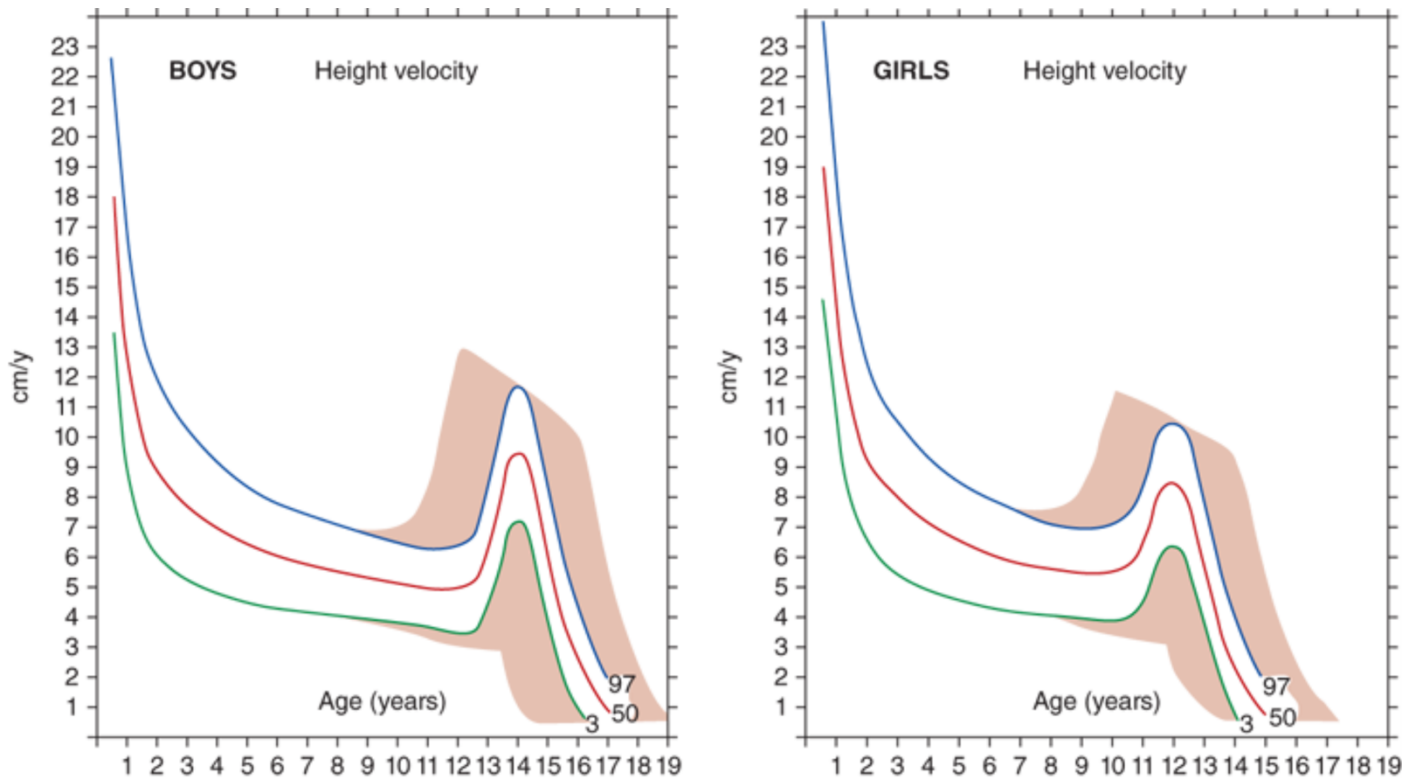






**Growth velocity: The annual rate of growth in height (cm/year).**



**It starts high, then declines, then increases again during growth spurt, and then declines once again.**

**Rule of Thumb (Length and Height):**

- Average length at birth is 50 cm
- Average Length at 1 year is 75 cm
- At 4 years, birth length doubles.
- Between 4 years and puberty, annual height increase by 5-8 cm/year

**Rule of Thumb (weight):**

- Newborns lose 5-10% of body weight in the first few days after birth.
- Newborns regain birth weight in 7-10 days.
- Birth weight doubles at 4 months
- Triples at 1 year
- Quadruples at 2 years.

