

Approach to Short Stature

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Learning Objectives

1. Understanding the physiology of growth
2. Familiar with the common causes of short stature
3. Clinical assessment and plan investigations of a short child
- 4- Follow up and treatment options

Physiology of Growth

- Important basic ingredients
 - Nutrition
 - Oxygen
 - Hormones
- And the more general components
 - Adequate sleep
 - Exercise
 - Psychosocial factors

Fetal Growth

- The most important factors involved in the control of fetal growth are
 - uterine function and size
 - maternal nutrition
 - Insulin
 - IGFs and IGFBPs

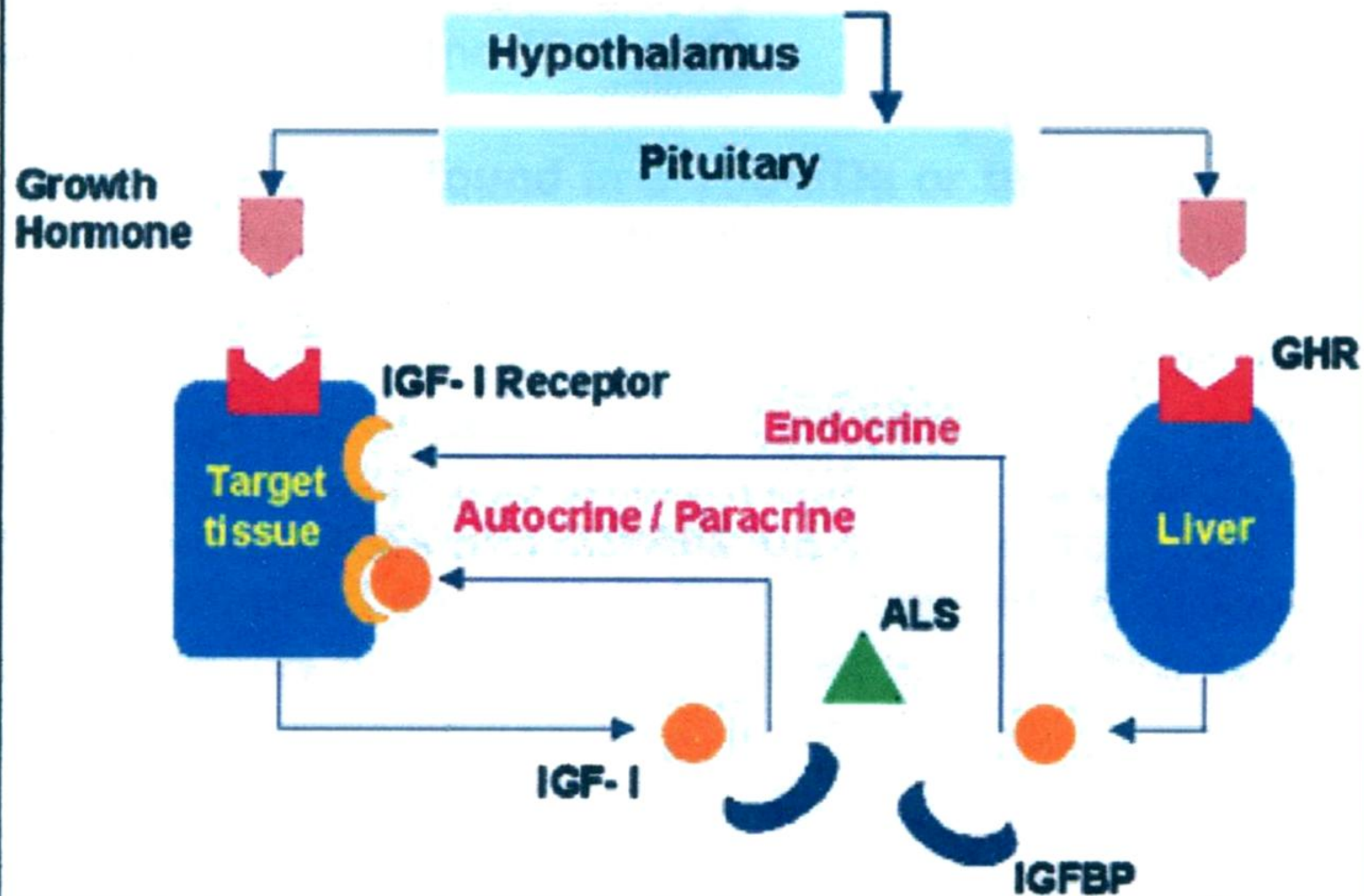
Pubertal Growth

- Pubertal growth spurt
- Occurs in girls approximately 2 years earlier than in boys
- girls (8.3 cm/y) , boys (9.5 cm/y)

Hormonal Factors

- Required in the right amounts and at the right times for optimal growth.
- Growth hormone (GH) & insulin-like growth factor-I.
- Other Hormones (Thyroid hormone, insulin, sex steroids, and glucocorticoids)

The Growth Hormone / IGF Axis



Growth Hormone

- GH, a polypeptide (191 amino acids).
- GH pulses occur during sleep, exercise, and physiologic stress.
- Regulation by
 - GH-releasing hormone (GHRH)
 - Somatostatin (SRIH)
 - Negative feedback systems

Growth assessment

- Height (or length) and weight: should be measured with care.
- Using a single steady stadiometer by a single person and obtaining more than one measurement provides accurate values.

Definition of short stature

- Standing height $> 2SD$ below the mean (< 2.5 percentile) for gender and chronological age.
