

Pediatrics TeamWork ^K
437

Growth & Puberty

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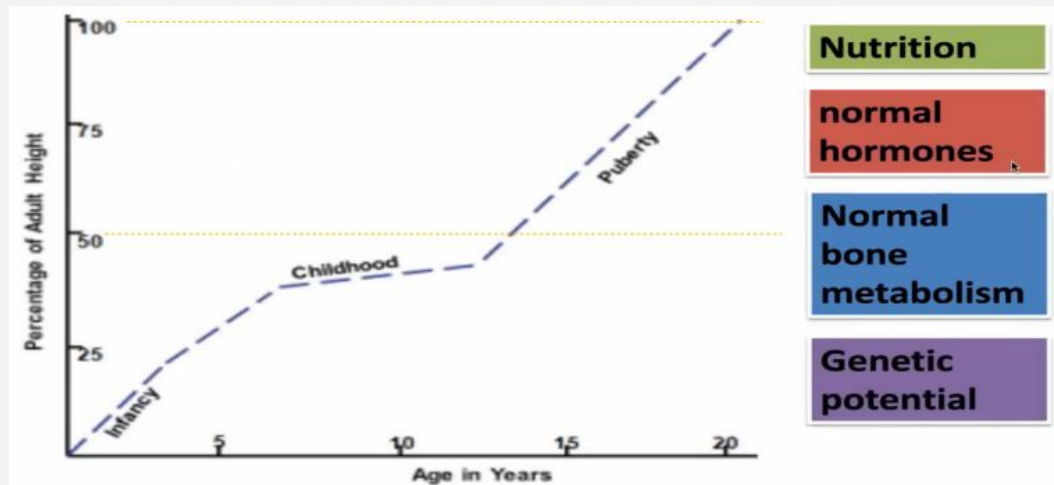
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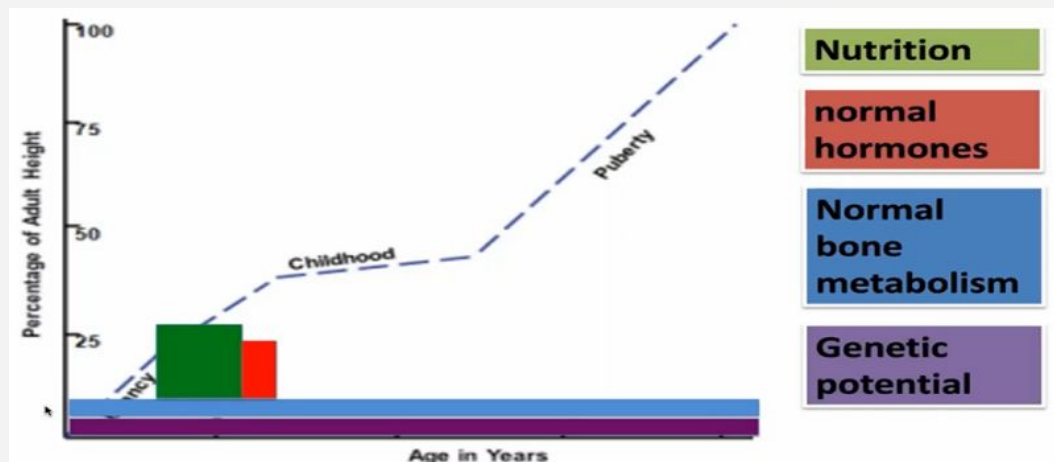
Puberty

The puberty topic only includes book!!

Normal Growth

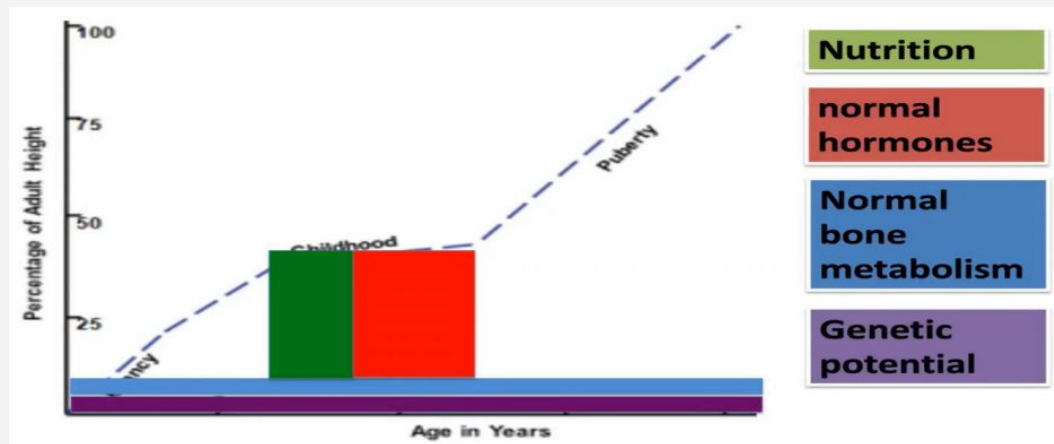


- When person is born, He/she grows in terms of height gradually till they reach childhood when the growth somehow plateaus and then they go through growth spurt during puberty. So, the majority of the attained adult height is attained during puberty.
- If you drew a line, you would find almost 50% of adult height is attained during puberty.
- Almost 10% of adult height is attained during childhood.
- And the rest is attained during early infancy.



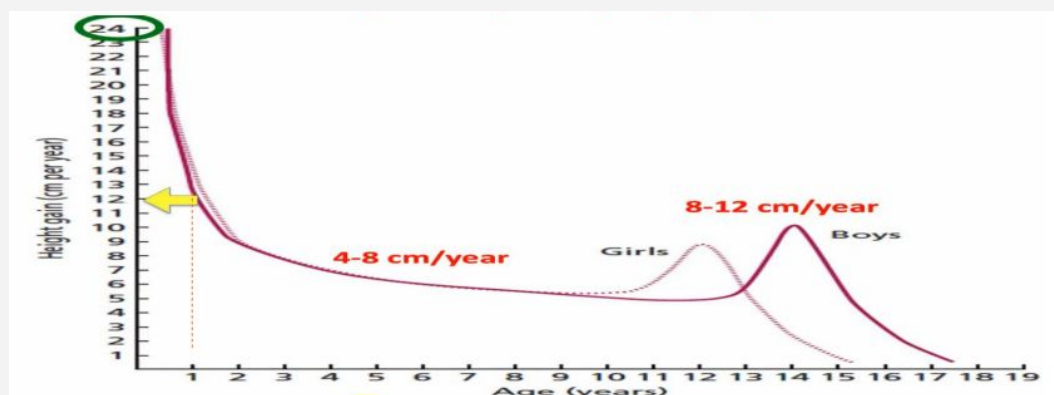
- What are the factors that contribute to growth?
 - Nutrition
 - Normal hormones (including Growth hormone)
 - Normal bone metabolism
 - Family history (genetic potentials)
- Which factor out of these 4 is the greatest contributor to growth during early infancy? **Nutrition.** Genetics is the second factor. Genetics and normal bone metabolism play major role during the whole life, but nutrition take the main bulk in early infancy, and normal hormones plays a role but not major role like nutrition in the early 2 years of life.

Normal Growth



- Then, both nutrition and normal hormones play almost an equal role during childhood and puberty. This is important to understand because we receive lots of questions about children who are born short, children who are born short are usually not short because of growth hormone deficiency. growth hormone deficiency play a major role on height after the first 2 years of life. Rarely it leads to severe short stature in early infantile age.

This plotting translates growth velocity meaning how many centimeters a child grows in a year as per age groups.



- If plot an imaginary line here crossing the first year of life you will notice that child grows almost 12 cm/year by the end of the first year.
- But early on they grow 24 cm. So, the growth velocity starts as being so high 24cm/year and then starts quickly dropping to 12 cm/year and then it reaches a plateau of 4-8 cm/year during the childhood period.
- Childhood period is the period when children attain 10% of their final adult height almost to 15%.
- The normal growth velocity is 4-8 cm/year. (This is very important information to remember).
- They also go through a peak that represents puberty. During the puberty, a children go through what we called growth spurt which equals to 8-12 cm/year.
- Girls go through growth spurt around 12 years, while boys go through it around 14 years. That is because girls go through puberty earlier than boys by almost 2 years. Therefore, girls enter growth spurt and finish growing before boys by 2 years.

Growth Assessment

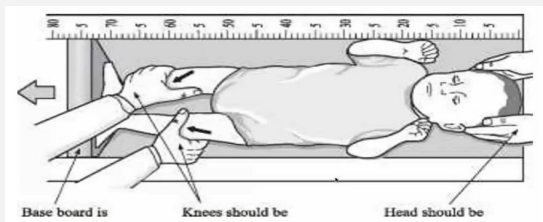


How can we measure height ?

- Infantometer for children who are < 2 years of age
- Stadiometer for children who are > 2 years

Infantometer

- This measures the child's length; we call it length because children are measured while they are lying down. The word Height is used when children are measured while standing.
- It requires 2 people to help in assessing child length. The first person holds the head against the headboard which is at the zero level, and make sure that the child does not move their head. The second person holds the legs and straighten the knees.
- You cannot just stretch one leg alone when you do so the hip will be tilted, and the child would be measured falsely taller. After stretching both legs and straightening the knees, push the baseboard against the feet. And take the measurement in centimeters.
- Usually, children don't like this position and they will scream cry and kick. Repeat it 3 times and then take the average.



