SHORT STATURE AND PUBERTY

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By the end of this lecture, we will be able to:

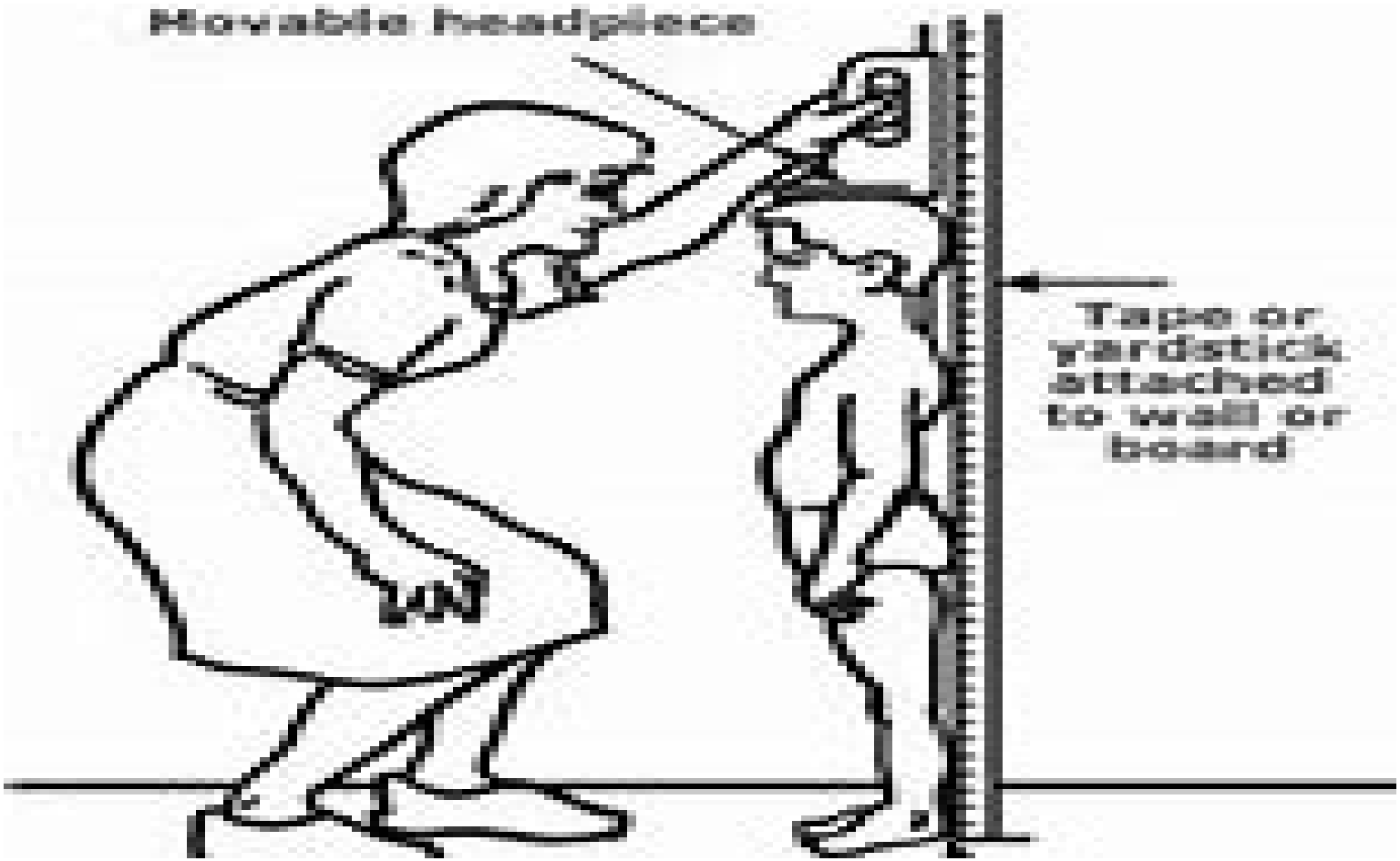
- Define short stature.
- • Mention types of short stature.
- • Mention the principles of diagnosis.
- • Identify the causes of short stature.
- • Outlines about Managements.

