tumors

a-Hypothalamic hamartomas

A congenital malformation

The most common type of CNS tumor that cause CPP

Size & shape do not change significantly over time

May be associated with seizures (the intrahypothalamic type)

Rapidly progressing CPP in a child < 2 Y suggest this Dx

GnRH Rx is satisfactory & safe

b-Optic glyomas

c-Craniopharyngioma

d-Dysgerminoma

e-Epindymoma

f-ganglioneuroma

3-CNS dysfunction

a-Space occupying lesion eg. Arachnoid cyst

b-Hydrocephalus

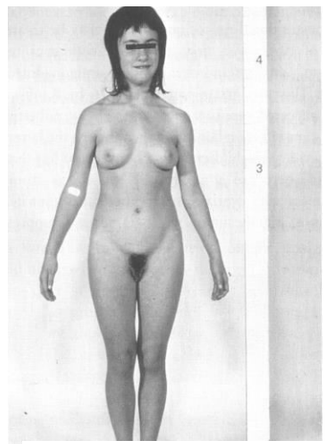
c-Irradiation

d-Trauma

e-Infection

f-Septooptic dysplasia (congenital)

g-Excessive exposure to sex steroids (congenital adrenal hyperplasia)



A 7 Y OLD CHILD WITH CPP

RX: GnRH analogues are the treatment of choice

Treatment of CPP

Purpose of treatment:

- ✓ To gain normal adult height (Pt with CPP will have an ultimately shortened adult height)
- ✓ Amelioration of the psychosocial consequences of ↑ size ⇨ unrealistic adult expectations

Who should be treated?

- ✓ Pt. with early puberty (<6Y) , accelrated growth & advanced skeletal age should be treated, (bone age >2Y>chronologic age. Menarche <8Y
- ✓ Pt. with early onset but without indication that puberty is advancing should be followed up

Treatment of CPP

1- GNRH analogues : {injection}

GnRH agonists (zoladex) ⇨ bind to GnRH receptors
(competitive inhibition) ⇨ down regulation of receptor function ⇨ ↓ gonadotropin secretion ⇨ inhibition of the HPO axis ⇨ ↓ estrogen secretion ⇨ regression of the manifestation of puberty
The goal of therapy is complete suppression of gonadotropin secretion ⇨ prepubertal GnRH stimulation test result
Adult Ht of Rx pt. > untreated
Adult Ht is related to skeletal age at the onset of Rx
Adult Ht of Rx pt. is still < target Ht / predicted Ht

- ✓ Rx is continued until the progress of puberty is age appropriate
- ✓ Best statural outcome ⇨ pt. treated until bone age 12 -12.5 years
- ✓ Growth hormone may be added to Rx
- ✓ After discontinuation of Rx resumption of puberty occurs & precedes at a normal pace
- ✓ Side effects: local injection reaction & sterile abscess

2-Medroxyprogestrone acetate :

- ✓ Used in the past
- ✓ Suppress the progression of puberty & menses
- ✓ NO effect on skeletal maturation & adult height

Peripheral precocious puberty
ppp / pseudo pp

- ✓ GnRH independent Due to inappropriate sex hormone secretion or exposure to exogenous sex steroids
- ✓ LH & FSH levels are low prepubertal , while estrogen ↑↑
- ✓ May present with some or all of the physical changes of puberty

CAUSES:

A-Exogenous sex steroids or gonadotropins

B-Abnormal secretion of gonadotropins (rare)
eg. Tumors secreting hCG (teratoma)

C-Functioning ovarian tumors UNCOMMON
- ✓ Granulosa cell } 70% present with PP
- ✓ Granulosa-thica cell }
- ✓ Mixed germ cell → usually benign