Stadiometer

- Another device is stadiometer that measures the height while child is standing. After age of 2 years.
- It can be done by one person but sometimes it is better done by two.
- You have to make sure you align all three points against the wall the heel the hip the shoulder and the head all against The wall and the child must be barefoot. The child should not bend their knees or be standing on tiptoes.
- The person taking the measurement should hold the head stabilizing the chin and child should be looking straight forward without looking up or down. Then, take the head bar slide till you reach child's head and then you read the measurement on the side of the wall.
- You take three reading and then you take the average of these readings.



Target Height

Target height of the child — Mid parental height

Boys:

$$\frac{[\text{Father's height (cm)} + \text{Mother's height (cm)}] + 13}{2} \quad \pm 8 \text{ cm}$$

Girls:

$$\frac{[\text{Father's height (cm)} + \text{Mother's height (cm)}] - 13}{2} \quad \pm 8 \text{ cm}$$

- Target height or mid parental height is estimating the final adult height for the child knowing the mother's height and father's height.
- The difference between boy and girls' formula is that we add 13 in boys' formula while we subtract 13 in girls'.
- The outcome is the average height. For every mean there is standard deviation, If we want to know the normal range for that height we add and subtract 8 from the result. Add/subtract 13 before you divide by 2.

Growth Curves

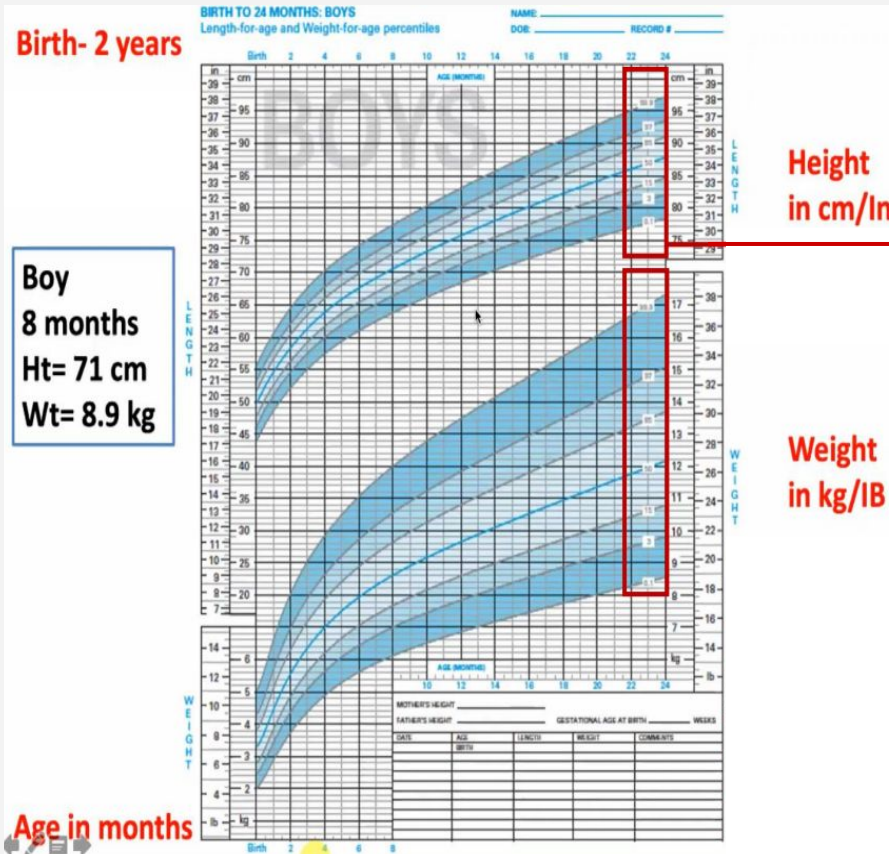


Types of Growth Curves

- WHO
- CDC
- Saudi Growth Charts

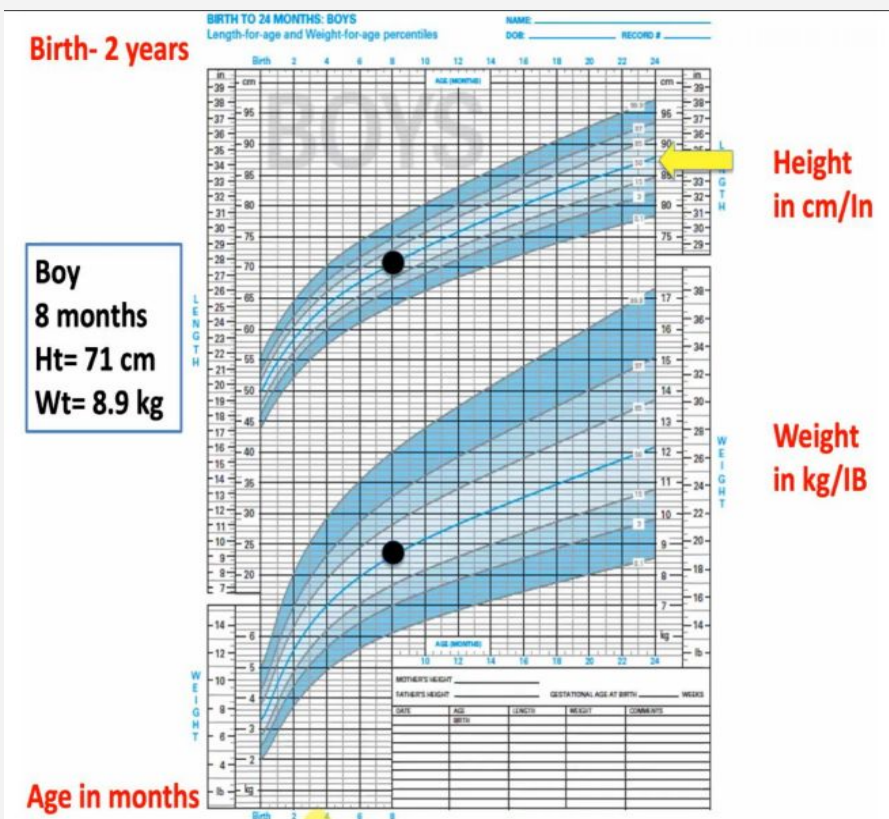
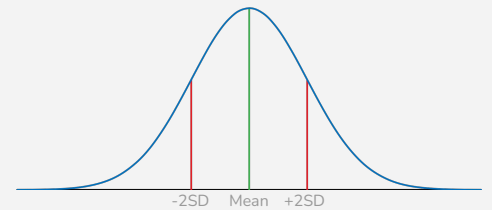
Boys:

This is WHO growth curve for boys from birth – 2 years.



These are the percentile, so we can compare the child to children in same age and gender.

- If we take any measurement, it should follow the normal distribution of the “Bell curve”.
- Where the 0 represents the mean, plus 2 standard deviation (+2SD) and minus 2 standard deviation (- 2SD).
- The growth curve idea was adopted from this. Where the mean represents 50th percentile + 2 SD represents 99th percentile -2 SD represents 3rd percentile.



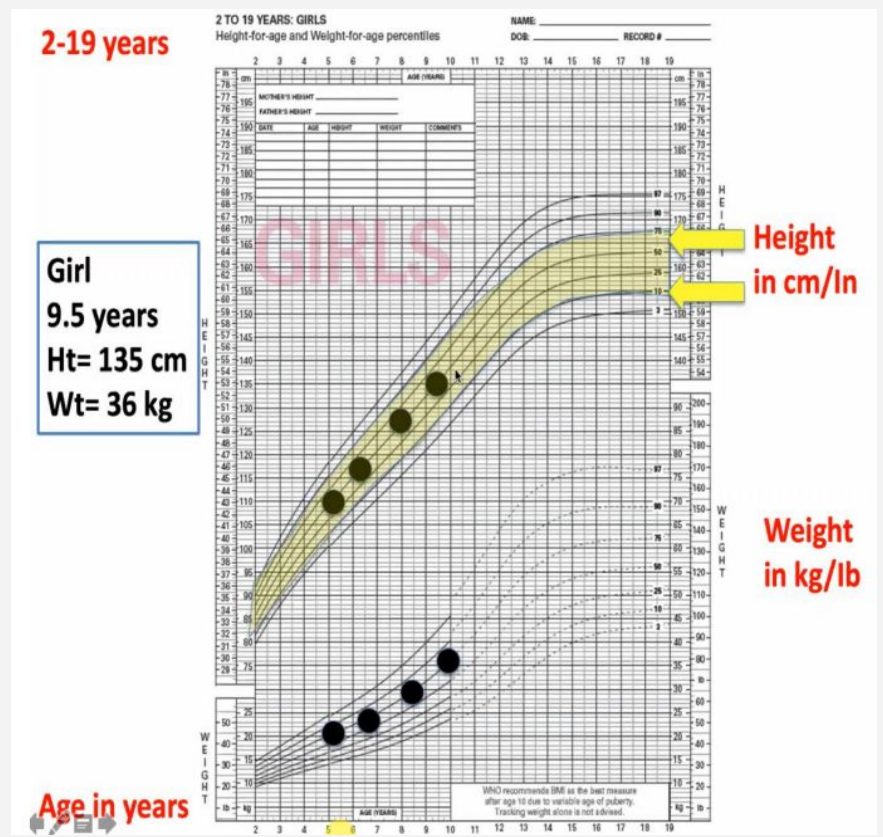
How to plot height / weight data of a baby who is 8 months old his height is 71cm and weight is 8.9?