- Compare the child's height with that of a larger population of a similar background and mid-parental target height.

Target height(Midparental height)

- BOYS:

$$\frac{[\text{Father's ht (cm)} + (\text{mother's Ht (cm)} + 13)]}{2}$$

- GIRLS:

$$\frac{[(\text{Father's ht (cm)} - 13) + \text{mother's Ht(cm)}]}{2}$$

Most children achieve an adult stature within approximately 10 cm of their target height

Growth velocity

- Most important aspect of growth evaluation
- Change in standing Ht over:
 - Infants: 4 mo
 - Children: 6mo

- **Normal (cm/yr)**
 - 1y: 25
 - 2y: 12
 - 3y: 8
 - **Then until puberty: 4-7 cm**

Body Proportions

- Proportionality: Inspect the child for proportionality of limbs and trunk. If disproportion is suspected, the following measurements may be taken:
 - **Arm span**: Measure outstretched arms from fingertip to fingertip.
 - arm span should approximate the height.
 - **Lower segment (LS)**: Measure from the symphysis pubis to the floor.
 - **Upper segment (US)**: Subtract the LS from the height.
- The **US/LS ratio** is calculated by dividing the US by the LS.
 - this ratio is about 1.7 at birth and decreases to 1 at about age 10, where it remains throughout adulthood

Causes of short stature

*Familial short stature

*Constitutional delay of
pubertal growth spurt

*lowbirth weight ;malnutrition

*Endocrine disorders:

A.growth hormone
deficiency

B.hypopituitarism

C.hypothyroidism

D.Cushing syndrome

*Chromosomal
disorders/syndrome:

A.Turner syndrome

B.Silver-Russell syndrome

*Skeletal dysplasias:

achondroplasia

*Emotional/psychosocial
deprivation dwarfism

*Chronic illness:

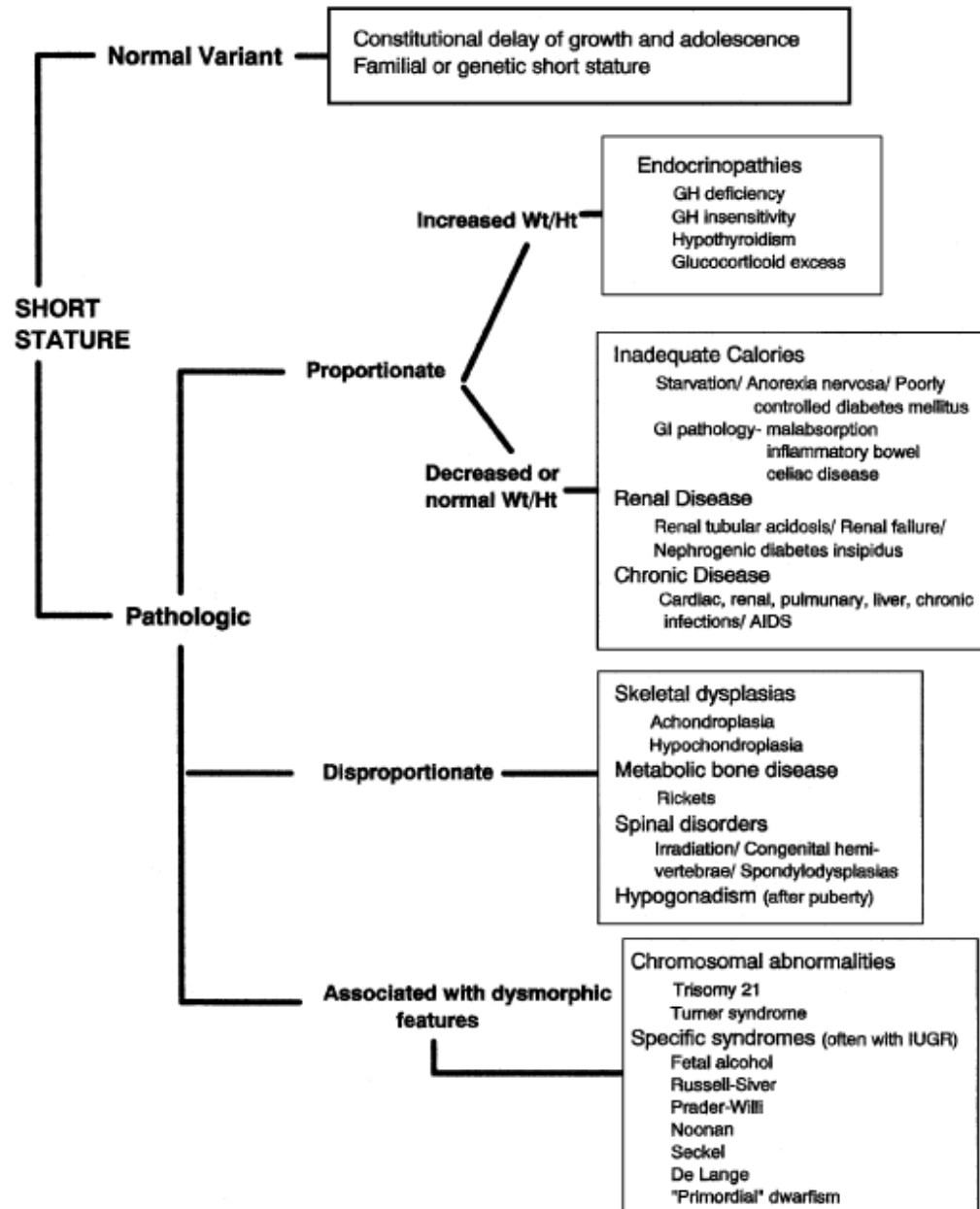
A.congenital heart disease

B.cystic fibrosis

C.cerebral palsy

D.chronic renal failure

Approach:



Common causes:

Familial (genetic)	Constitutional
$BA = CA$	$BA < CA$
N growth veloc	N growth veloc
Appropriate target height	Appropriate target height

Familial short stature

- **Familial short stature:**
 - history of parents with short stature.
 - normal growth velocity (thus, they do not exhibit true growth failure).
 - Bone age is not delayed.
 - puberty at a normal time and most often finish their growth with a short adult height.