**Example:**

- Mohammed came today to the general pediatrics clinic for his annual health check up.
- His date of birth is 7-3-2014. His mother states that he is 4 years old.
- His height is today is 97 cm and his weight is 15 Kg
- Mohammed's mother asks: "Is his growth normal?"





**Short stature:**

Define it by either the single point data or the serial measurement data

Single measurement data: Height > 2 SDS below mean of age and sex ( $\leq 2^{\text{nd}}$  %ile).

Or height velocity less than 25% (- 2 SD for age)

Normal height velocity is: 4-5 cm per year, in puberty: 8-12 cm per year

**Growth failure:**

Height Velocity > 2 SDS below the mean for age and sex ( $< 3^{\text{rd}}$  %ile)

**Causes:**

| Short Stature (Normal growth velocity)  | Growth Failure   |
|---|--|
| Constitutional Delay of Growth and Puberty (CDGP)/ Constitutional short stature   | <b>Endocrinopathies:</b><br>1- Growth hormone deficiency<br>2- Hypothyroidism<br>3- Cushing syndrome   |
| Nutritional deficiency  |  |
| <b>Chronic illnesses:</b><br>1- GI diseases, Malnutrition, malabsorption...<br>2- DM<br>3- Cystic fibrosis<br>4- Congenital heart disease<br>Heart failure, renal failure, liver disease... | Genetic (Turner syndrome, Silver-Russell Syndrome, Noonan Syndrome, Prader-Willi syndrome, SHOX gene insufficiency, Pseudohypoparathyroidism Skeletal Dysplasias<br><br>Familial Short stature |

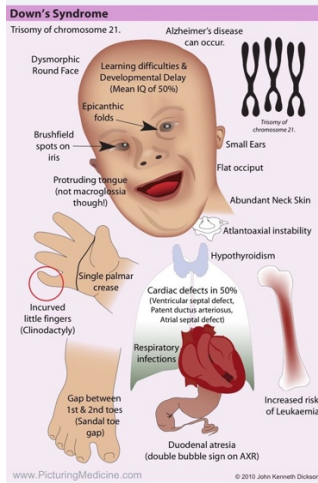
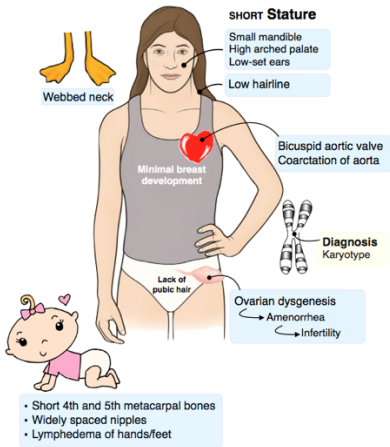
**Assessment:**

- Midparental Height
- Body proportions
  - Arm span (normal arm span = height)
  - lower body segment (Symphysis pubis to floor while standing), Upper segment = height – lower segment) (normal = 1:1 by 10 years of age)
- Bone age:
  - Left hand and wrist x-ray compared to a standard. (Used to assess skeletal maturity and to predict remaining growth and final adult height)

| Dx                               | Clinical features  |
|----------------------------------|--|
| Constitutional Short stature     | Usually in a healthy boy with normal height early in life, associated with delayed puberty and delayed bone age, FHx of delayed puberty.   |
| Familial short stature           | Height within genetic target as per midparental height. Bone age = chronological age, no pubertal delay  |
| <b>Endocrinopathy</b>            | Growth failure (usually), weight is not affected (well-nourished child), bone age is delayed.<br>No growth spurt, stopped growing, gaining weight (mainly Cushing) or well-nourished child Endocrinopathies<br>If a child is hypothyroid, they will just stop growing! (thyroid hormone controls growth more than the growth hormone itself) (hockey stick appearance) |
| <b>Chronic illness</b>           | Growth failure, weight is also affected.   |
| <b>GI disease/ Malabsorption</b> | Growth failure, weight is more affected than height  |
| <b>Genetic</b>                   | Down syndrome, turner syndrome, Russel silver syndrome<br>Can never achieve the mid parental height, clues come from physical examination  |