Definition

- Height below 3rd centile or less than 2 standard deviations below the median height for that age & sex according to the population standard
  OR
- • Even if the height is within the normal percentiles but growth velocity is consistently below 25th percentile over 6-12 months of observation
- • The term 'Dwarfism' is no longer used for short stature
- • It should not be confused with FTT as it is associated with greater impairment in wt.gain than linear growth resulting in decresd W/H.& THE LINEAR GROWTH affected is almost always SECONDARY.

Normal Measuring

- **Supine length < 2 y of age**
- • For measurement of supine length it is best to use a firm box with an inflexible board against which the head lies, with a movable footboard on which the feet are placed
- **Erect height > 2 y**
- • The head is held in a horizontal plane • Upward pressure is applied to the mastoid processes in order to encourage the child to stand up straight.


Movable headpiece
Tape or yardstick attached to wall or board

Short child

- **FIVE GOLDEN POINTS •**
- 1- Accurate & Serial measures .
- • 2- Mid Parental Height (MPH).
- • 3- Height age.
- • 4- Bone Age.
- • 5- appropriates Investigations.

Important Definitions

- Chronological age – Actual age of the child.
- • Height age – it's the age at which the height of the child is at 50th centile.
- • Bone age - is an indicator of skeletal maturation.
- • Target MPH: F+M/2 +6.5 for boys and -6.5 for girls.
- • Then plot the result on Growth Chart at Age 20 to form Family chart ±10 to form centile

- Disproportionate (ie, involves one more than the other).
- • U/L > Increase ratio ---------- short lower limb. • (e.g. Achondroplasia, Skeletal dysplasia)
- • U/L < Decrease ratio : • Short trunk (Scoliosis, MPS)
- • Short neck (Turner Syndrome

Features	Familial Short Stature	Constitutional Delay
Parent's Stature	Small one or both	Average
Parent's Puberty	Usual timing	Delayed
Birth Length	Normal	Normal
Growth	Normal	Normal to slow
Growth Puberty	Normal	Slow
Bone Age	Normal	Delayed
Timing of Puberty	Normal	Delayed
Puberty Growth Rate	Low range of Normal	Diminished
Adult Height	Short	Normal

Factors affecting height

Intra uterine Growth factors	Nutrition Thyroid harmon		Growth Hormone	uterine Growth factors Nutrition Thyroid hormone Growth Hormone FSH LH GH Thyro	
	Birth	1 year	2-8 years	Puberty	Adult

Growth factors at various stages

- **PRENATAL GROWTH:** Uterine function & size, maternal nutrition, insulin ,IGF
- • **POSTNATAL GROWTH:** GH& THYROXINE

Cont.

- • **3YEARS TO PUBETY**: GH& THYROID HORMONE Constant linear growth @4-7cm/yr.
- • **PUBERTY:** Sexsteroids (estrogen & testosterone) in concert with GH,THYROID,&NUTRTION□
- Acceleration of growth□ pubertal growth spurt. - Spontaneous growth hormone elevation in response to sex steroids.

- • First sign of puberty in females preceeds the first sign of puberty in males by 6months.
- • Pubertal growth spurt in females is 2 years earlier than males but the peak height velocity is slower in females than males(8.3cm/yr <9.5cm/yr) resulting in on an average of 13cm difference in between them.

SKELETAL MATURATION

- Growth usually results from increased length of bones coupled with rate of skeletal maturation.
- • BONE AGE RADIOGRAPHY: Assessing skeletal maturation by examining the epiphyseal maturation at hand&wrist. In <18 months- hemiskeleton x ray due to immature hand &wrist growth plates.
- • Delayed bone age –indicates short stature is partially reversible coz linear growth continues until epiphyseal fusion completes

Causes Of Short Stature:

- ***A) Proportionate Short Stature***
- **1) Normal Variants:**
- i) Familial – ii) Constitutional Growth Delay
  2)Prenatal Causes:
- i) Intra-uterine Growth Restriction Placental causes, Infections, Teratogens
- ii) Intra-uterine Infections
- iii) Genetic Disorders (Chromosomal & Metabolic Disorders)

Cont.

