Short stature

Shoug AL-anezi
Samer Balasmeh
Taha Obaid
Hala Qawasmeh
Fadel Shereer

Introduction

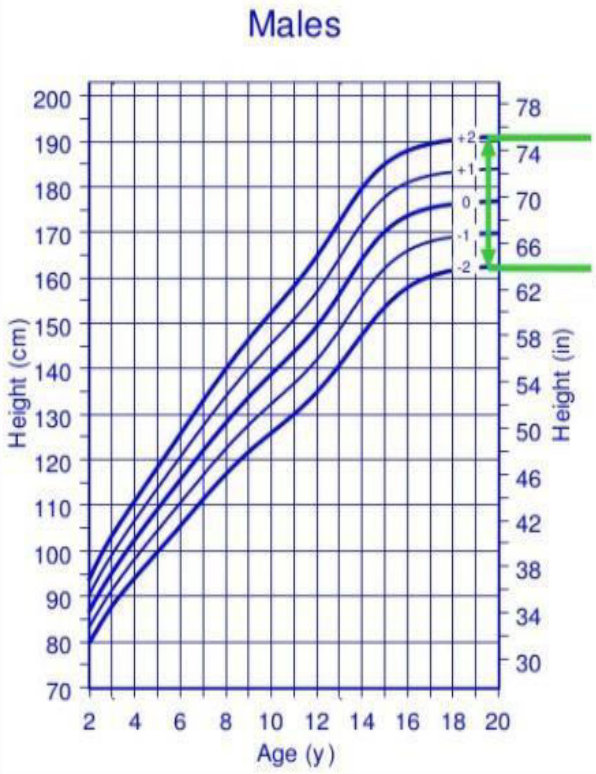
- Growth is the fundemental physiological process that charecterizes childhood.
- Growth can be worrisome among 2 variables;

Height (short stature) and Velocity (growth failure).

- Height less than 3rd percentile or 2SD below the mean for age of the population reference standart.
- Normal height range differs from one country to another
- Excessively short i.e. More than 2SD below the med parental height or target height even if the height recorded is within the normal population percentiles for age.
- Growth velocity less than 25th percentile on a velocity curve over 6-12 months (less than 4cm).
- Dwarfisim refers to more severe short stature defined as height below 3SD for age and gender norms.

Definition

- HSDS < -2SD
- Ht velocity < 3rd percentile .