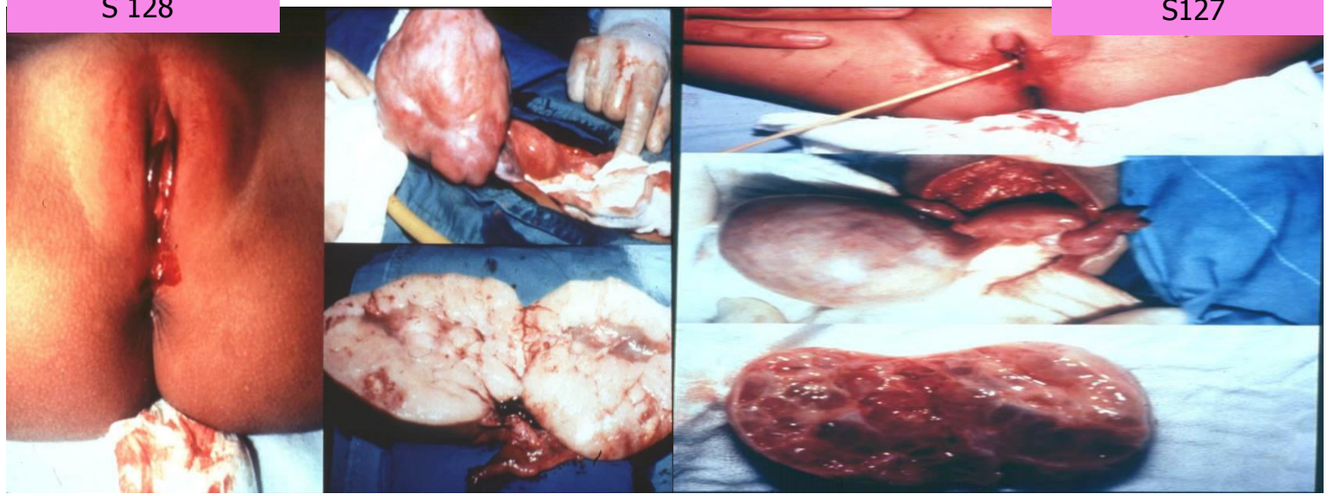
Present with rapid progression of breast development , vaginal bleeding & abdominal pain
Palpable mass & dulling of vaginal mucosa
Estradiol level excessively elevated
U/S, CT, MRI, are helpful in confirming the Dx
Rx ⇨ Excision ⇨ regression of 2ry sexual characteristcs

Peripheral precocious puberty
ppp / pseudo pp

Causes :

- Malignant ovarian trs are responsible for 2-3% of all cases of precocious pseudopuberty (PPP) in girls.
- The most common are the granulosa cell tumors

8 Y old, 3 M Hx of vaginal bleeding , breast &pubic hair Tanner III ,Ht 70th
% Wt 95th %, pelvic mass. FSH 4.1 LH 3.2
TSH 2.3 prolactin 21 LDH 192
HCG 103 AFP 5.
Laparotomy BSO ,appendectomy , omentectomy.
Dx Bilateral Dysgerminoma arising in a Gonadoblastoma , Karyotype XY
RX 8 coarses of chemotherapy, no recurrence at 20 M



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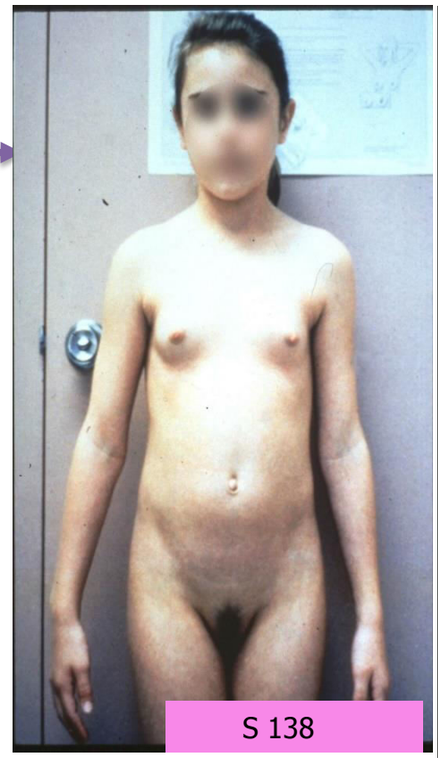