- iii) Psychosocial Short Stature (emotional deprivation)
- iv) Endocrine Causes: (With increased W/H) - Growth Hormone Deficiency/ insensitivity - Hypothyroidism - Juvenile Diabetes Mellitus - Cushing Syndrome - Pseudohypoparathyroidism

Cont.

- ***B) Disproportionate Short Stature***
- 1) **With Short Limbs:** - Achondroplasia, Hypochondroplasia, Chondrodysplasia punctata, Chondroectodermal Dysplasia, Diastrophic dysplasia, Metaphyseal Chondrodysplasia - Deformities due to Osteogenesis Imperfecta, Refractory Rickets
- 2) **With Short Trunk:** - Spondyloepiphyseal dysplasia, Mucolipidosis, Mucopolysaccharidosis - Caries Spine, Hemivertebrae

Genetic Syndromes:

- ***A) Chromosomal Disorders –***
- *Turner syndrome (XO)*: an incidence of 1 in 2000 live births - should be ruled out even if typical phenotypic features are absent - Other Eg: Noonan,-looks like turners but both sexes are afectd. Silver- Russel – with iugr child Seckle syndrome- bird headed dwarfism.
- ***B) Inborn Errors of Metabolism*** -eg. Galactosemia, Aminoaciduria

Intra-uterine Growth Restriction

- Arrest of fetal growth in early embryonic life causes reduction in total number of cells, leading to diminished growth potential in postnatal life
- • BW -<10th centile for GA.
- • Most of these babies show catch-up growth by 2yrs of age, but 20-30% may remain short. • AETIOLOGY: Subtle defects in the GH-IGF axis • Growth Velocity- normal
- • BA = CA
- • Learning disabilities could be present

Under nutrition:

- One of the commonest cause of short stature.
- • Aetiology: PEM, Anemia & trace element deficiency such as Zinc , calcium def are common causes.
- • Child usually appear STUNTED, with POOR Wt. gain, Wasted muscles.
- • BA < CA.:
- • Usually child achieves catch up growth with restoration of nutrition & may be dwarf if under nutrition is profound.
- • Diagnosis: good dietary history, anthropometric measurements

Chronic Systemic Illness:

- **1) Chronic Infections -**eg:TB, Malaria, Leishmaniasis, Chr. pyelonephritis - Growth retardation is due to impaired appetite, decreased food intake, increased catabolism, poor utilization of food, vomiting & diarrhea
- **2) Malabsorbtion Syndromes** - eg: chronic recurrent infective diarrhoea, lactose intolerance, cystic fibrosis, celiac disease, giardiasis, cow's milk allergy, abeta lipoproteinemia
- IBD&COELIAC DISEASE- manifest with growth delay even before onset of GI symptoms.

- **3) Birth defects**: CHD, urinary tract & nervous system anomalies
- **4) Miscellaneous**:(EVIDENCED CLINICALLY) Cirrhosis of liver, bronchiectasis, acquired heart diseases, cardiomyopathies, SDH
- RTA& Nephrogenic DI- may present from birth with FTT.