Draw imaginary line starting from the age going down till you reach the height of 71 cm, the intersection between age and height is where you can plot this child.

The same for weight draw imaginary line from age going up until it meets the child’s weight.

Girls:

This is WHO growth curve for girls 2 – 19 years.



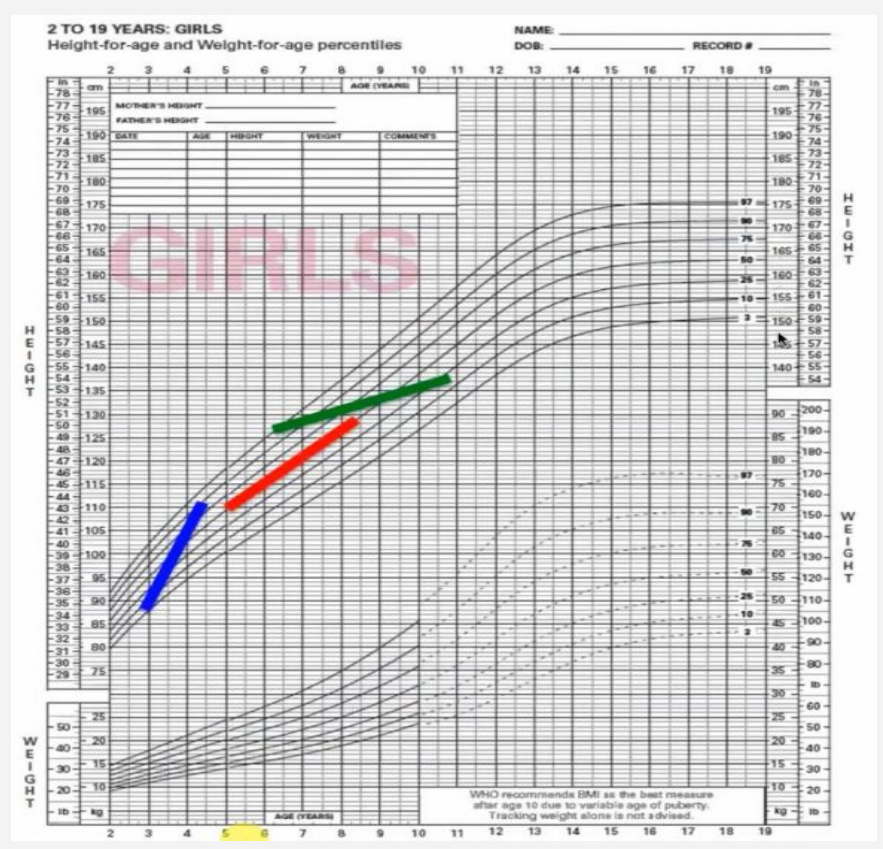
- Plotting height data of 9.5-year-old girl the same principle applied/
- Other dots means previous growth measurement.
- Why is it important to look at previous growth data? Because it tells you about the pattern of growth.
- What does the yellow arrows represent? The standard deviation of mid parental height calculated using the formula.
- That means the normal mid parental height of this child is between the 10th percentile and 55th percentile.
- We can also plot the average after calculating the mid parental height instead of putting 2 arrows of the normal range (putting the result of the equation without adding/subtracting 8).

• All these values lie within the range of mid parental height. That means the child is following their genetic potential.

We learned three things:

1. The value needs to be normal within normal population we have the comparison to other children in the same age and gender.
2. Child growth pattern follows the same tracking of the same line that he started since birth and growth velocity is normal.
3. These values are lying within mid parental height, so the child is following the same distant genetic potentials.

- If these 3 information are normal so most likely the child growth is normal.
- The average weight gain for children after 2 years of life is 1-2 Kg/ year. **Why does weight curve plotting disappear?** Because it is not important to follow the weight, we should follow the BMI instead, so we don't miss children with obesity.

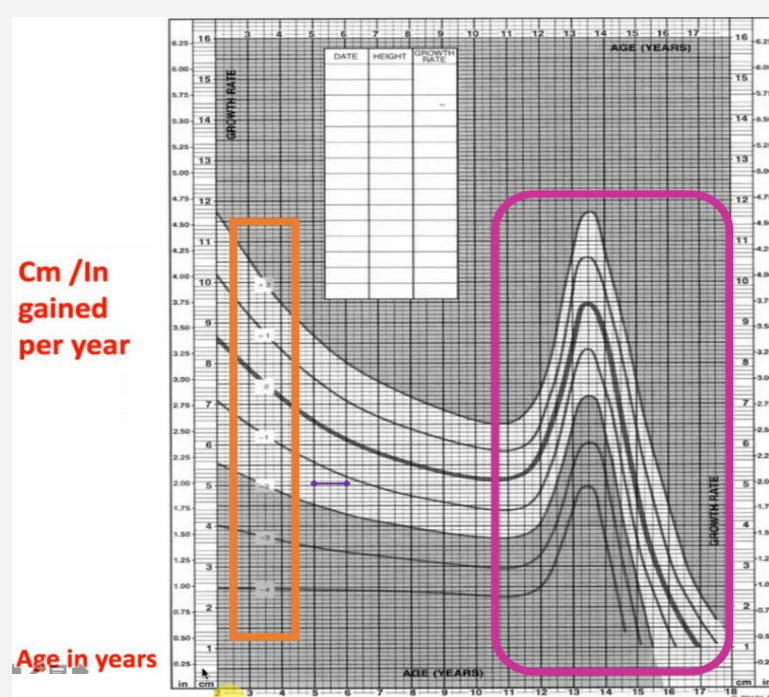


These are growth patterns of three children:

- The first one (in **BLUE**) started to grow in height in 3rd percentile and through years progressively gained height till she reach 90th percentile.
- The second child (in **RED**) started at 50th and continued at 50th.
- The third child (in **GREEN**) started at the 97th percentile and then reached 25th percentile.

Which one is normal?

- The one in **RED** because the child started at 50th percentile and continued at 50th percentile. Even if she started at 10th percentile and continued at 10th percentile, she is considered normal as long as she continued at the same pattern.
- The blue line means the child was short and suddenly she became taller (Abnormal).
- The green line means the child was tall and then she progressively became shorter (Abnormal).

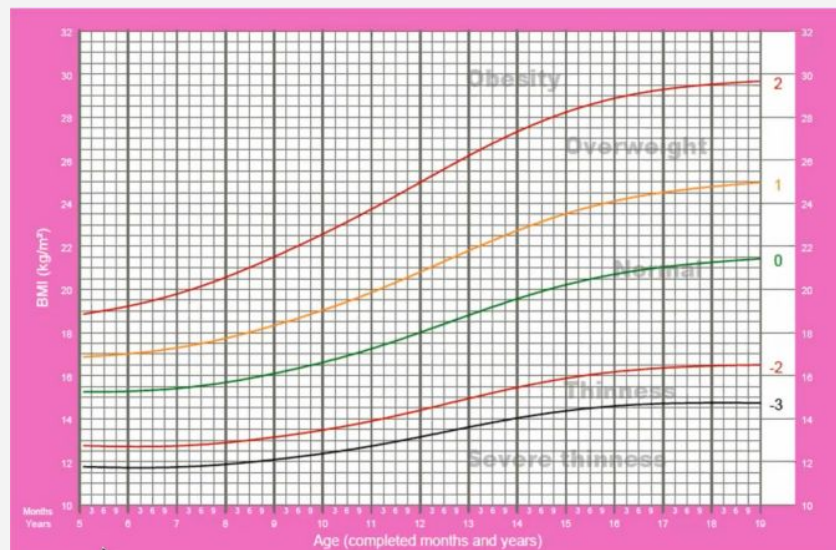


- This is growth velocity curve where x-axis represents ages in years and Y-axis represents the cm gained per year.
- This is marked by Z score as you can see -4, -3, -2, -1, 0, +1, +2.
- Some of growth curves are marked similarly using -3,-2,- 1,0,+1,+2 not translated in percentiles.
- **If you want to translate it to percentiles:**
 - 2 = 3rd percentile
 - 1 = 25th percentile
 - 0 = 50th percentile
 - +1 = 75th percentile
 - +2 = 95th percentile

• **To plot a child in growth velocity curve:**

If we have child who grew 5cm between 5 & 6 years of age, we drew a line from 5-6 years at the level of 5cm.

- There is peak and decline that represents the puberty (growth spurt), and then you complete your growth while growth velocity declines. once you reach the final adult height you don't grow anymore therefore your growth velocity becomes zero.