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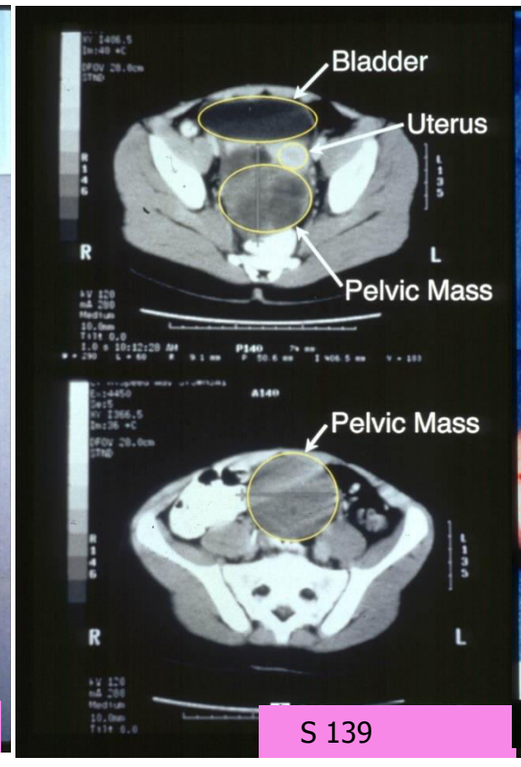

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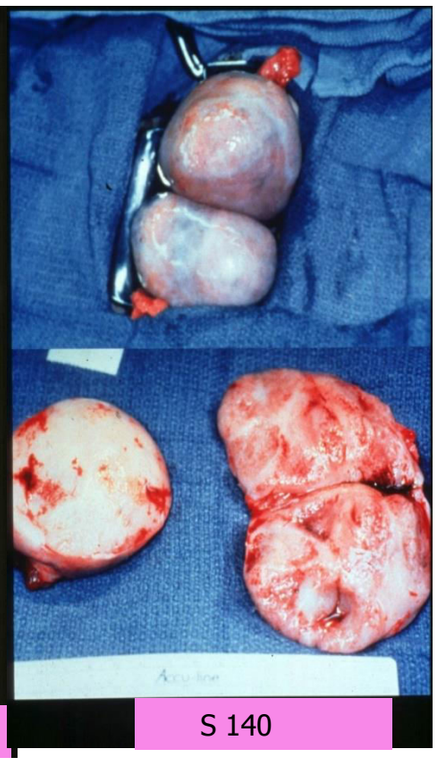

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Peripheral precocious puberty
ppp / pseudo pp

Causes :

C-Functioning ovarian tumors

- ✓ Cystadenoma
- ✓ Gonadoblastoma both
- ✓ Lipoid

} May produce estrogen or androgen or Rare

D-Functional ovarian cysts

Secrete estrogen ⇨ breast development

Rupture or resolution ⇨↓ estrogen ⇨ vaginal bleeding

*Surgery should be avoided

E-Adrenal tumors RARE

F-Congenital adrenal hyperplasia

G-CHRONIC 1RY HYPOTHYROIDISM

↑ TSH ⇨ acts on FSH receptors ⇨ PPP

RX ⇨ thyroxin ⇨ resolution of the PPP

Ht	20th%
Wt	95th%
Thyroid	slightly prominent
Breasts	Tanner lll
Pubic hair	Tanner ll
Hymen	Well estrogenized
P/R	Pelvic mass 5cm
FSH	5.4 IU/L
LH	0.3
Estradiol	94 pg/ml
TSH	50 mIU/ml