Constitutional growth delay

- Growth pattern similar to those with familial short stature
- Have a delay in skeletal maturation and onset of puberty
- Pubertal catch-up growth
- Growth continues beyond the time the average child has stopped growing
- Final height is normal

Lowbirth weight(IUGR)

- Intrauterine growth retardation
- Secondary to poor maternal environment ,fetal malnutrition,congenital infection etc
- Many children with IUGR exhibit catch-up growth during first 2-3 years of life
- 15%-20% will remain short through life

Diagnostic Approach to the Short Child

Table 1. The Medical History

Family History

- Parents' and siblings' heights, age of onset and tempo of puberty, age of attaining adult height
- Medical problems (parents, siblings, grandparents)
- History of consanguinity or familiar congenital anomalies

Birth History

- Maternal problems during pregnancy
- Birthweight and length (presence or absence of intrauterine growth restriction)
- Preterm birth, difficult birth, or breech delivery
- Postnatal problems or complications

History of Parents Growth

- Timing of puberty in parents: Constitutional delay in growth and maturation may have a family history.
- Most mothers can remember their age at menarche (average age, 12-12.5 y).
- Eliciting pubertal history from a father is more difficult because no specific landmark is recognized.
- Evidence of delayed puberty may include continuing to grow after high school or not shaving until age 20 years or older.

History

Development

- Developmental milestones
- Age of tooth eruption and loss
- School performance

Nutrition

- Calcium
- Protein
- Calories
- Vitamins

Medications

- Methylphenidate or other stimulants
- Anticonvulsants
- Antidepressants

History

General Health

- Frequent ear infections
- Urinary tract infections
- Constipation
- Poor appetite
- Diarrhea
- Stomach aches

Activity

- Physical activity
- Exercise tolerance
- Stamina

Age of Pubertal Development

- Body odor or deodorant use
- Acne
- Breast development
- Genital development
- Axillary and pubic hair development

History

Significant Medical Events

- Examples: head injury, surgery, illnesses

Other Persistent Symptoms

- Headaches
- Vision or hearing problems
- Dry skin
- Cold intolerance (covers at night)
- Allergies

Physical Examination

- Examination of Growth
 - Height
 - Weight
 - Head circumference
 - Upper to lower segment ratios
 - Arm span
 - MPH
 - Ht velocity
- Pubertal Assessment (Tanner staging)
 - Axillary hair
 - Pubic hair & staging
 - Breast development & staging
 - Genital development & staging

PHYSICAL EXAMINATION

Table 2. The Physical Examination

- Facial appearance and apparent maturation; abnormal facies
- Dysmorphic features: palate shape, ear placement, size and shape of hands and feet
- Skin: acne, facial hair, skin temperature, birthmarks
- Body proportions: arm span, upper-to-lower ratio, head circumference
- Hands: short metacarpals, nail beds <80% of fingertip width, palmar creases, clinodactyly
- Chest: widely spaced nipples, pectus excavatum, shield-shaped chest
- Breast development: breast buds (male or female) or breast stage

PHYSICAL EXAMINATION

- General examination: heart, lungs, abdomen, neurologic
- Genitalia:
 - Female: pubic hair stage, clitoris size, labia, vagina, estrogen effect
 - Male: pubic hair stage, genital stage, including phallic and testicle length (>2.5 cm maximum length signifies entry into puberty)

PHYSICAL EXAMINATION

Carefully examine the midface.

A single, central, maxillary incisor reflects a defect in midline facial development.

Similarly, a bifid uvula suggests the possibility of a submandibular cleft palate, which may be palpable, yet not visible on inspection.