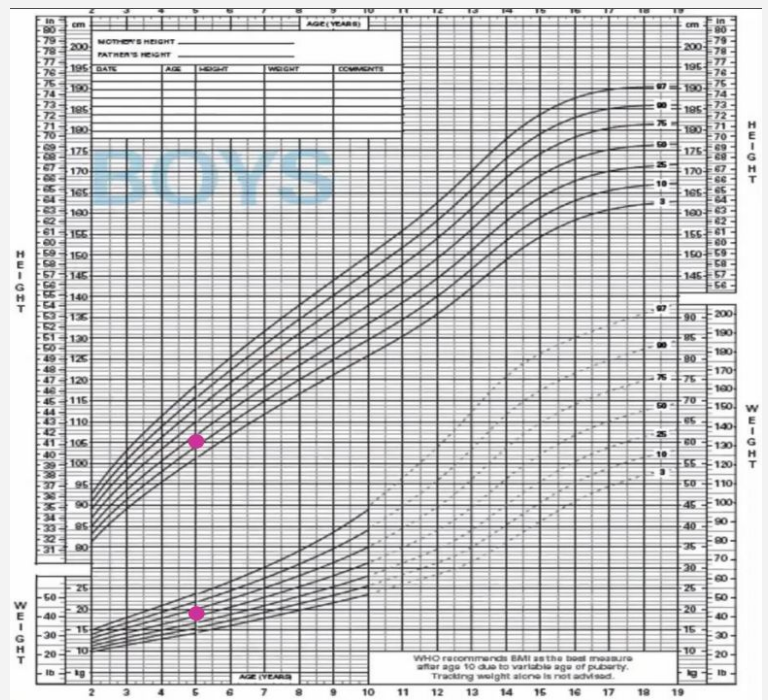
- This the BMI growth curve age in the x-axis and BMI in y-axis.
- Numbers are in Z score.
- Zero is the zone for normal (-2 to +1).
- **BMI curve give a little information about nutritional status:**
 - Those who are less than -2 standard deviation, are thin.
 - Those who are less than -3 are severely thin or malnourished.
 - Those who are between +1 and +2 standard deviation are overweight.
 - Those who are more than +2 are obese.
- Some BMI curves shows percentile where +1 standard deviation equals to 85th percentile.
- It is important in counselling children with obesity. We have to catch them before they reach the obesity zone. And to work on children who are severely thin.

Plot the following



1.

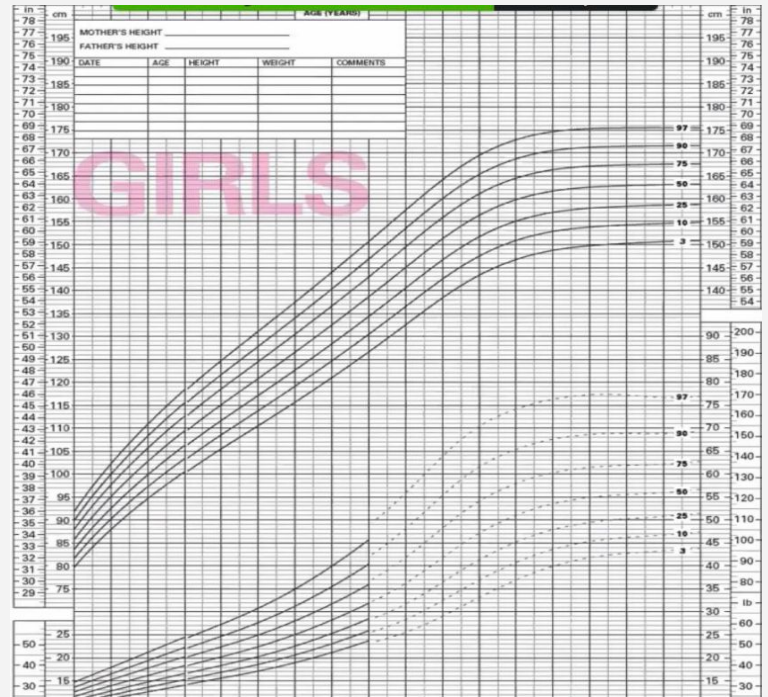
- 5 year old boy
- Height: 105 cm
- Weight: 18 Kg
- BMI
- Father height: 170 cm
- Mother height: 160 cm
- Mid parental height = $((170+160) + 13 / 2) \pm 8 = 171.5 \pm 8$



2.

- 5 year old girl
- Father height: 170 cm
- Mother height: 160 cm

Age	5	6	7	8
Ht	105	106	107	108
Wt	18	18	19	20



Is she short?

Short Stature

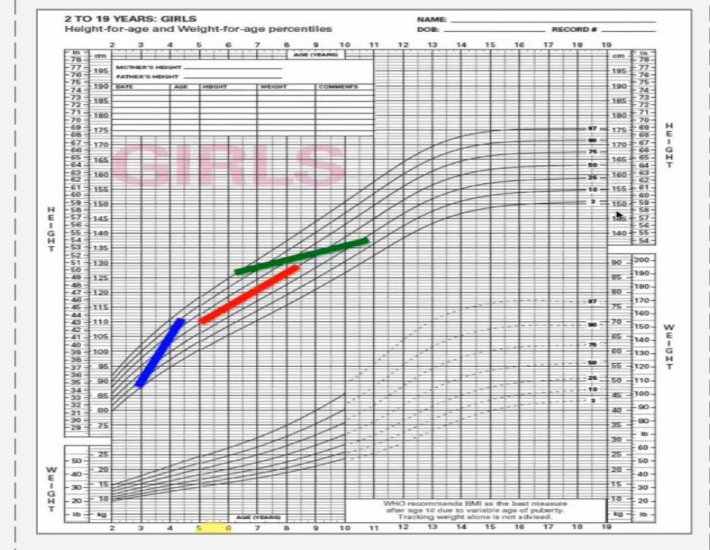


- Height < 2 standard deviations below the mean for the population
- Height < 2nd or 3rd centile
- Height velocity < 25th ile
- Crossing percentile

What do we mean by crossing percentile? In the growth curve the child who was taller, then she became short (the green line) and the child who was short and then she became taller (the blue line) they crossed lines of percentile across time. Once a child crosses percentile line that means the child has abnormal growth.

Causes

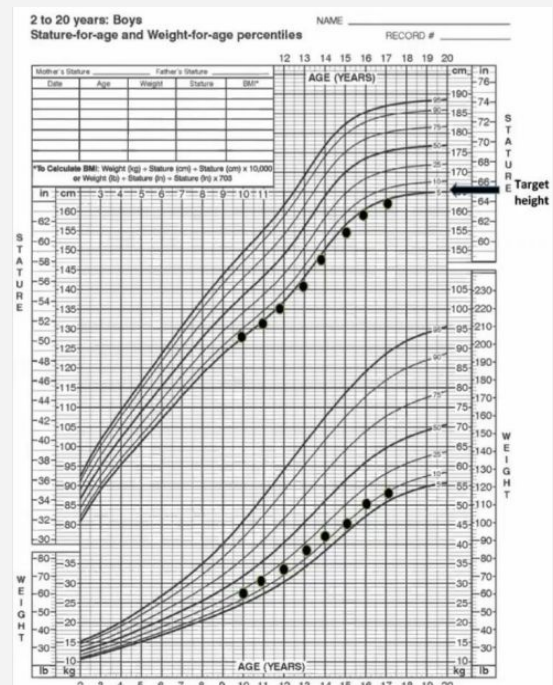
- Normal variants:
 - Constitutional
 - Familial (genetic)
- IUGR
- Chronic illness
- Malnutrition
- Endocrine:
 - Growth hormone deficiency
 - Hypothyroidism
 - Cushing Disease
- Syndromes



Familial Short Stature

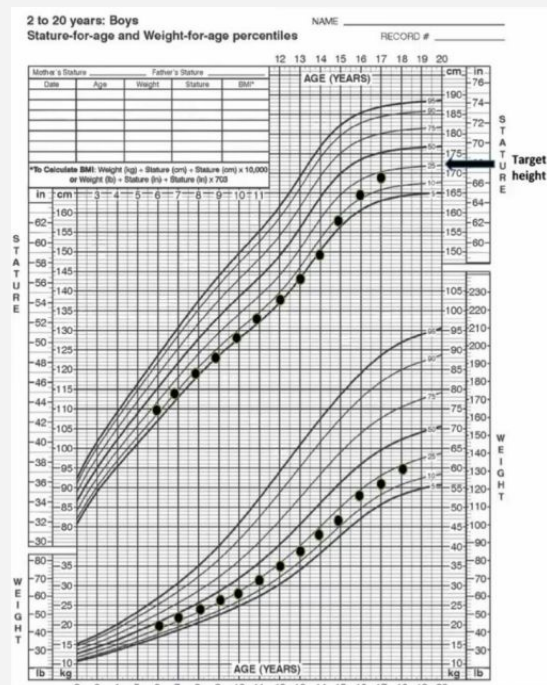
- Short family (MPH)
- No chronic illness
- Normal growth velocity
- Normal physical exam
- No dysmorphic features
- Normal puberty
- Normal bone age

Here the child growth pattern follows the 5th percentile and falls in the normal range of mid parental height and did not cross percentile and this is normal familial short stature. Which is normal variant of height, if the parents are short then the child is destined to be short.