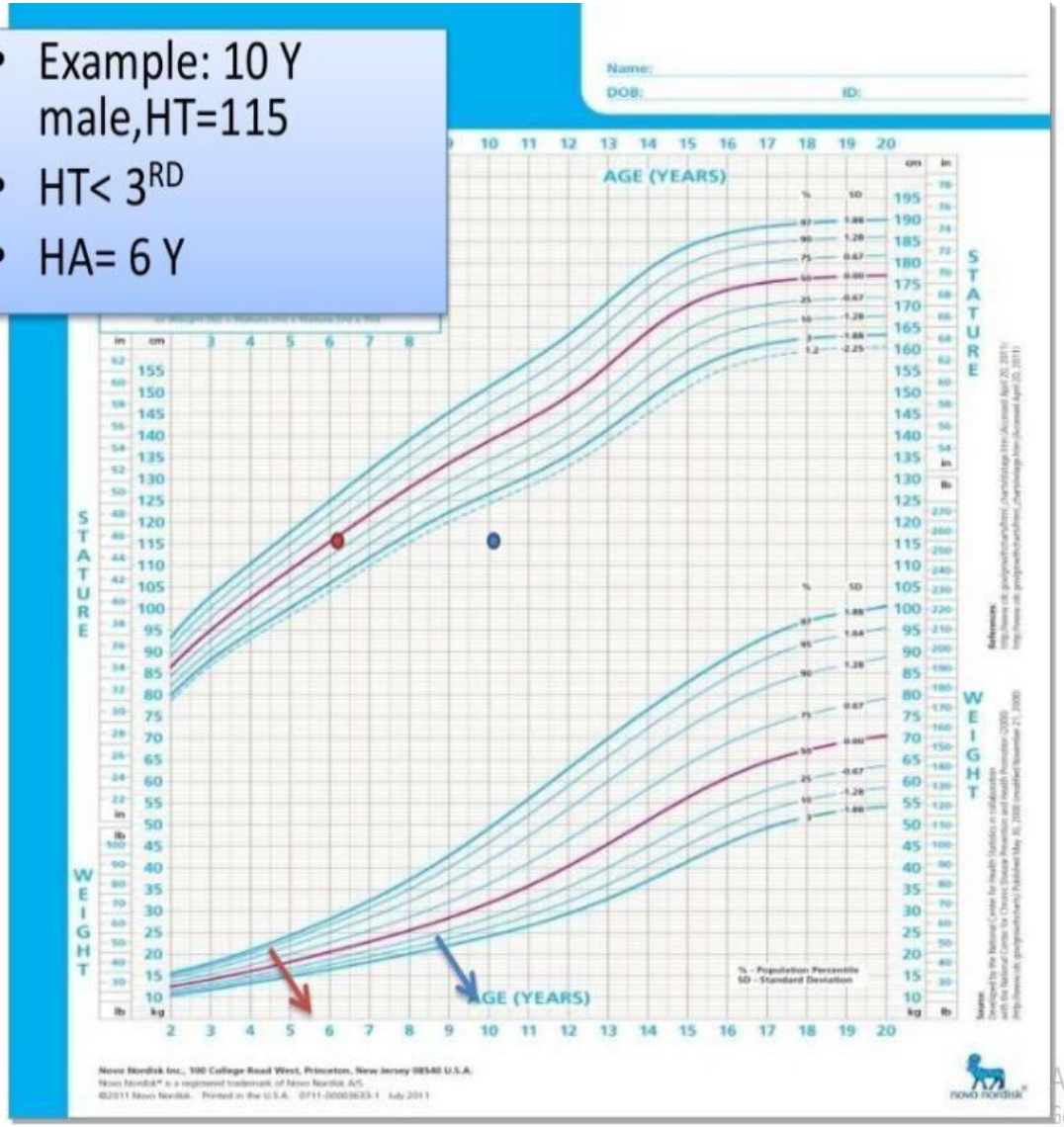
-2.0 SD **(2.3 percentile)**

Generally accepted definition of normal range

Important definitions

- Chronological age – actual age of a child
- Height age – its the age where the height of the child is at 50th percentile
- Bone age- indicator of skeletal maturation
- Target MPH - (F+M+13)/2 for boys and -13 in girls then plot the result on growth chart at age 20 to form family chart , for boys+- 10 and +-8.5 for girls.

- Example: 10 Y male,HT=115
- HT< 3RD
- HA= 6 Y



Accurate height measurment

- <2 years; supine length by infantometer
- >2 years; standing height by stadiometer

1. Infantometer;
- Bulky diapers should be

Removed.

- Supine baby with head

held against a fixed upright

headboard by one person

Legs straight with feet at

Right angles to leg

Accurate height measurment

Stadiometer:
Without footwear , with heels,buttocks,scapula and occipit touching the wall
Frankfurt plane – lower border of the eye socket in the same horizontal plane as EAM
Looking straight ahead
Harpenden Stadiometer determains the height accurately (within 0.1 cm)

Evaluating a child with short stature

- Maternal history
- Birth history
- Growth pattern
- Developmental milestones
- Family history
- Medical history
- Dietary history
- **History and presentation :**
- Hypoglycemia, prolonged jaundice , small penis
- Antenatal
- Puffy extremities
- Fever , weight loss ,anorexia
- Chronic diarrhea ,bulky frothy stool
- Dyspnea ,cough ,cyanosis
- Headache ,vomiting ,diplopia
- Polyuria
- Weight gain ,obesity
- Constipation, lethargy, delayed milestones
- Congenital GH deficiency
- IUGR ,turner ,chronic infections
- Malabsorption
- Systemic disease
- Pituitary or hypothalamic SOL
- CRF ,RTA
- Cushing syndrome
- Hypothyroidism

Physical examination

- Measurements : weight , standing height , sitting height ,HC
- Height in relation to previous height (height velocity)
  parents height ,stage of puberty
- Genitalia and pubertal development
- Unusual dysmorphic features
- Signs of specific disease .

Clues on Examination

• Pallor	- Anemia
• Hypertension	- CRF, Cushing syndrome
• Dysmorphism	- Genetic disorders
• Midline defect	- Hypopituitarism
• Vitamin deficiency, ↓ Wt for Ht	- Malabsorption, PEM
• Frontal bossing, depressed nasal bridge	- Congenital GH deficiency
• Disproportionate body proportion	- Skeletal dysplasia, Rickets
• Central obesity, proximal weakness	- Cushing syndrome
• Papilloedema, visual defect, optic atrophy	- Pituitary Tumor
• Goiter, delayed dentition, Short lower limbs	- Hypothyroidism

Growth Velocity

Definition: the change in measurements or increments in weight and length/height from one visit to the next. This provides information on growth monitor progress. It indicates the velocity or the rate of growth per unit of time.