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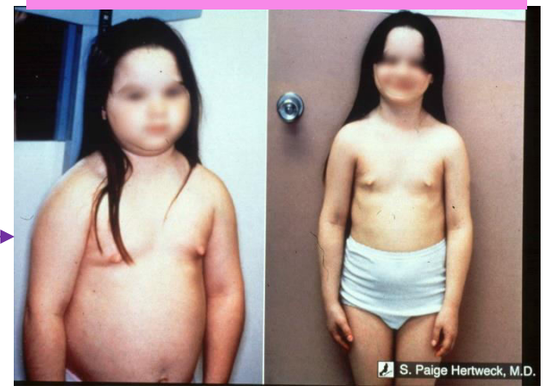

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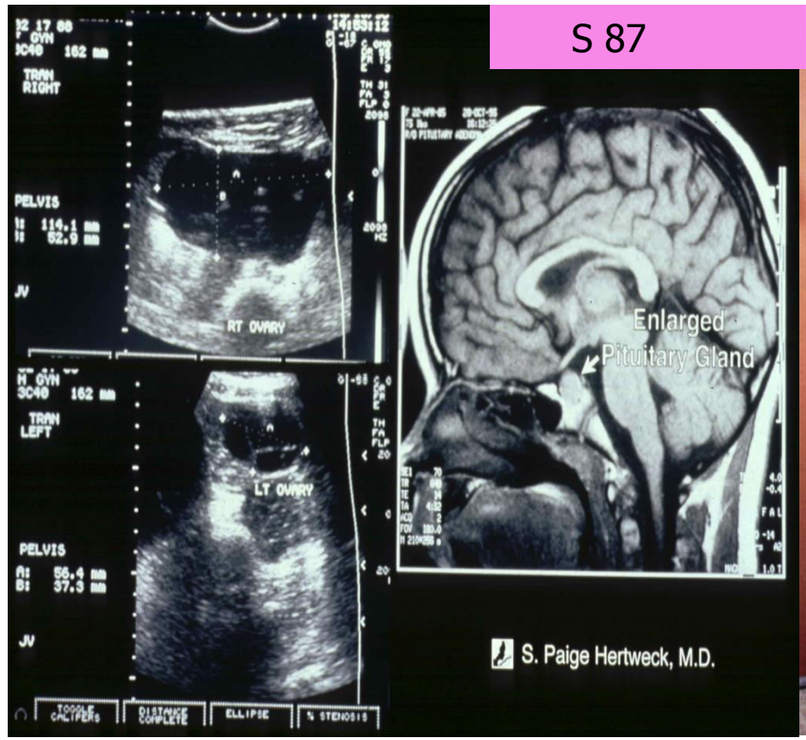

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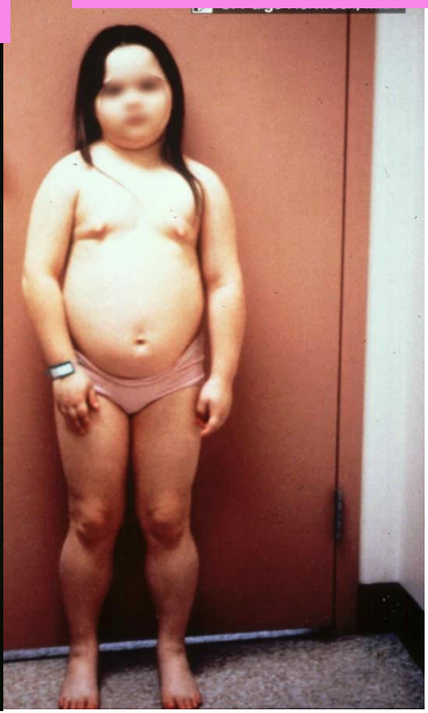
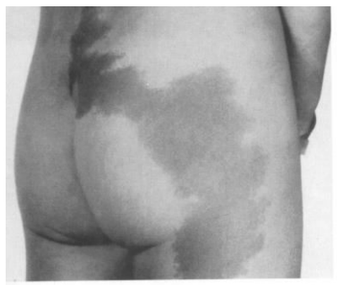


Peripheral precocious puberty
ppp / pseudo pp

Causes :