## Turner Syndrome 45 XO



**Table 4. Suggested Laboratory Tests for Children with Short or Tall Stature**

| Test   | Indication                 |
|--|----------------------------|
| <b>Short stature</b>                               |                            |
| Complete blood count                               | Anemia                     |
| Comprehensive metabolic panel                      | Hepatic and renal diseases |
| Erythrocyte sedimentation rate, C-reactive protein | Inflammatory bowel disease |
| Follicle-stimulating hormone, karyotyping          | Turner syndrome            |
| Insulinlike growth factor 1*                       | Growth hormone deficiency  |
| Thyroid-stimulating hormone, free thyroxine (T4)   | Hypothyroidism             |
| Tissue transglutaminase and total immunoglobulin A | Celiac disease             |
| Urinalysis   | Renal disease              |

## Investigations for the cause of short stature?

- Rule out chronic illnesses: CBC, renal profile, electrolytes, ABG, celiac
- Thyroid profile
- Chromosomal analysis
- Bone age

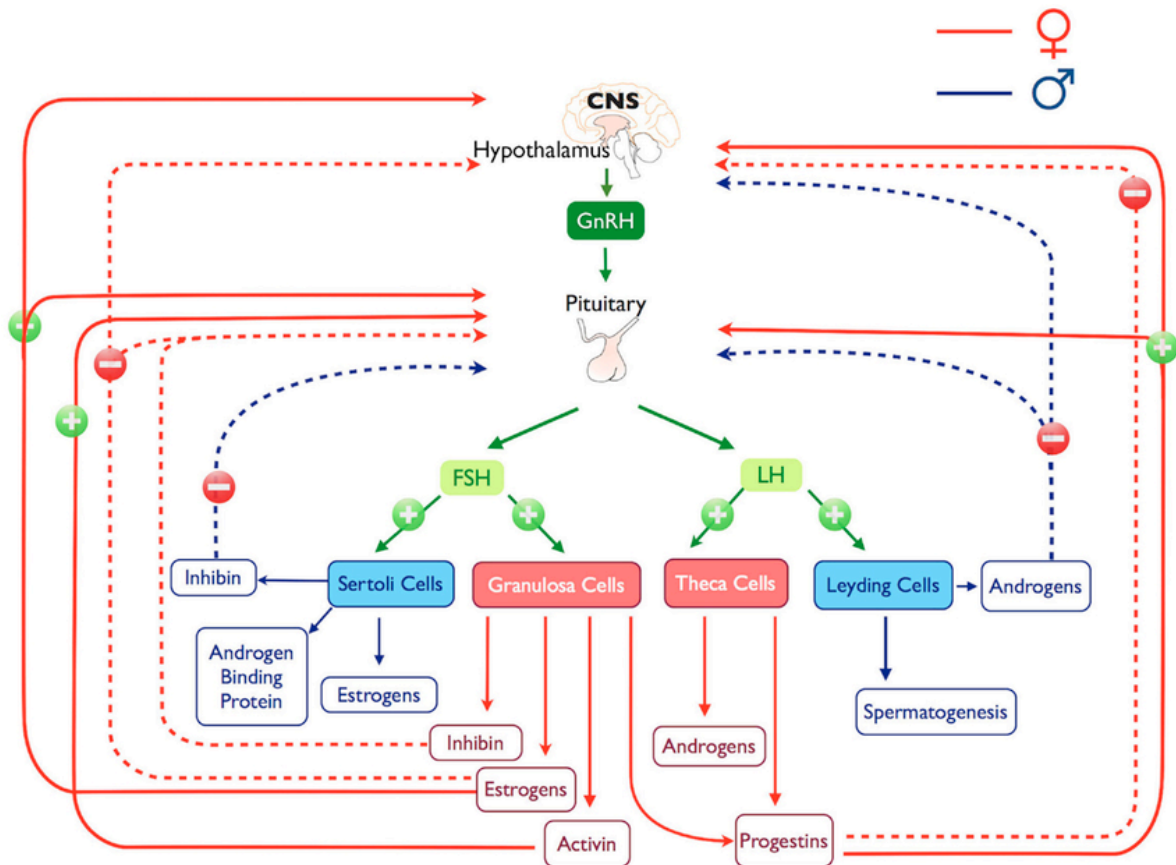
## Treatment:

Familial: no treatment

Malnutrition, Chronic illness: correct

Growth hormone deficiency, turner syndrome, IUGR, renal failure, HIV: Growth hormone

## How is Hypothalamic – Pituitary – Gonadal Axis regulated?



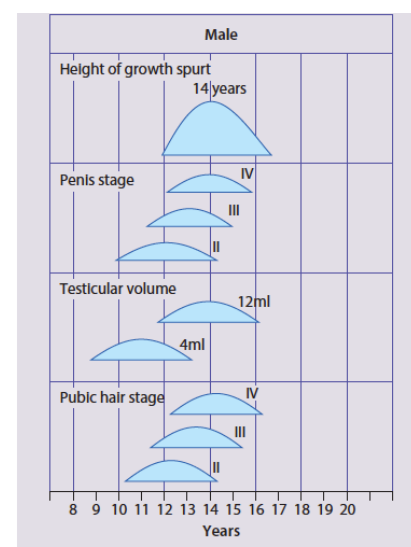
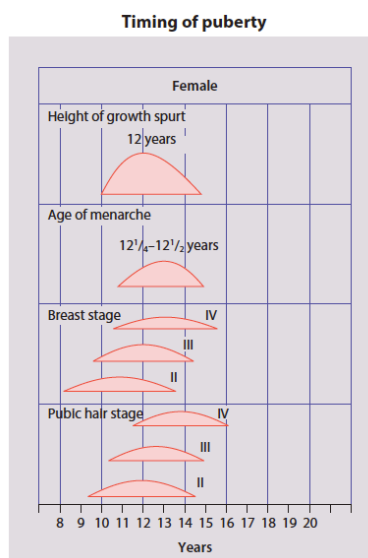
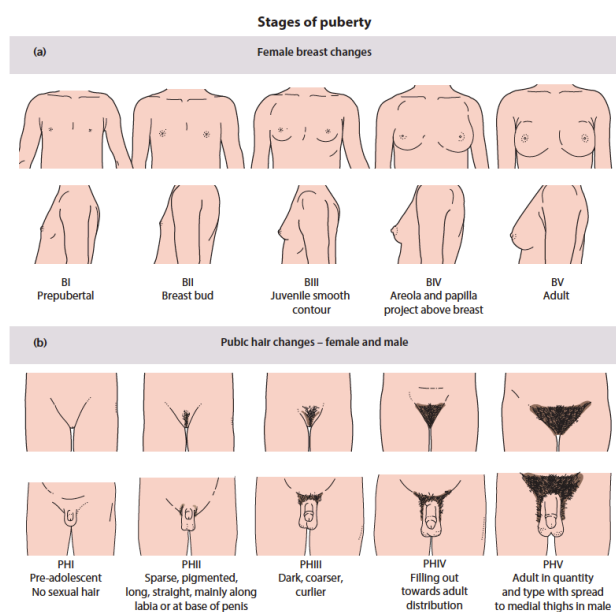
| Term       | Signs  | Result of                                |
|------------|--|--|
| Gonadarche | Testicular enlargement                                       | Testicular activation by FSH/ LH         |
| Adrenarche | Body odor, skin oiliness, Pubic hair, Axillary hair and acne | Adrenal gland 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         |

When baby is in uterus, levels of LH & FSH are higher than in puberty and they go down dramatically prior to birth, when the child is born, they go up again (mini puberty, almost resemble the levels in puberty stage), it is normal, because the axis is going to be turned off 3 months later until the time of puberty. God knows what turns it on and off.

## Pubertal Assessment:

### 1- Tanner staging

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



- In girls peak growth happens prior to menarche (stage 4), then decelerates.

### 2- Orchidometer

- Testicular volume in boys of 4 ml indicates the onset of puberty
- 2.5 cm, more than 2.5 cm means puberty had started
- Testicular volume increases (1<sup>st</sup>) then genitalia size and pubic hair, then growth accelerates, peak happens in stage 4 and spermarche happens in stage 5



## Delayed Puberty:

In boys: Absence of pubertal signs by age 14.