Psychosocial short stature:

- emotional deprivation dwarfism, maternal deprivation dwarfism, hyperphagic short stature
- • Functional hypopituitarism - low IGF-1 levels & inadequate response to GH stimulation
- • Type1- below 2 yrs, failure to thrive, no GH deficiency.
- • Type2- in > 3 yrs ,due to emotional deprivation.
- • Slow GV, delayd BA, resume normal growth if stimulus is removed
- • Other behavioral disorders: enuresis, encopresis, sleep & appetite disturbances, crying spasms, tantrums
- • Dental eruptions & sexual development delayed

Skeletal dysplasias:

- **chondrodysplasias**
- Inborn error in formation of components of skeletal system causing disturbance of cartilage & bone
- • Abnormal skeletal proportions & severe short stature
- • Diagnosis family history, measurement of body proportions, examination of limbs & skulls, skeletal survey

Diagnosis

- • Detailed history
- • Careful examination
- • Laboratory evaluation

Now Look At the Proportions

- Is the Child Disproportionate ?
- • Take sitting height and standing height
- • Calculate Subischeal leg length • Use proportion charts or tables
- • Short legs – Skeletal Dysplasia
- • Short spine – Metabolic and storage disorders and rare skeletal dysplasia

Clues to etiology from history

History	Etiology
History of delay of puberty in parents	Constitutional delay of growth
Low Birth Weight	SGA
Neonatal hypoglycemia, jaundice, micropenis	GH deficiency
Dietary intake	Under nutrition
Headache, vomiting, visual problem	Pituitary/ hypothalamic SOL
Lethargy, constipation, weight gain	Hypothyroidism
Polyuria	CRF, RTA
Social history	Psychosocial dwarfism
Diarrhea, greasy stools	Malabsorption

Pointers to etiology of short stature

Pointer	Etiology
Midline defects, micropenis, Frontal bossing, depressed nasal bridge, crowded teeth,	GH deficiency
Rickets	Renal failure, RTA, malabsorption
Pallor	Renal failure, malabsorption, nutritional anémia
Malnutrition	PEM, malabsorption, celiac disease, cystic fibrosis
Obesity	Hypothyroidism, Cushing syndrome, Prader Willi syndrome
Metacarpal shortening	Turner syndrome, pseudohypoparathyroidism
Cardiac murmur	congenital heart disease, Turner syndrome
Mental retardation	Hypothyroidism, Down/ Turner syndrome, pseudohypoparathyroidism

Physical examination

- Weight measurement –
- W/A >H/A i.e. fat & short- Endocrine.
- -H/A> W/A but both are below the chronological age with thin & short- Under nutrition / chronic illness.
- Systemic examination to rule out systemic illness
- skeletal system examination including spine Dysmorphic features
- Tanner staging

Investigations

- **Level 1 (essential investigations):**
- Complete blood counte with ESR
- • BONE AGE
- • Urinalysis (Microscopy, pH, Osmolality) • Stool (parasites, steatorrhea, occult blood)
- • Blood (RFT, Calcium, Phosphate, alkaline phosphatase, fasting sugar, albumin, transaminases)

Level 2:

- Serum thyroxine,T3, T4, TSH
- • Karyotype to rule out Turner syndrome in girls
- • Observe height velocity for 6-12 months
- • If height < 3SD□ level 3 investigations

Level 3:

- Celiac serology (anti- endomysial or anti- tissue transglutaminase antibodies)
- • Duodenal biopsy
- • GH stimulation test with Clonidine or insulin & serum insulin like GF-1 levels

GH secretion

- GH secretion occurs in discrete irregular pulses
- • Between the pulses, circulating GH falls to levels that are undetectable with current assays
- • Greatest GH levels at night, generally correlating with the onset of sleep
- • GH secretion is influenced by other physiological stimuli such as nutrition and exercise

Provocative test(GH Stimulation test)

- Random sampling of serum GH is insufficient to diagnose GH deficiency; GH stimulation tests are required
- • A limited number of provocative agents should be used after an overnight fast in a well standardized protocol.
- • Insulin tolerance test (ITT)
- • Glucagon test (100 microgrammes/kg BW IM(max.1 mg)
- • L-dopa test • Arginine test(0.5g/kg BW , slow IV infusion (max,30g) ,
- • Clonidine test (0.1- 0.15 mg/kg BW orally).