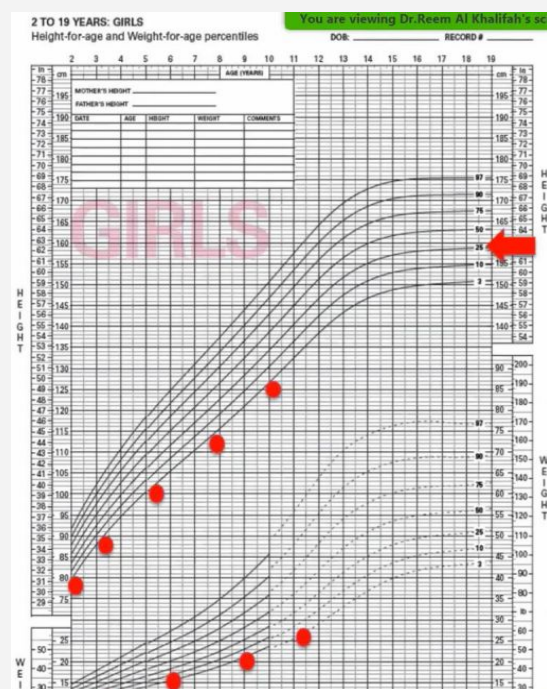
Constitutional Short Stature

- Family history of delayed puberty
- Appropriate height for MPH
- Normal growth velocity
- Delayed puberty
- Delayed bone age
- This is a bit difficult to get because most of the clues you get through the history and small clues in the growth chart.
- They usually have a family member who had delayed puberty and was the short and once they go through puberty, they stretched out and they became the tallest in the family.
- The height although it lies at the 5th percentile it is still within the normal mid parental height.
- If you take an x-ray of the hand, it will show delayed bone age.
- No treatment needed only reassurance and follow up, because they are going to have delayed puberty just like their family and they will grow and be the tallest in their family.



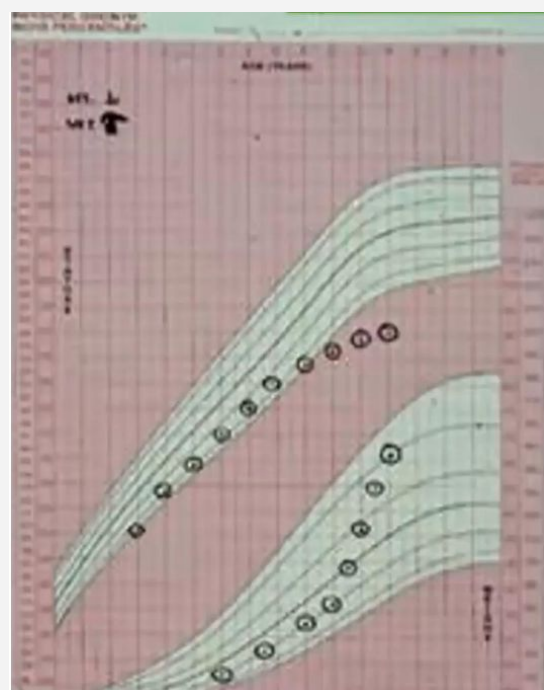
Intrauterine Growth Restriction

- Short since birth
- Low birth weight
- Never catch up !
- They are born with low birth weight and if they are well nourished, they will have catch up growth in the first 2 years. To catch up for whatever growth was missing when they were in Utero. If this does not happen, usually they will continue to be short for the rest of their life.



Endocrinopathy

- Deceleration in a well-nourished or obese child:
 - GHD
 - Hypothyroidism
 - Glucocorticoid excess
- The child becomes shorter with time although he is well nourished or obese.

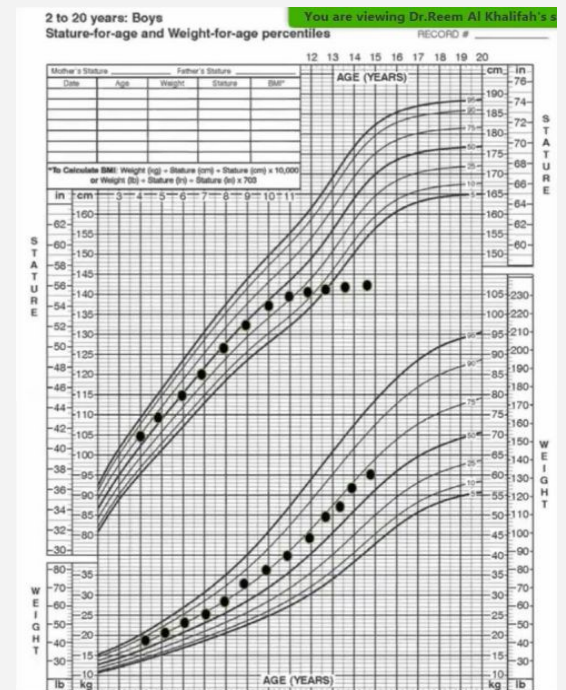


Hypothyroidism

- Stopped growth
- Hockey stick pattern
- Increased weight

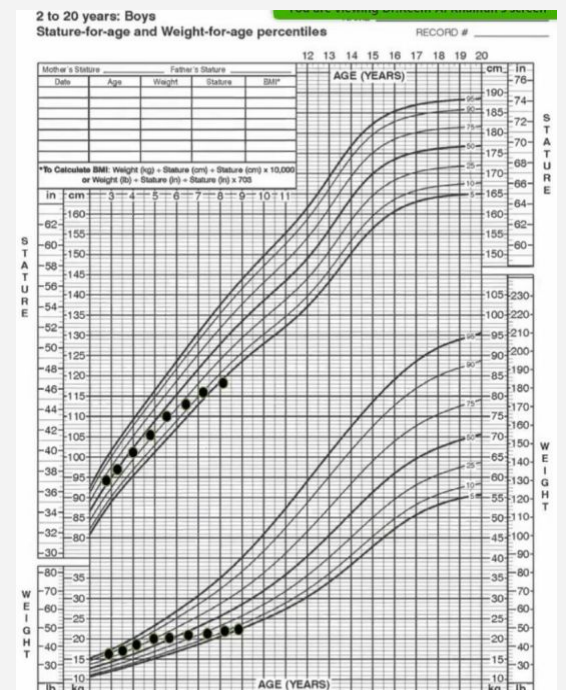


The child becomes shorter over time although he is well nourished. And that is endocrinopathy pattern, most likely hypothyroidism the child stops growing. Hypothyroidism stop child growth more than GHD.



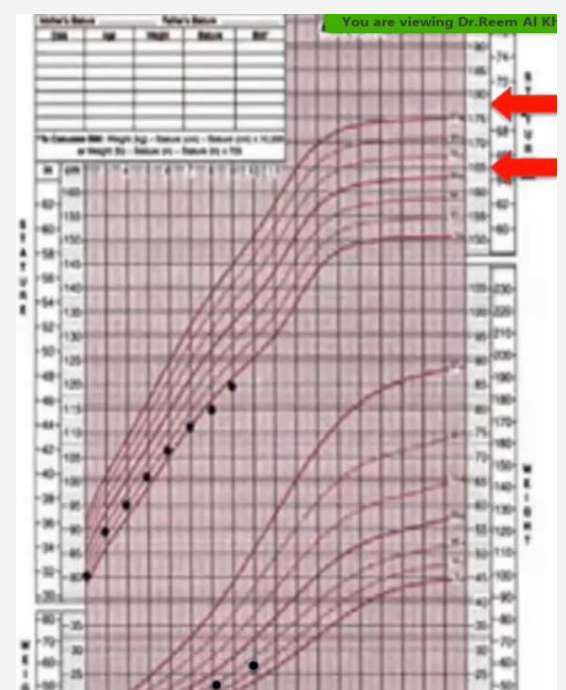
Chronic Illness Undernutrition

- Weight affected more than height
- Celiac disease
- Malabsorption
- Cystic fibrosis
- Renal failure
- Crohn's disease
- Child crosses the percentiles in both height and weight, but the weight was first. he was malnourished and that what affects their height.
- So, in this pattern the weight is more affected than height. The weight is first to be affected and the height after that.
- The differential diagnosis could include all GI diseases.



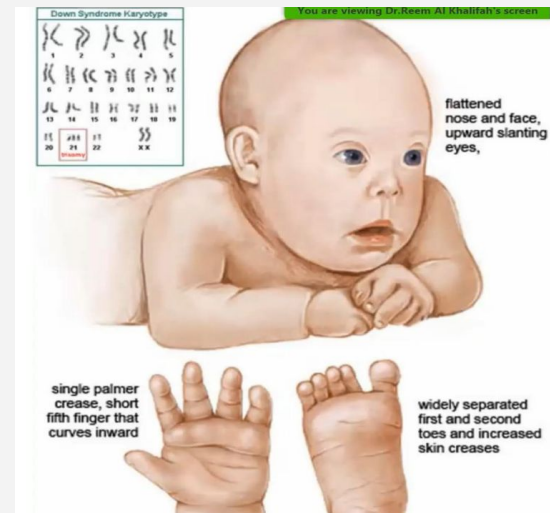
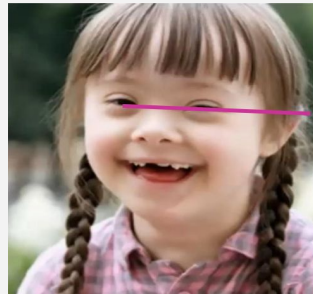
Syndromic Causes

- Not appropriate for MPH
- Dysmorphic features
- Child crosses the percentiles in height. He is at the 3rd percentile which is very far from MPH. This pattern is syndromic.



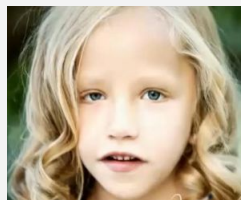
Down Syndrome

- Trisomy 21.
- One of the feature is low-set ear.
- If we draw a line crossing the eyes, we will find that most parts of the ears are below that line.
- Doctor did not skip the features.



