IN THE NAME OF GOD
Endocrine physiology of puberty
females

- In females, thelarche is usually the first sign of puberty (10-11 yr of age), followed by the appearance of pubic hair (pubarche) 6-12 mo later.
- The interval to the onset of menstrual activity (menarche) is usually 2-2.5 yr, but may be as long as 6 yr. internal and external genitalia.
In males, growth of the testes (≥4 mL in volume or 2.5 cm in longest diameter) and thinning of the scrotum are the first signs of puberty (11-12 yr).

These are followed by pigmentation of the scrotum and growth of the penis and by pubarche.

Appearance of axillary hair usually occurs in midpuberty.

In males, acceleration of growth is maximal at genital stages IV-V (typically between 13 and 14 yr of age).
males

- In males, the growth spurt occurs approximately 2 yr later than in females, and growth may continue beyond 18 yr of age.
Breast development

• M1: only the papilla is elevated
• M2: Breast bud stage: Breast & papilla are elevated as small mound
• M3: further enlargement of breast, not separation
• M4: areola & papilla project
• M5: only the papilla project (mature)
Pubic hair stages

• P-1: No pubic hair
• P-2: Sparse growth of hair along the labia
• P-3: Hair is more darker, coarser & curlier, over junction of pubic area
• P-4: Adult type but smaller than most adult & not to medial side of thigh
• P-5: Adult type
Female Tanner Stages

<table>
<thead>
<tr>
<th>Tanner Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tanner 1:</td>
<td>None</td>
</tr>
<tr>
<td>Tanner 2:</td>
<td>Few darker hairs along labia</td>
</tr>
<tr>
<td>Tanner 3:</td>
<td>Curly pigmented hairs across pubis</td>
</tr>
<tr>
<td>Tanner 4:</td>
<td>Small adult configuration</td>
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<tr>
<td>Tanner 5:</td>
<td>Adult configuration with spread onto inner thighs</td>
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Genital development

- G-1: preadolescent
- G-2: scrotum & testes are enlarged & scrotal skin changed & some reddening
- G-3: penis enlarged (most in length) & enlarged others
- G-4: Development of glans
- G-5: adult size
Pubic hair

• P-1: preadolescence
• P-2: hair in base of penis
• P-3: more hair & in junction of pubes
• P-4: smaller than adult type & not in medial thigh
• P-5: adult type
Precocious Puberty
Definition (Nelson 2016)

• Precocious puberty is defined by the onset of secondary sexual characteristics before the age of 8 yr in girls and 9 yr in boys.
During the past 15 to 20 years, studies from the United States and Europe reported earlier breast development in girls, as compared to historical data. However age at menarche occurred at the same time or slightly earlier. Thus the time span from breast development to menarche seemed to have increased.
Types:

1 - **central. P.P.** true precocious puberty **GnRH dependent.** (80%)

2 - **peripheral. P.P.** false (pseudo-precocious puberty) **GnRH independent** (20%)

3 - **Incomplete** precocious puberty (Variations of pubertal development)
   - Precocious Thelarche
   - Precocious Adrenarche
   - Precocious Menarche
Central precocious puberty

• It occurs 5-10–fold more frequently in girls than in boys and is usually sporadic.
• A high prevalence of idiopathic central precocious puberty has been reported in girls adopted from developing countries, with the limitation that the exact date of birth may be uncertain.
Central precocious puberty

• **Idiopathic precocious puberty**
  – Although approximately 90% of girls have an idiopathic form, a structural CNS abnormality can be demonstrated in up to 75% of boys with central precocious puberty.

• **Neurogenic precocious puberty**
  – **A: Acquired disorders:**
    – traumatic brain injury, meningitis, encephalitis, brain abscess, brain tumor as glioma, craniopharyngioma, ...
    – chemotherapy, radiation, granulomas inflammation
  – **B: Congenital anomalies:**
    – Arachnoid cysts, hydrocephalus, hypothlamic hamartoma, septooptic dysplasia, suprasellar cyst.
• Patient (A) at 3 11/12, (B) at 5 8/12, and (C) at 8½ yr of age. Breast development and vaginal bleeding began at 2½ yr of age. Bone age was 7½ yr at 3 11/12 and 14 yr at 8 yr of age. Intelligence and dental age were normal. Growth was completed at 10 yr; ultimate height was 142 cm (56 in). No effective therapy was available at the time this patient sought medical attention.
Photographs at 1.5 (A) and 2.5 (B) yr of age. In early infancy, the patient began having frequent spells of rapid, purposeless motion; later in life, he had episodes of uncontrollable laughing with ocular movements.