Provocative test

- In healthy volunteers peak GH levels are 10 ng/ml (20 mU/ml).
- •If peak GH level of 10 ng/ml (20 mU/ml) is detected , it exclude classical GHD
- •In a classical GHD case a GH peak is not detected or GH peak is less than 3 ng/ml (6 mU/ml) in all these tests.
- •In partial GHD cases GH peak of 8-10 ng/ml (16-20 mU/ml) may be seen.

Familial Short Stature	Constitutional Short Stature	Pathological Short Stature
↓3rd Centile	↓3rd Centile	↓3rd Centile
↔ MPH	↓ MPH	↓ MPH
BA = CA Normal	BA = Height Age < CA	BA < HA<CA

GH THERAPY

- DOSE: 0.1U/KG/DAY s.c. at night time □
- Follow up & watch for atleat one year before starting the treatment.
- Earlier is always better&ideal is 3-4yrs
- Never delay beyond 7-8yrs □
- Usually growth velocity is maximum in first year of therapy. □

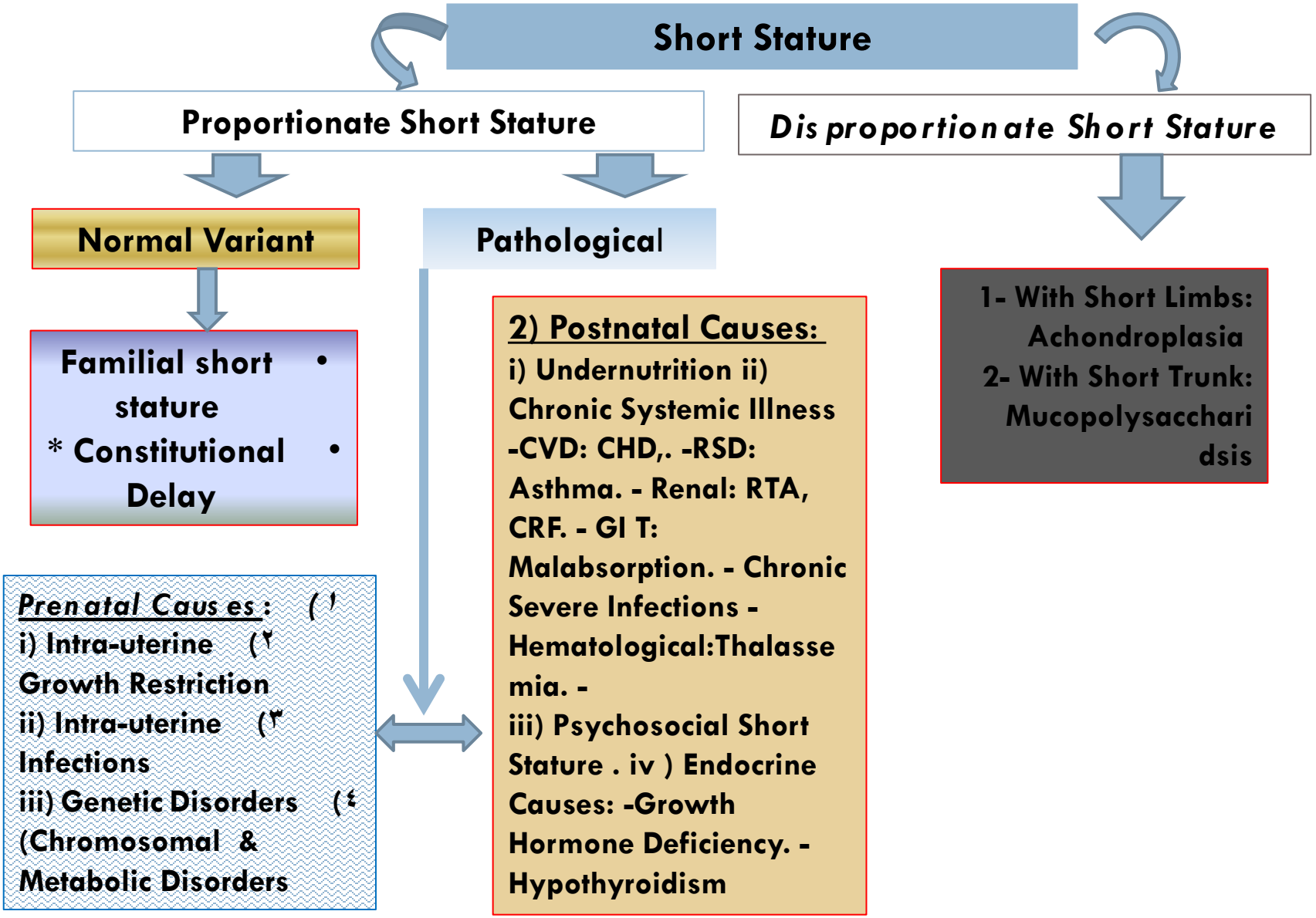
- **Routes of administration**:
- S.c- currently using
- Intranasal- under trials
- **Timing:** 2-3 times/wk
- **Response to Rx:**
- Max response in 1st year with growth velocity >95th percentile
- With each increasing year the growth rate tends to decline.
- If falls <25th percentile: assess compliance before increasing dose