Turner Syndrome

- Female X 0 45
- Dysmorphic features are:
 - Broad chest
 - Short stature
 - Webbed neck
 - Edematous hand and feet that disappears with time
 - Increased nuchal fold
- They could look normal just like the girl in the picture.



Russell-Silver

- Characterized by:
 - Short stature petite
 - History of hypoglycemia at birth
 - Café au lait spots
 - Low-set ears
 - Triangular face
 - Sclerodactyly



Achondroplasia

- Large head
- Short arms and short legs (their arms barely touch the pelvis)
- Trident hands
- Lordosis in the back
- Scoliosis
- Small chest



Investigations

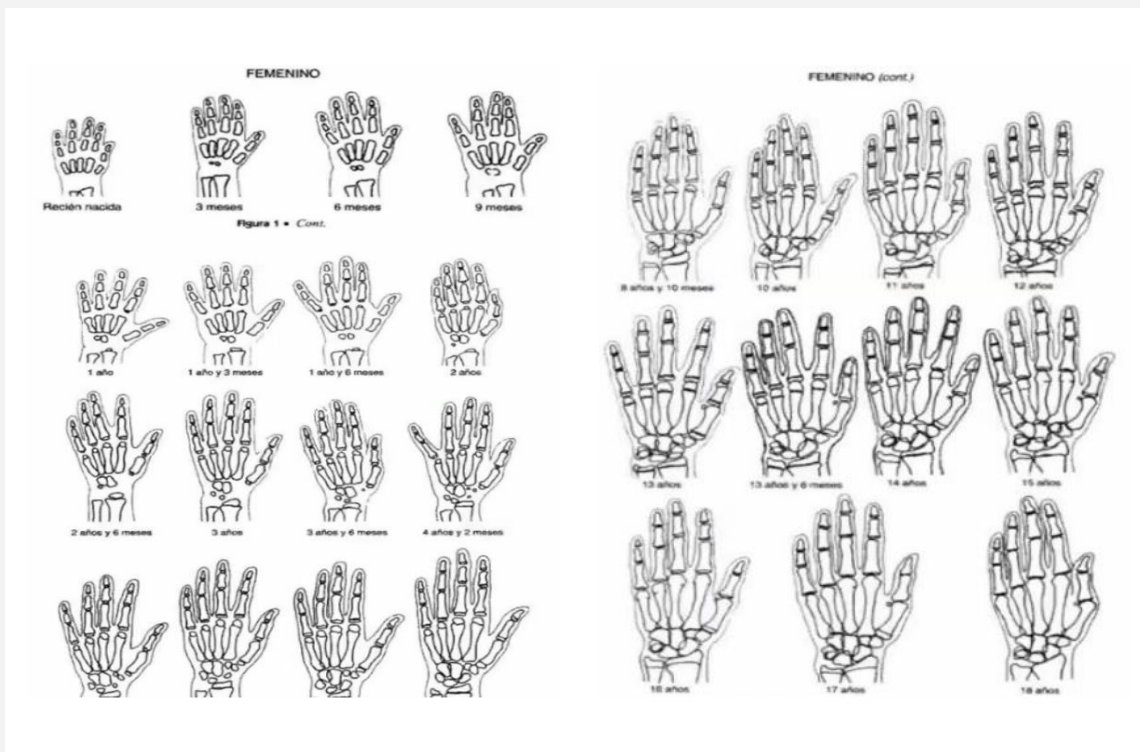


- **1st line testing:** ordered by primary physician or general pediatrician
 - CBC
 - BUN, Creatinine, Electrolytes (Renal profile)
 - TTG to rule out coeliac
 - Karyotype to rule out turner and trisomy 21
 - TSH, FT4
 - Bone age
- **2nd line testing:**

If basic investigations are done, then refer to endocrine who will order the 2nd line tests

 - GH testing
 - MRI pituitary

Greulich & Pyle Atlas



- The first investigation we should order is Bone age.
- We have an atlas for bone age that looks at bone maturity across all age groups, which is taken through an x-ray of the left hand and wrist. You look at maturation of all growth plates.
- This is hand of female who is 1 year old and female who is 11 years old.
- You can observe the difference female 11 y: all carpal bones achieved major part of their maturation compared to 1 year old. And even all growth plates here are more mature while in 1yr old there is no growth plates that start maturation.



Treatment



Indications for GH Therapy:

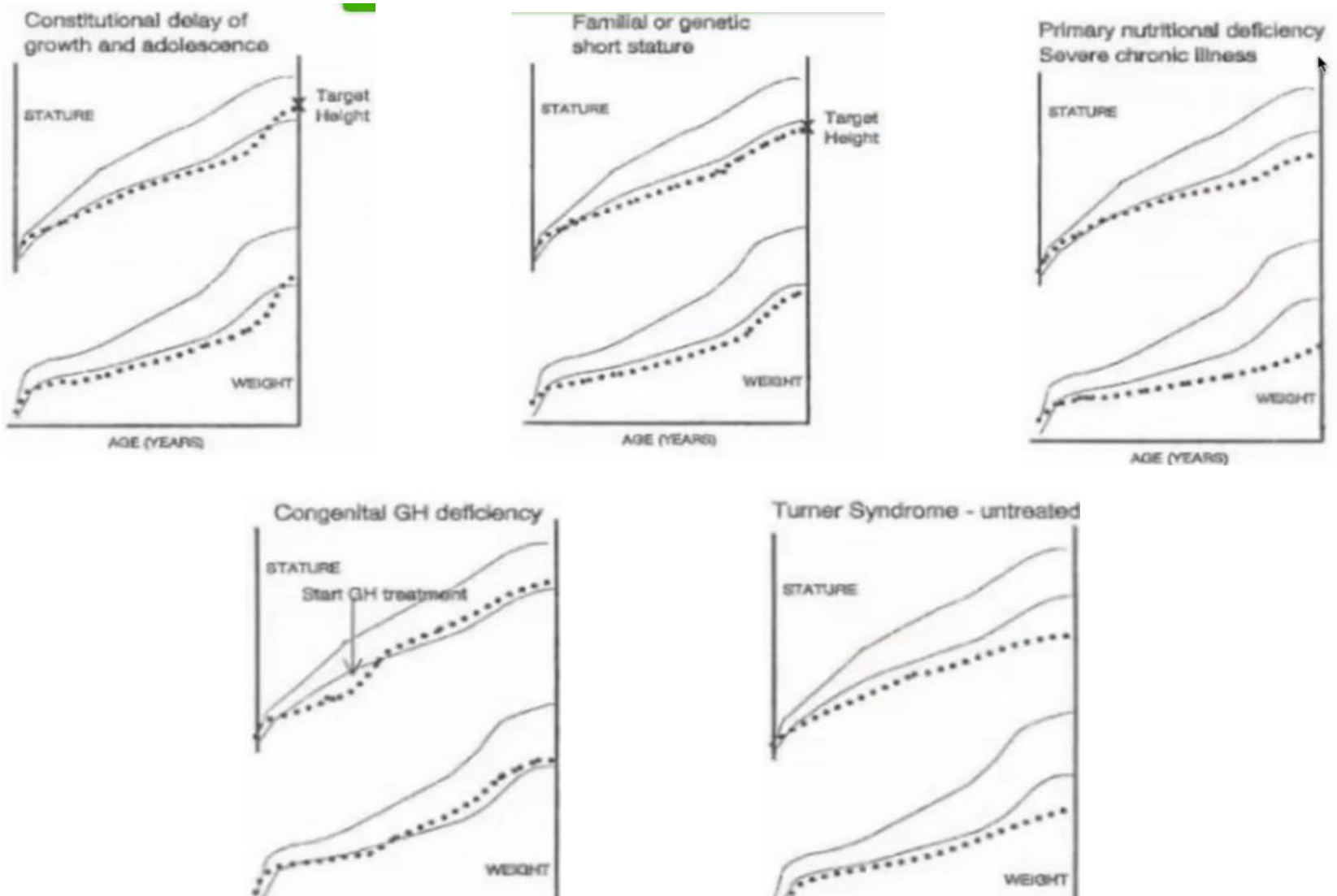
- GH deficiency
- Turner
- Prader-willi syndrome
- SGA/IUGR who didn't catch up
- Renal insufficiency
- HIV

We don't treat familial short stature and constitutional short stature they are normal variants.

Q. You are evaluating a **6 yo girl** for short stature. Her growth chart reveals a **birth length at 60th percentile**, and a current **height at 5th percentile**. Her growth velocity in the last 3 yrs has been **2 cm/yr**. Her **weight is at the 90th percentile**. On PE: her intelligence appears normal. There are **no** midline defects or dysmorphic features. Her **bone age is 4 yrs**. **What is the most likely dx?**

1. Crohn disease
2. GH deficiency
3. IUGR
4. Turner

Summary of all growth curves you have to remember for life.