In girls: Absence of pubertal signs by age 13.

## Approach:

| Constitutional delay of growth and puberty  | Hypogonadotropic hypogonadism  | Hypergonadotropic Hypogonadism  |
|---|--|---|
| <ul style="list-style-type: none"><li>- In an otherwise healthy child.</li><li>- Family Hx of delayed puberty in a parent</li><li>- Short stature, delayed bone age.</li><li>- Spontaneous recovery at Bone age 12-13</li><li>- FSH/LH and sex steroids in prepubertal range</li><li>- A retrospective diagnosis.</li></ul> | <ul style="list-style-type: none"><li>- Difficult to differentiate from CDGP</li><li>- If congenital, could be associated with, cryptorchidism and/ or micropenis in boys.</li><li>- Due to Pituitary/ Hypothalamic pathologies</li><li>- No spontaneous recovery</li><li>- <b>FSH/LH and sex steroids in prepubertal range</b></li></ul> <p><b>DDx:</b></p> <ul style="list-style-type: none"><li>- Pituitary hypoplasia (associated with other pituitary deficiencies, septo-optic dysplasia, CHARGE)</li><li>- Isolated Gonadotropin Deficiency [<b>Kallman syndrome</b>] (associated with anosmia/hyposmia).</li><li>- Secondary (Trauma, Tumor, Radiation, Autoimmune, under nutrition anorexia, excessive exercising, hypothyroidism, hyperprolactinemia, cushing's)</li></ul> | <ul style="list-style-type: none"><li>- Difficult to differentiate from Hypogonadotropic hypogonadism in prepubertal age range.</li><li>- If congenital, could be associated with Ambiguous genitalia, cryptorchidism and/or micropenis in boys.</li><li>- Due to a gonadal pathology</li><li>- <b>FSH/LH are extremely elevated in pubertal age range.</b></li></ul> <p><b>DDx:</b></p> <ul style="list-style-type: none"><li>- Gonadal failure (congenital dysgenesis, Turner Syndrome, Klinefelter syndrome)</li><li>- Secondary:</li><li>- Trauma, Tumor, infection (mumps), radiation, Autoimmune, galactosemia.</li></ul> |

## 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 (US to abdominal pelvis)

LH FSH level 35 and estradiol is 18, where is the problem? Very low estradiol, very high FSH LH =

**Hypergonadotropic Hypogonadism (primary gonadal failure)**



### Precocious Puberty:

- Appearance of pubertal signs before age 8 in girls.
- Appearance of pubertal signs before age 9 in boys.

### Causes:

Central (hypothalamic-pituitary axis) and peripheral (gonadal)

| Hypothalamic-pituitary axis |                          | Gonadal                       |
|-----------------------------|--------------------------|-------------------------------|
| - Pituitary tumor           | - Infection              | - Ovarian cyst                |
| - Infiltrative disease      | - Post trauma            | - Adrenal hyperplasia/ cancer |
| - Idiopathic                | - Post cranial radiation | - Gonadal tumor               |
| - Genetic / inherited       |                          | - Exogenous steroids          |

### McCune- Albright Syndrome

Caused by auto activation of the gonadotropin receptor

Gonadotropin independent precocious puberty (Suppressed FSH/LH)

CALMs respect midline and have rough borders

Associated with fibrous dysplasia  
Café-au-lait macules (CALMs) & Cyst in the ovary

Caused by somatic GNAS mutations

### Red flags for pathological causes:

- Abnormal sequence of puberty
- Rapid progression (Tanner 1 this month then tanner 4 the next month)
- Virilization in females (testosterone involved, most likely tumor there) feminization in boys (estrogen, most likely tumor)
- Neurological symptoms

### Premature thelarche:

- Between 6months to two years
- Only breast growth (isolated)
- No neurological symptoms
- Self-limiting, no treatment

### 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)

**Treatment: depends on cause**

**Tumor? Take it out**

**Idiopathic? Suppress puberty by GNRH agonist, because puberty happens when GNRH is pulsatile.  
So we give Lepron injections every 1-3 months**