SIDE EFFECTS

: Pseudotumour cerebri, hyperglycemia, acute □ pancreatitis, liver abnormalities, gynaecomastia

Regardless of symptoms all children with significant short stature should be screened for hypothyroidism. •

Rx: thyroxin usually started at 100 micro grams to be started,


Short Stature
Proportionate Short Stature
Disproportionate Short Stature
Normal Variant
Pathological
Familial short stature
* Constitutional Delay
1- With Short Limbs: Achondroplasia
2- With Short Trunk: Mucopolysaccharidsis
2) Postnatal Causes:
i) Undernutrition ii) Chronic Systemic Illness -CVD: CHD,. -RSD: Asthma. - Renal: RTA, CRF. - GI T: Malabsorption. - Chronic Severe Infections - Hematological:Thalassemia. -
iii) Psychosocial Short Stature . iv) Endocrine Causes: -Growth Hormone Deficiency. - Hypothyroidism
Prenatal Causes :
i) Intra-uterine Growth Restriction
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Physical Changes
Early Adolescent

- **Girls:**
- Growth and growth spurts begins
- Beginning of pubertal changes breasts/genitalia/pubic hair
- Weight changes-body shape and size

Cont.

- **Boys:**
- Development of the testes and scrotum is usually the first sign of puberty in boys
- Pubic hair
- Voice changes
- Gynecomastia common

- Boys and Girls:
- Wide range of normal
- Acne
- Girls tend to lose less of their body fat than boys
- An awkwardness as various body parts grow at different rates
- Biologic changes in the brain causing dynamic emotional and cognitive changes