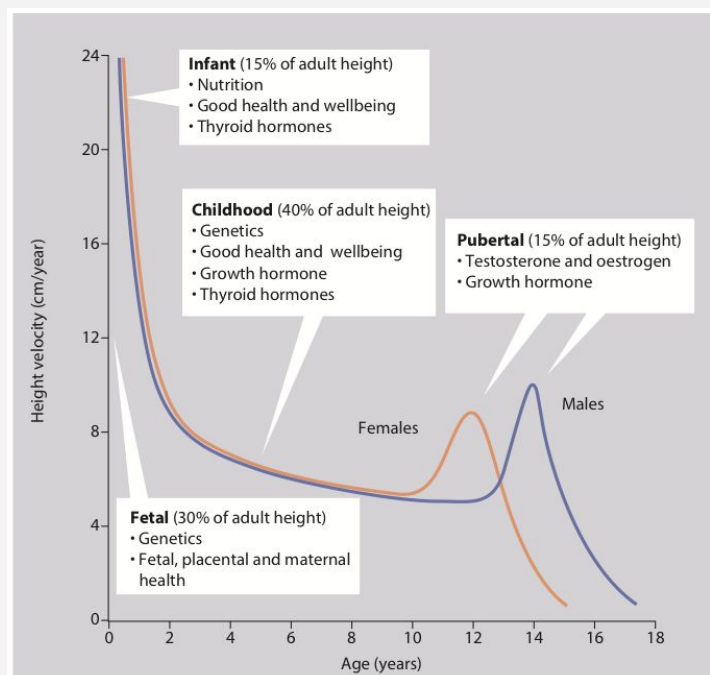


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Growth

- Growth phases (the graph shows the determinants of each phase):



- **Fetal phase** is the fastest period of growth. It is stimulated by raised maternal glucose resulting in **raised glucose and increased IGF-1 in the fetus**.
- Growth in fetal phase is restricted by pre-existing or pregnancy related maternal disease, maternal drugs, smoking or starvation or uteroplacental insufficiency and congenital infection and other disorders of the fetus
- **Infantile phase** is characterized by rapid but decelerating growth rate. An inadequate rate of weight gain during this period is called 'faltering growth (FTT)'
- **Childhood phase** is a steady and prolonged period. Thyroid hormone, vitamin D and steroids also affect cartilage cell division and bone formation
- **Pubertal growth spurt:** height acceleration. Sex steroids cause fusion of the epiphyseal growth plates and cessation of growth
- You should consider Turner syndrome **in all short girls**
- **Abnormalities of SHOX (short stature homeobox)** located in chromosome X can cause short stature in Turner syndrome (absence of one gene) while additional copies cause tall stature like in Klinefelter syndrome.
- **Long term illness that can cause short stature:**

Celiac disease (slow growth can be the only feature)	IBD (especially Crohn's disease)
Chronic kidney disease	Cystic fibrosis (malabsorption, recurrent infections, increased work of breathing and reduced appetite)
Congenital heart disease (increase work of breathing)	Idiopathic juvenile arthritis (chronic inflammation)

- Emotional deprivation may cause short stature and underweight with delayed puberty due to affect on hypothalamic-pituitary function (low GH)

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Growth

- Investigations for short stature:

Standard investigations for all	Notes
Full blood count	Anaemia may indicate nutritional deficiency, coeliac or Crohn disease
Creatinine, electrolytes and liver function tests	Look for evidence of renal or hepatic dysfunction as there may be few symptoms present
Thyroid stimulating hormone	Acquired hypothyroidism is the most common endocrine cause of short stature and may have few symptoms
Anti-tissue transglutaminase (anti-TTGa) immunoglobulin A antibodies	Coeliac disease is common and symptoms are variable, so this is important to exclude
Karyotype or microarray	Check in all girls, looking for Turner syndrome (45,XO) as dysmorphic features may be subtle
IGF-1	This is a useful screening test for growth hormone deficiency
X-ray of the left hand and wrist for bone age to determine skeletal maturation (Fig. 12.10)	Mild delay in constitutional delay of growth and puberty. Marked delay for hypothyroidism or growth hormone deficiency
Specialist investigations	Notes
C-reactive protein (acute-phase reactant) and erythrocyte sedimentation rate	Check if symptoms suggestive of inflammatory conditions, for example Crohn disease
Calcium, phosphate, alkaline phosphatase, Vitamin D	Consider if renal dysfunction present and check for suspected bone disorders if bone deformity, such as bowing of the legs noted on examination
Limited skeletal survey	If evidence of disproportion, aiming to find skeletal dysplasia. Scoliosis may also cause short stature.
Growth hormone provocation tests (using insulin, glucagon, clonidine, or arginine in specialist centres)	Consider if growth rate is slow and IGF1 low to diagnose growth hormone deficiency
MRI brain scan	If child has headache or neurological signs to rule out intracranial tumour, e.g. craniopharyngioma
Immunoglobulins and functional antibodies	If child has recurrent infections, to rule out immunodeficiency

- Most tall stature inherited from tall parents
- Obesity causes tall stature in childhood but they will get their puberty earlier hence their final height doesn't increase
- In Marfan syndrome you need to screen for aortic root dilation
- **Causes of tall stature:**

Genetic	Familial – most common cause Klinefelter syndrome (47,XXY karyotype) Marfan syndrome Homocystinuria Beckwith Wiedeman syndrome Sotos syndrome – associated with large head, characteristic facial features, and learning difficulties
Nutritional	Antenatal – maternal diabetes mellitus Obesity – puberty is advanced, so final height centile is less than in childhood
Hormonal	Hyperthyroidism Excess sex steroids – precocious puberty Excess adrenal androgen steroids – congenital adrenal hyperplasia Excess growth hormone secretion

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Growth

- Most head growth occurs in the first 2 years of life and 80% of adult head size is achieved before the age of 5 years
- Sutures and fontanelle are open at birth. Posterior fontanelle normally closes by 8 weeks, and the anterior fontanelle by 12 months to 18 months
- **Rapid increase in head circumference >> exclude increased intracranial pressure (hydrocephalus) (do US or CT scan)**

Abnormal head shape

Box 12.2 Forms of craniosynostosis

Localized

- Sagittal suture – long narrow skull
- Coronal suture – asymmetrical skull
- Lambdoid suture – flattening of skull

Generalized

- Multiple sutures resulting in microcephaly and developmental delay
- Genetic syndromes, e.g. with syndactyly in Apert syndromes, with exophthalmos in Crouzon syndrome




Figure 12.13 Long flat head of a preterm infant. This can be avoided by lying preterm infants on a soft surface and regularly changing their head position.

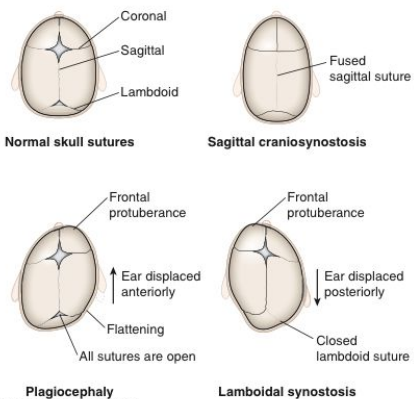


Figure 12.14 Differentiating craniosynostosis from plagioccephaly.

Figure 12.15 Crouzon syndrome showing the typical shallow orbits and exophthalmos. Craniofacial reconstructive surgery is required to prevent visual loss and cerebral damage from raised intracranial pressure and for cosmetic appearance.

- **Craniosynostosis:** The condition can be treated surgically in specialist centres for craniofacial reconstructive surgery if there is raised intracranial pressure, or for cosmetic reasons

Box 12.1 Causes of a large head

- Familial macrocephaly
- Raised intracranial pressure (in an infant):
 - chronic subdural haematoma
 - brain tumour
 - neurofibromatosis
- Cerebral gigantism (Sotos syndrome)
- Central nervous system storage disorders, e.g. mucopolysaccharidosis (Hurler syndrome)

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Puberty

- In girls normal puberty starts between the age of 8 and 13 years. In boys normal puberty starts between the age of 9 and 14 years.
- **Menarche** – occurs on average 2.5 years after the onset of puberty and signals that growth is coming to an end, with only around 5 cm height gain remaining
- In both sexes, there will be development of acne, axillary hair, body odour, and mood changes.
- The growth spurt in boys occurs later and is of greater magnitude than in girls, accounting for the greater final average height of men compared to women.

Summary

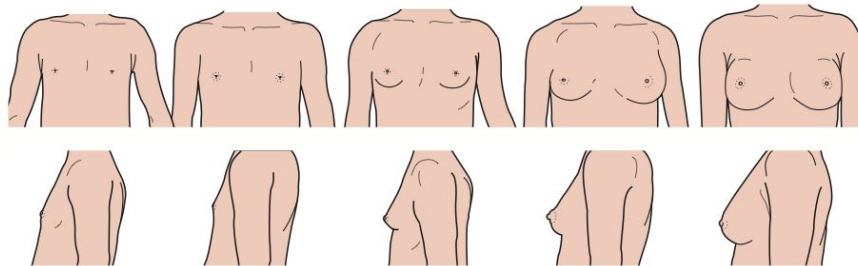
Puberty

- The first sign of female puberty is a palpable breast bud; the first sign of male puberty is testicular volume >4 ml.
- In females, height acceleration starts shortly after breast development; in males, it starts almost 18 months after the first signs of puberty.