H-McCune-Albright syndrome



- ✓ Café-au-lait spots
- ✓ Polyostotic fibrous dysplasia
- ✓ GnRH independent PP
- ✓ Endocrine disorder (hyper thyroidism, hyperparath, Cushing S)
- ✓ Autonomous functioning ovaries with 1 or 2 ovarian cysts ⇨↑ estrdiol

Rx ⇨ Testalactone ⇨inhibit aromatase activity

⇨↓ estrogen synthesis

Rx of PPP :

1-TREAT THE CAUSE (IF POSSIBLE)

2-Drugs

-Testolactone ⇨ aromatase inhibitor , inhibit conversion of testosterone to estrogen 35mg/kg/D 3 divided doses

-Ketoconazole ⇨ inhibit steroid biosynthesis 200mg tds

-Cyproterone acetate ⇨ Potent progestin & antiandrogen, inhibit androgens at the receptor level / supress gonadal & adrenal steroidogenesis : antigonadotrophic 100 mg/m2 2 divided doses

-Spironolactone ⇨ inhibit androgens at the receptor level, ↓ ovarian androgen production, antimineralocorticoid 50-100mg bd

-Medroxyprogestrone acetate

Girls with prolonged PPP ⇨ prolonged exposure of the CNS to estrogen ⇨ central precocious puberty CPP

Incomplete precocity

- ✓ **Partial (often transient) pubertal development in the absence of other stigmata of puberty.**
- ✓ **Slow progression , no change or waning of the physical finding may occur.**

1-PREMATURE THELARCHE

Premature beast development in the absence of other
signs of sexual maturation
Estradiol level ↑↑
Unilateral or bilateral , without areolar development
< 2 Y of age & non progressive
Follow up should distinguish cases of slow progressing CPP
No Rx is indicated & subsequent normal puberty occur

2-PREMATURE PUBARCHE

THE APPEARANCE OF PUBIC HAIR BEFORE 8 Y OF AGE IN GIRLS
Early maturation of the normal pubertal adrenal androgen production "Adrenarche"
It is evidence of premature adrenarche without activation of the HPO axis
Beast development is absent
Slightly accelerated growth velocity & advanced skeletal maturation
Puberty occur normally at the appropriate age
Dx by exclusion of CAH, androgen secreting tumors & CPP
50% of pt. with premature pubarche progress to PCO

Hyperandrogenism & insulin resistance are chct of PCO

Late onset CAH may have a similar presentation
Dx ---ACTH stimulation test ➪
Marked ↑ of 17-OH progestrone
--- ↑ plasma level of 17-OH progestrone, AND, DHEA
Rx ---- glucocorticoids
CPP can occur 2ry to late Dx or inadequate Rx of CAH

Incomplete precocity

3-ANDROGEN SECRETING TUMORS

ADRENAL TUMORS:

RARE
Function autonomously
↑ DHEA , DHEAS, testosterone
↑ Cortisol
Could benign or malignant with poor prognosis

OVARIAN TUMORS:

Arrhenoblastoma, lipoid cell tumors
↑ Testosterone , AND
DHEA, DHEAS → NORMAL

4-PREMATURE MENARCHE

Uncommon
We should role out serious cause of bleeding
1-Neonatal period
Due to withdrawal of estrogen produced by the fetoplacental unit
2-Spontaneous regression of ovarian cysts
3-Hypothyroidism
4-McCune Albright Syndrome
D. Dx

- Vulvovaginitis
- Foreign body in the vagina
- Trauma
- Sexual abuse
- Vaginal tumors

Evaluation of patients with sexual precocity

We have to differentiate between CPP & PPP

1-HISTORY

- ✓ Onset & progression of symptom
- ✓ (N tempo ⇨CPP, Abrupt & rapid ⇨estrogen sec Tr)
- ✓ Hx of CNS trauma or infection
- ✓ Symptoms associated with neurological dysfunction
- ✓ Symptoms associated with endocrine dysfunction
- ✓ Exposure to exogenous steroids
- ✓ Hx of abdominal pain or swelling
- ✓ Family Hx ⇨ early puberty, short stature