Associated anomalies of midline structures, such as the pituitary gland, are common in patients with major midline facial anomalies

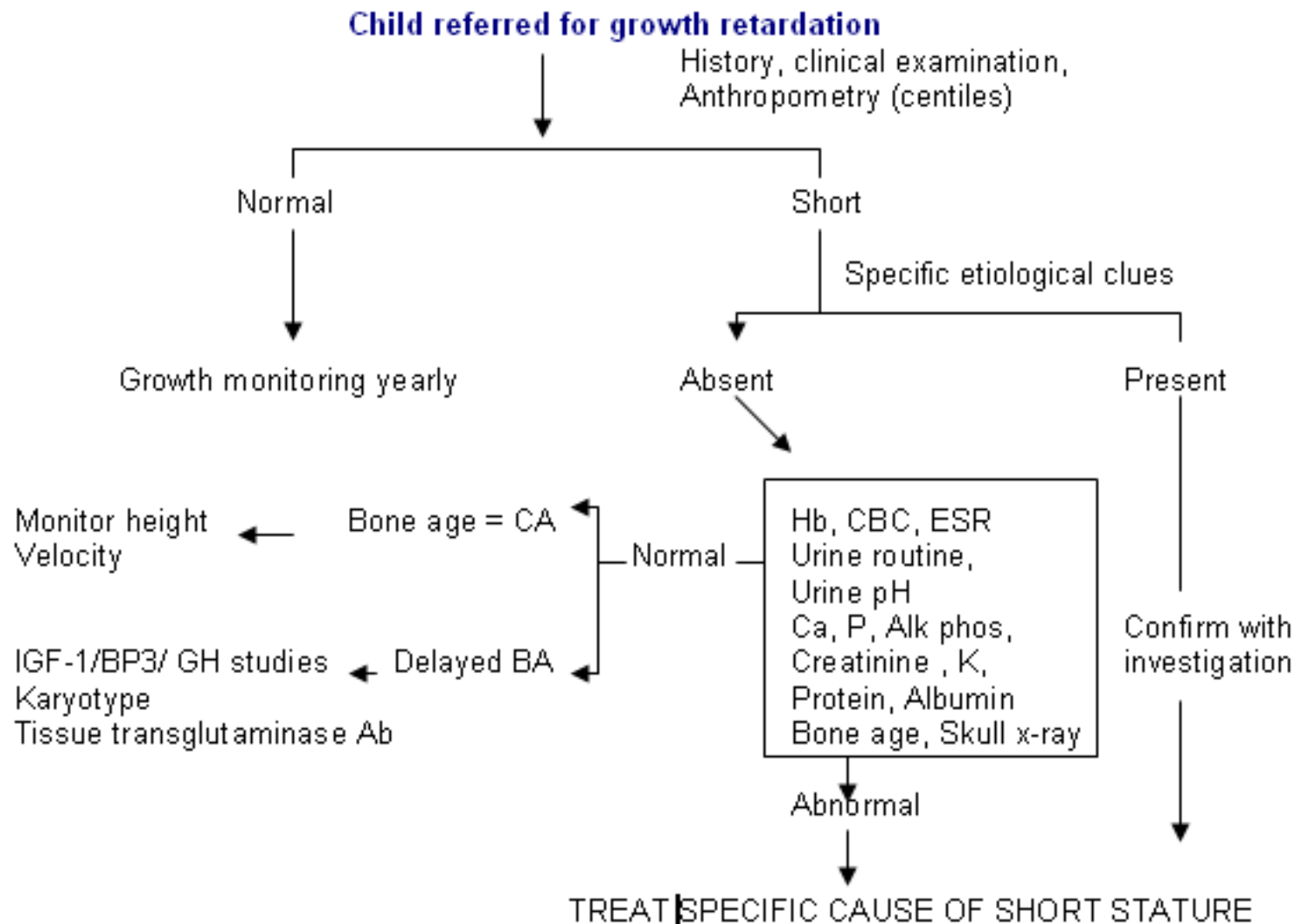
PHYSICAL EXAMINATION:

- Look for signs of specific syndromes:
 - Turner syndrome, look for webbing of the neck, a wide carrying angle (cubitus valgus), a low hairline, a high-arched palate, short fourth metacarpals, and multiple nevi.
 - Noonan syndrome and Russell-Silver syndrome, among others, should be considered.