Stages of puberty

(a)

Female breast changes



B1

Prepubertal

B2

Breast bud with elevation of breast and papilla plus enlargement of the areola. A key stage of female puberty as it signifies the onset of puberty

B3

Juvenile smooth contour

B4

Areola and papilla project above breast

B5

Adult with projection of papilla only as areola has recessed

(b)

Male genital stages



G1

Pre-pubertal

G2

Enlargement of scrotum and testes, with reddening and change of texture of scrotal skin

G3

Enlargement of penis, length at first. Further growth of testes

G4

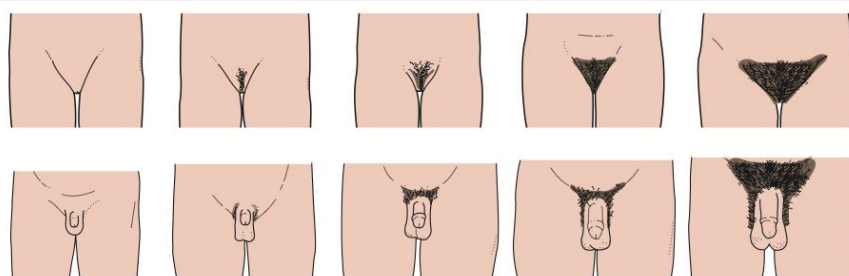
Increased breadth of penis, development of glans penis and darkening of scrotal skin

G5

Adult genitalia

(c)

Pubic hair changes – female and male



PH1

Pre-pubertal

PH2

Sparse, pigmented, long, straight, mainly along labia or at base of penis

PH3

Dark, coarser, curlier

PH4

Hair adult in type, but covering a smaller area

PH5

Adult in quantity and type

Tanner stages

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Early Puberty

- It is the development of puberty before 8 years of age in girls and 9 years of age in boys:

<p style="text-align: center;">Thelarche</p>	<p>-in girls between 6 months and 2 years due to high maternal levels of prolactin usually</p> <p>-breast enlargement may be asymmetrical and fluctuate in size</p> <p>-rarely progress beyond stage 3 of puberty</p> <p>-No other features of puberty or significant acceleration in growth</p> <p>-Self limiting and no need of investigations</p>
<p style="text-align: center;">Adrenarche</p>	<p>-Sensitivity to androgen NOT excessive production!!</p> <p>-Pubic hair growth with no other signs of puberty nor significant growth acceleration</p> <p>-There may be a slight increase in growth rate and bone age</p> <p>-Girls with adrenarche have increased risk of PCOS later in life</p> <p>-If the child is growing rapidly, or there is significant virilization, excess production of adrenal hormones should be excluded</p>
<p style="text-align: center;">Precocious puberty (PP)</p>	<p>See the graph below</p>

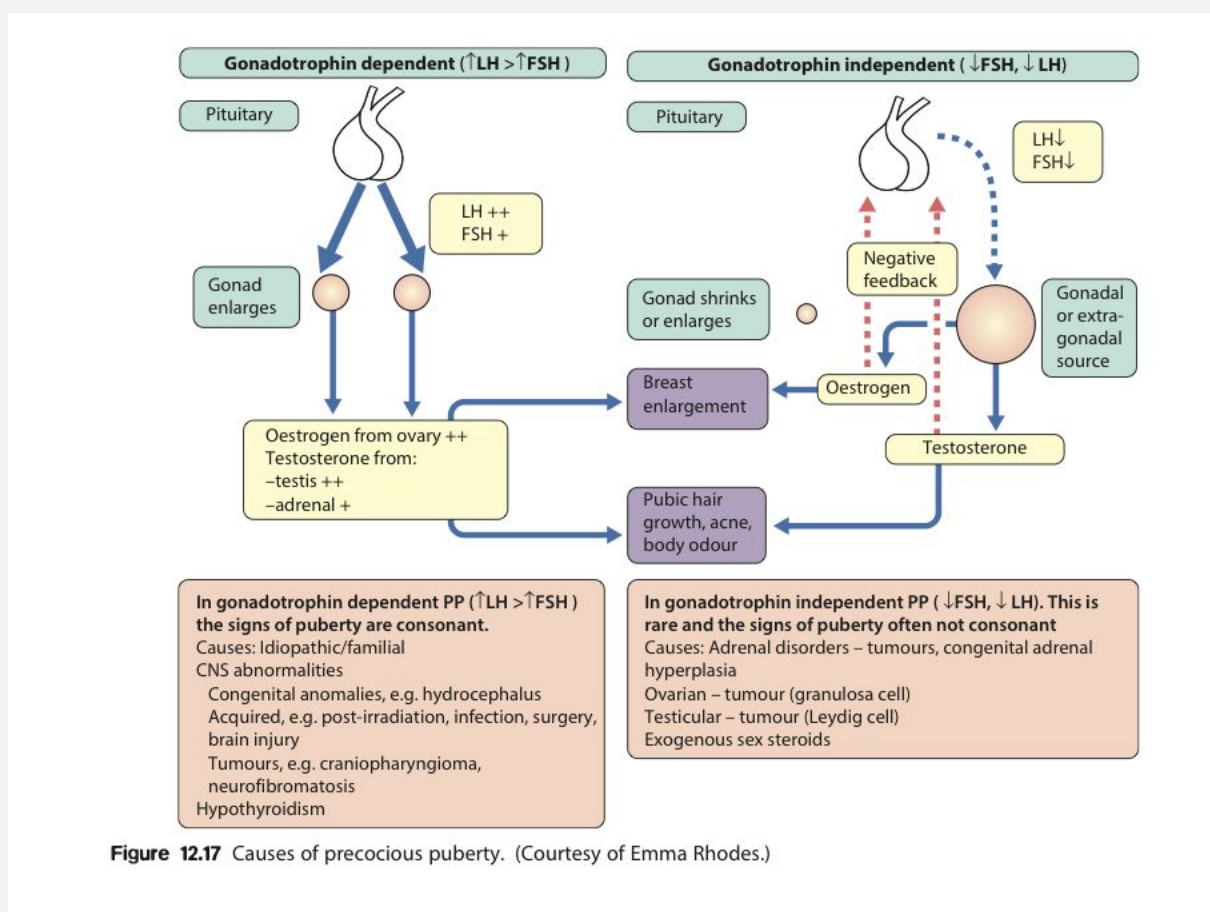


Figure 12.17 Causes of precocious puberty. (Courtesy of Emma Rhodes.)

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Early Puberty

- **PP in girls:** The uterus will change from an infantile 'tubular' shape to 'pear' shape with the progression of puberty and the endometrial lining can be identified close to menarche.
- **Precocious puberty in girls is common and usually due to the premature onset of normal puberty. Precocious puberty in boys is rare and a pathological cause must be excluded**
- **Examination of the testes is important in PP:**

Bilateral enlargement of the testes, with testicular volumes greater than or equal to 4 ml, suggests gonadotropin-dependent PP. This can be caused by a change in the structure of the pituitary gland.

Prepubertal testis suggest a gonadotropin- independent cause, e.g. adrenal pathology.

A unilateral enlarged testis suggests a gonadal tumour.

- Gonadotropin releasing hormone analogues to delay gonadotropin dependent puberty. Adult height of treated patients is higher than untreated and is related to skeletal age at the onset of treatment
- **Labs:**

○ **Decreases LH: LH/FSH ratio < 1 → Prepubertal gonadotropin secretion**

○ **Increased LH: LH/FSH ratio > 1 → Pubertal gonadotropin response CPP**

GnRH stimulation test (100 ugm of GnRH IV, Check FSH & LH at baseline, 20,40,60 min):

○ **Prepubertal(PPP): FSH > LH, LH rise is minimal < 10 IU/ml.**

○ **Pubertal(CPP): high LH > FSH, LH peak above upper limit for prepubertal.**

McCune Albright syndrome (one of the causes of peripheral PP)(EXTRA)

- Also known as Polyostotic fibrous dysplasia
- **Autonomous functioning ovaries with 1 or 2 ovarian cysts → increased estradiol.**
- Café-au-lait spots and multiple cystic bone lesions
- **GnRH independent PP**
- Endocrine disorder (hyperthyroidism, hyperparathyroidism, Cushing syndrome).
- Rx: Testolactone inhibit aromatase activity → decreased estrogen synthesis.



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Delayed Puberty

- It is the absence of pubertal development by 13 years of age in girls and 14 years in boys. **Causes are:**

Constitutional delay of growth and puberty/familial

- By far the most common in boys

Low gonadotrophin secretion (hypogonadotropic hypogonadism)

- Systemic disorders:
 - cystic fibrosis, severe asthma, Crohn disease, organ dysfunction, anorexia nervosa, starvation, excess physical training
- Hypothalamo-pituitary disorders:
 - pituitary dysfunction
 - isolated gonadotrophin or growth hormone deficiency
 - intracranial tumours (including craniopharyngioma)
 - Kallmann syndrome (luteinizing hormone-releasing hormone deficiency associated with absent sense of smell)
- Acquired hypothyroidism

High gonadotrophin secretion (hypergonadotropic hypogonadism)

- Chromosomal abnormalities:
 - Klinefelter syndrome (47,XXY)
 - Turner syndrome (45,XO)
- Acquired gonadal damage:
 - After surgery, chemotherapy, radiotherapy, trauma, torsion of the testis, autoimmune disorder

It is a variation of the normal timing of puberty rather than a pathological condition

- Delayed puberty is common in boys and is usually due to constitutional delay of growth and puberty. Delayed puberty is uncommon in girls and a cause should be sought (karyotyping for Turner syndrome, thyroid and sex hormones should be measured. Pituitary pathology should be excluded by an MRI)
- Treatment can be offered to induce puberty in boys after 14 years of age, usually using low-dose intramuscular testosterone injections, which will accelerate growth as well as inducing secondary sexual characteristics.
- Girls may be treated with oestradiol for several months to induce puberty.