2-PHYSICAL EXAMINATION

- ✓ Tall stature for age / changes in HT velocity
- ✓ 2ry sexual chct (Tanner staging) ⇨ synchronous ⇨ CPP
- ✓ Neurological examination
- ✓ Fundoscopy & gross visual field evaluation
- ✓ Virilization
- ✓ Evidence of hypothyroidism or hyperadrenalism
- ✓ Examin the skin for acne, odor, café-au-lait spots, hirsutism

Abdomen ⇨ masses

- ✓ PR

Evaluation of patients with sexual precocity

INVESTIGATIONS

1-LAB STUDIES

↑DHEA, DHEAS ⇨ adrenarche

⇨ adrenal origion of PPP

TSH, T4, hCG

LH, FSH, Estradiol

↓LH ⇨ LH/FSH ratio < 1 ⇨ Prepubertal gonadotropin secretion

↑ LH ⇨ LH/FSH ratio > 1 ⇨ Pubertal gonadotropin response CPP

-GnRH stimulation test

100 ugm of GnRH IV

Check FSH & LH baseline, 20,40,60 min

Prepubertal:

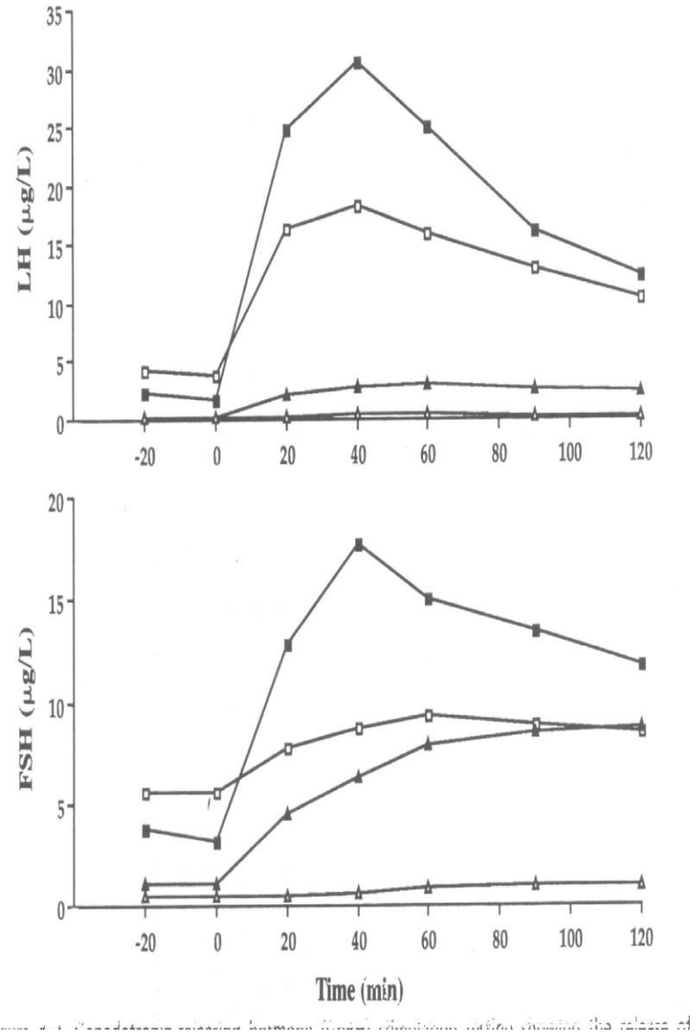
⇨ FSH > LH

⇨ LH rise is minimal < 10 IU/ml

Pubertal:

⇨ ↑ LH > FSH

⇨LH peak above upper limit for prepubertal



■ 6 Y old with CPP

□14Y old with normal puberty

▲ 16Y old with H-P destruction 2ry to cranio-pharyngioma

△5Y old prepubertal

Evaluation of patients with sexual precocity

INVESTIGATIONS

2-Bone age radiography : X-Ray

- ✓ Advanced in both CPP & PPP
- ✓ Premature adrenarche ⇨ slightly ↑
- ✓ Premature thelarche ⇨ Normal