Physical Changes
Mid Adolescence

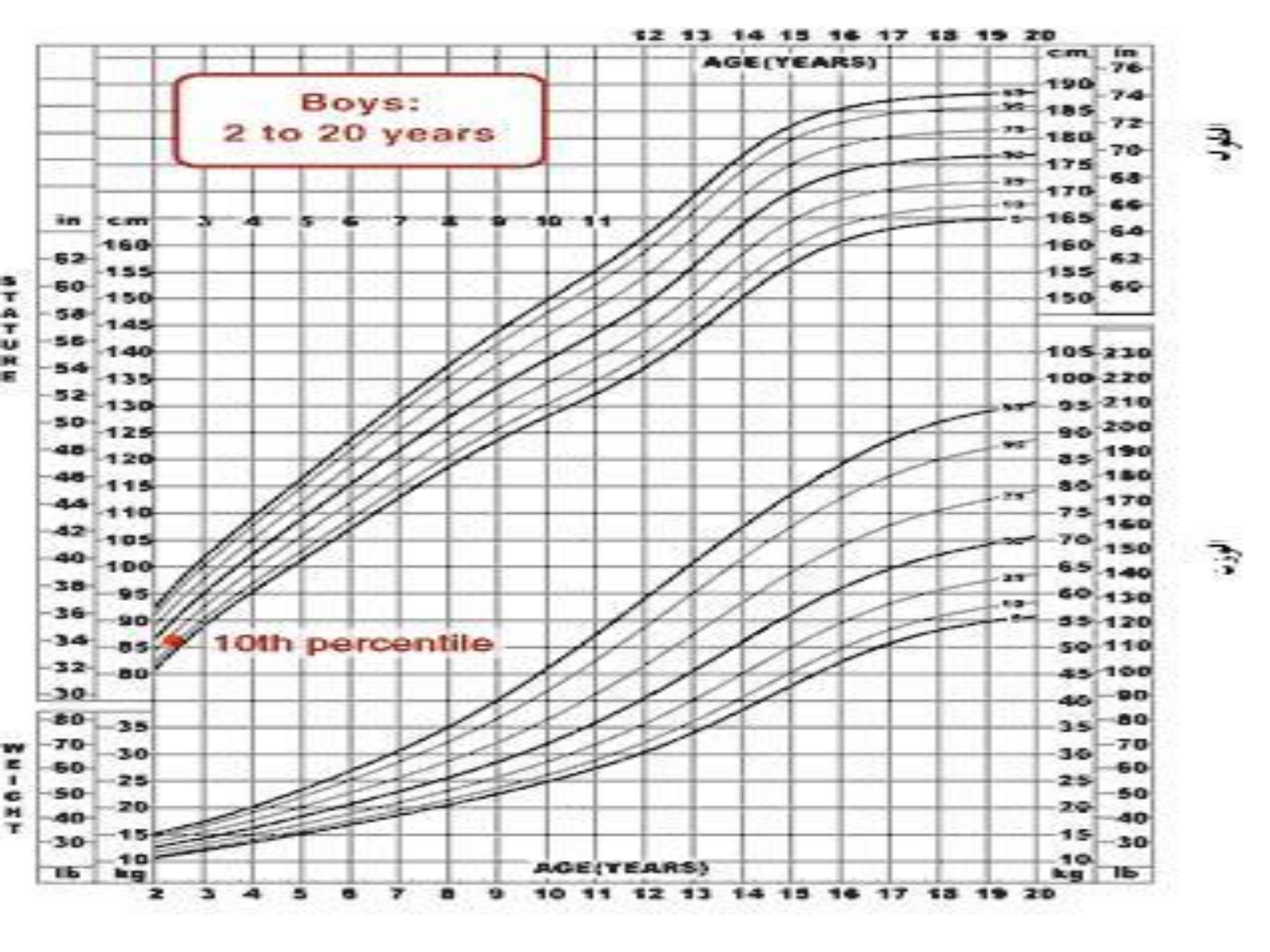
- **Girls:**
- Breast development
- Nipples swell , breasts may feel tender and sensitive
- Breasts fill out over three to four years. One breast may grow faster than the other
- One or both breasts may secret a small amount of milky fluid
- Broadening hips leading to rounded feminine figure

- **Boys:**
- Growth spurt in height usually occurs
- Often the arms and legs lengthen before the trunk of the body, can cause awkwardness
- Faster muscle growth in boys leads to greater strength
- Penis growth
- Development of pubic, facial and body hair. Typically facial and body hair appear about two years after pubic hair

Physical Changes
Late Adolescence

- **Females**
- By 16 years most young women have completed puberty, the growth rate slows, there is pubic and body hair, a rounded and curved figure because of widened pelvis, hips and breasts
- With a well established menstrual cycle, a young woman at this point is physically able to produce offspring

- **Males**
- By 16 to 18 years most males have completed puberty, their growth rate begins to slow, their shoulders have broadened, limbs and trunk are muscular and they have adult body and facial hair
- Produce sperm and are physically able to produce offspring


Boys:
2 to 20 years
AGE(YEARS)
STATURE
WEIGHT
10th percentile
cm
in
kg
lb

Thank You !!