PHYSICAL EXAMINATION

- Palpate for thyroid enlargement
- Test visual fields for signs of pituitary and hypothalamic tumors, initially by gross confrontation.
- Inspect fourth metacarpals, which are shortened in persons with Turner syndrome, pseudohypoparathyroidism, Albright hereditary osteodystrophy.

Table 3 : Investigations in a short child



Lab studies

- **TSH & Ft4**

- Because of the possibility of subtle signs, evaluation of thyroid hormone levels in all children with slow growth is advised.
- With hypothyroidism, the growth rate is extremely slow, and with replacement of thyroid hormone, catch-up growth is rapid.

Lab studies:

- Tissue transglutaminase
- IGF-1 and IGFBP-3:
are growth hormone (GH) dependent. Low values suggest growth hormone deficiency.

Lab studies (cont.):

- Karyotype:

Girls with otherwise unexplained short stature should have karyotype determined to rule out Turner syndrome.

some girls with Turner syndrome have short stature as the only recognizable feature.

Imaging:

- **MRI of the head:**
- **to rule out a brain tumor, such as a craniopharyngioma.**
- **10% of children with a craniopharyngioma present with growth failure as the only sign.**
- **15% of patients with growth hormone deficiency have an abnormality of the pituitary gland, such as an ectopic bright spot, an empty sella, or a small sella.**

INDICATION FOR GH TESTING

- Extreme short stature is less than 3 SD
- Low height velocity
- Clinical features suggestive of Endocrinopathy

GH stimulation test

➤ Exercise stimulation test

- if level is less than 20 u/l proceed to LDOPA propranolol stimulation test.
 - if less than 20 u/l proceed to Insulin induced hypoglycemia.
- Insulin-induced hypoglycemia: most powerful, but more risk.
 - OTHER (2 serial tests):
 - Arginine
 - levodopa, propranolol with glucagon, exercise, clonidine
 - **GHD: GH peak after stimulation < 10 ng/ml**

GHD

- GHD may be congenital or acquired
- Maybe isolated or with other pituitary hormone deficiencies
- Idiopathic GHD and GH insensitiveness syndrome (mutation in the GH receptor)
- Infants with GHD are of normal birth weight, slightly reduced in length
- Excess truncal adiposity
- Delay in skeletal maturation

GENETIC CAUSES OF GH DEFICIENCY

- Hypothalamic – GHRH
- Pituitary – combined hormone deficiency isolated GH deficiency septo optic dysphasia.
- Peripheral tissues
 - GH receptor defects
 - GH receptor signaling defects
- Primary defects of IGF (Laron)
 - Associated with IUGR

AQUIRED CAUSES OF GH DEFICIENCY

- Tumours
- Cranial irradiation
- Histocytosis
- Head injury
- Intrauterine infection

The management of short stature

Familial & constitutional short stature:
reassurance/ F/U ht velocity

Treat identified underline cause

FDA-Approved Indications for GH Therapy in U.S.

- Childhood GH deficiency (1985)
- Growth failure secondary to chronic renal insufficiency before transplantation (1993)
- Wasting syndrome associated with HIV infection in adults for 12 wk (1996)
- Turner syndrome (1996-1997)
- Adult GH deficiency (1997)
- Prader-Willi syndrome (2000)
- SGA without growth recovery by 3 yr (2001)
- Idiopathic short stature

S/E OF GROWTH HORMONE

- **Injection site discomfort**
- **Curvature of the spine (scoliosis)**
- **Joint pain Hip or knee pain**
- **Puffy hands and/or feet (caused by fluid retention)
(carpel tunnel)**
- **Changes in vision, a bad headache, or nausea with
or without vomiting**
- **Allergic reaction**

Growth hormone insensitivity (primary IGF-1 deficiency):

- Sometimes called Laron dwarfism, this disorder appears to be similar to growth hormone deficiency, except that large amounts of growth hormone are produced but levels of IGF-1 are low.
- This is a rare condition, except in populations where the gene is present with a greater frequency (eg, in Ecuador).

Tall stature

- Definition
- Causes
- Examination
- Investigations