3- CT / MRI OF THE HYPOTHALAMIC PITUITARY REGION :

- ✓ Important in all Pt. with suspected CPP or Pt. with neurological symptoms & signs

4-U/S :

- ✓ Adrenal
- ✓ Ovaries ⇨ role out ovarian cysts or tumors & to assess size
- ✓ Uterus ⇨ to assess size

5-Vaginal smear for pyknotic index :

- ✓ A simple method of assessing the level of estrogen stimulation
- ✓ Result is expressed in the form of % of basal , parabasal & superficial cells
- ✓ The greater the % of superficial cells the greater the estrogen effect

Psychosocial consequences of precocity

1-Children with PP are taller & appear older than their peers ⇨ unrealistic expectation from parents , teachers & others ⇨ child will be under stress.

2-They perceive them selves as different ⇨ however this does not have any long term effect & they do well psychologically.

3-Sexual maturity at an immature age make them vulnerable to be victims of sexual abuse.

Delayed puberty

Definition:

-Absence of pubertal development /No breast development by age 13
-No menarche by age 15
-No menarche by 3 years after the onset of breast development.
-Lack of progression to next Tanner stage in a year.
- Physiologic delays in puberty tend to be familial.

✓ Sexual hair onset does not mean the onset of puberty / it is due to adrenal androgen secretion.

Delayed puberty

A-Hypergonadotrophic Hypogonadism:

FSH / LH ↑

1-Auto immune ovarian Failure
2-Turner's Syndrome
3-previous radiation or chemotherapy
4-Galactosemia
5-Gonadal dysgenesis (XX, XY)

B-Hypogonadotrophic Hypogonadism :

1-REVERSABLE CAUSES
-constitutional { without problems} delay (most common 30%)
-Systemic disease (hypothyroidism, prolactinoma,excessive exercise, Congenital adrenal hyperplasia , anorexia nervosa, brain tumor,,chronic diseases)

2-IRREVERSIBLE CAUSES:
-Kallmann's Syndrome(most common)
-Hypopituitarism
-Congenital CNS lesion
-GnRH receptor defects

C-Euogonadotropic Eugonadism:

(Describes normal pubertal onset but lack of menarche)
1-Mullarian agenesis (most common)
2-vaginal septum/ imperforate hymen
3-Androgen insensitivity
4-Hypothalamic amenorrhea with onset after puberty (excessive exercise, extreme weight loss, psychogenic stress)

*Kallmann syndrome :

-They have isolated GnRH deficiency (no secretion of GNRH) → ↓ LH / FSH → Ovaries will not produce follicles → ↓ Estrogen

-It is associated with anosmia (decreased sense of smell).

-These individuals may have other anomalies of midline structures of the head.

- We cannot treat it, but we can treat the symptoms (e.g. LH/FSH for ovulation, or Estrogen as a replacement if she is not planning to get pregnant)

Evaluation

1-history

2-physical examination

3-investigations:

-Hormonal profile :

(FSH,LH , PROLACTIN , TFT , PROGESTERONE)

-IMAGING:

- ✓ pelvic US
- ✓ MRI / CT
- ✓ Bone Age (X-ray)
- ✓ Brain MRI

Management

Treat underlaying cause :

1-Turner syndrome → hormone replacement therapy.

2-HIGH FSH / NORMAL KARYOPTYPE XX
(Autoimmune ovarian failure or Gonadal dysgenesis) → Hormone replacement therapy.

3-HIGH FSH / XY KARYPTYPE (Gonadal dysgenesis) → Hormone replacement therapy+ Gonadectomy (to prevent malignant changes).

4- LOW / NORMAL FSH

- ✓ Exclude sysyemic disease
- ✓ If no systemic sisease :

-MRI of the brain

-GnRH stimulation test

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