At 7 yr, he exhibited emotional lability, aggressive behavior, and destructive tendencies. Although a hypothalamic hamartoma had been suspected, it was not established until CT scanning became available when the patient was 23 yr of age.

Epiphyses fused at 9 yr of age; final height was 142 cm

At 24 yr of age, he developed an embryonal cell carcinoma of the retroperitoneum.
MRI of a central nervous system lesion in a child with central precocious puberty. A 6-yr-old girl was referred for stage IV breast development and growth acceleration. Serum luteinizing hormone and estradiol concentrations were in the adult range. The midsagittal T1-weighted image shows an isointense hypothalamic mass (arrowheads), typical of a hamartoma.
Peripheral Precocious Puberty

Autonomous ovarian follicular cysts
Mc Cune Albright synd.
Ovarien Tumor
CAH
Virilizing Adrenal Tumor
Feminizing Adrenal Tumor
Glucocorticoid Resistance Syndrome
Testicular Tumor
Exogenous steroid
Other
McCune-Albright syndrome in a girl 4.5 yr of age; at this time, her height age and bone age were normal. Menarche occurred at 4 yr of age.

A, Note the bilateral breast development, hyperpigmented spots on the abdomen, and prominence of the left side of the face.

B, Roentgenograms revealed fibrous dysplasia in the distal end of the left ulna and thickening of the bones about the left orbit and the maxillary portion of the frontal bones.
FIGURE 92-4. Fourteen-year-old girl with McCune-Albright syndrome. Note the rough borders to the café au lait spot (coast of Maine) and the significant scoliosis, due to extensive bony lesions causing a leg length discrepancy.
DIAGNOSIS

- Hx
- P/E
- Growth velocity
- Bone age
- Lab test
1: History:

- *Exogenous estrogen or androgen.*
- Family pubertal history
- CNS abnormality
- *Growth velocity*
- *Accelerated growth*
- Advanced bone age (>20% Ht age)
2. Physical examination:

- **Tanner stages**
  - Thyroid exam, BP
  - Neurologic and ophthalmologic exam.
  - Skin pigmentation, Abdominal exam

Vaginal mucosa: glistening red/pink mucosa (E+)

- Galactorrhea, Hirsutism
2. Physical examination:

- **Testicular Enlargement (>2.5-3cm/4ml)**
  - *Symmetrical Enlargement*: C.P.P, Testotoxicosis
  - *Asymmetrical*: Leydig cell tumor
  - CAH + adrenal.rests

- **Penile Enlargement**: CAH, Adrenal tumor
Imaging

c. **Ultrasonography**. **CT or MRI** : to R/O ovarian or adrenal tumor.

Pelvic U.S: Uterine > 3.5 cm / > 1.8 ml ⇒ pub

- Ovarian cysts : >9 m.m ⇒ P.P.P
- Endometrial thickness ⇒ P.P
- Ovarian vol. > 1.2 ml ⇒ P.P
- skeletal scintigraphy ⇒ MC-Cune Alb.
- **CNS MRI**
Hormonal assay:

Testosterone > 20 ng/dL or
Estradiol > 9 pg/ml

LH and FSH by RIA:
Basal LH > 0.6 IU/L, FSH > 2 IU/L \( \Rightarrow \) C P P
T4, TSH, \( \beta \)-hCG

GnRH test

Pubarche: DHEAS, \( A_4 \), Testo, 17.OH prog
IX of therapy:

- Rapidly progressive pubertal changes
- **Abnormal height potential:**
  - Advanced B. age (>2yr/C.A)
  - Accelerated growth (>6cm/yr)
  - B. age >HT age>C. age
  - Girls with HP < 150 cm or 10 cm < T.H
  - Boys with HP < 160 cm or 10 cm < T.H
- **Psychological difficulty**
- Inoperable hypothalamic tumors
Treatment
central precocious puberty

• Long-acting, superactive analogues of GnRH are the treatment of choice for central precocious puberty.
• psychological support or even counseling for children and families
GnRH-independent precocious puberty

- Patients with precocious puberty from a hormone-secreting tumor require surgical removal, if possible.
- An inhibitor of testosterone synthesis (e.g., ketoconazole), an antiandrogen (e.g., spironolactone), or an aromatase inhibitor (e.g., testolactone) or antiestrogen, such as tamoxifen.