Height unit: cm/year

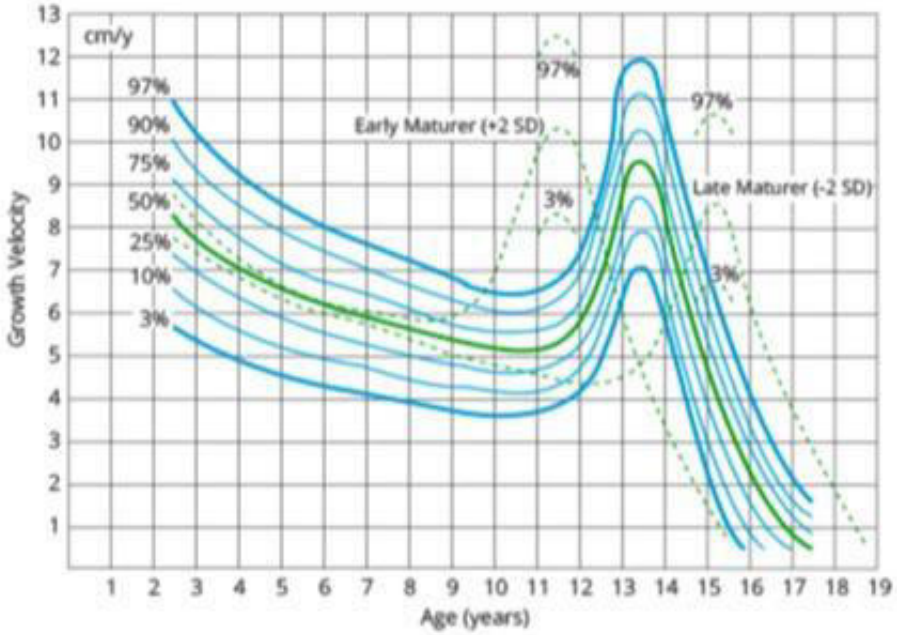
Weight unit: kg/year

Table 2. Normal Growth Velocity by Age

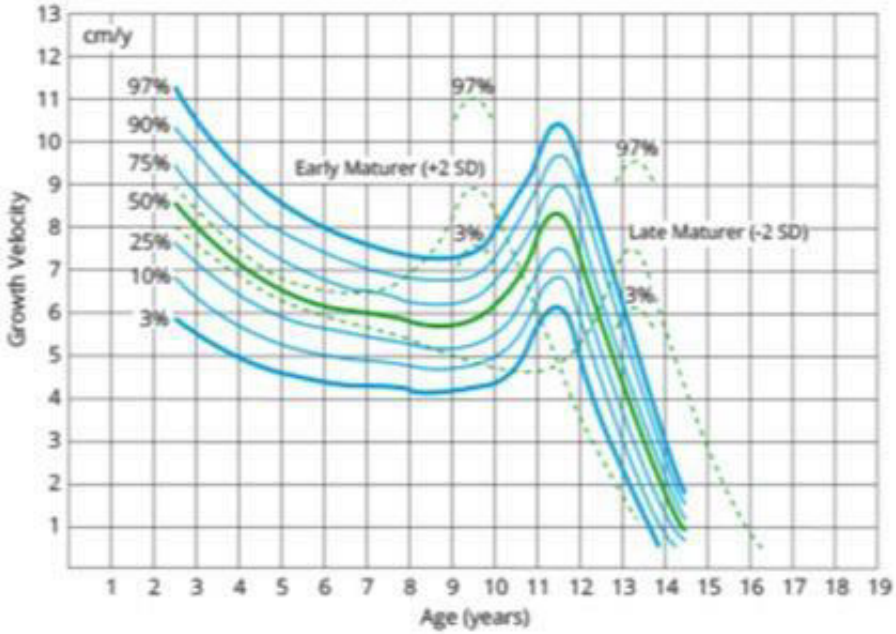
Age	*Growth velocity per year*
Birth to 12 months	23 to 27 cm (9.06 to 10.63 in)
12 months to 1 year	10 to 14 cm (3.94 to 5.51 in)
2 to 3 years	8 cm (3.15 in)
3 to 5 years	7 cm (2.76 in)
5 years to puberty	5 to 6 cm (1.97 to 2.36 in)
Puberty	Girls: 8 to 12 cm (3.15 to 4.72 in)
	Boys: 10 to 14 cm (3.94 to 5.51 in)

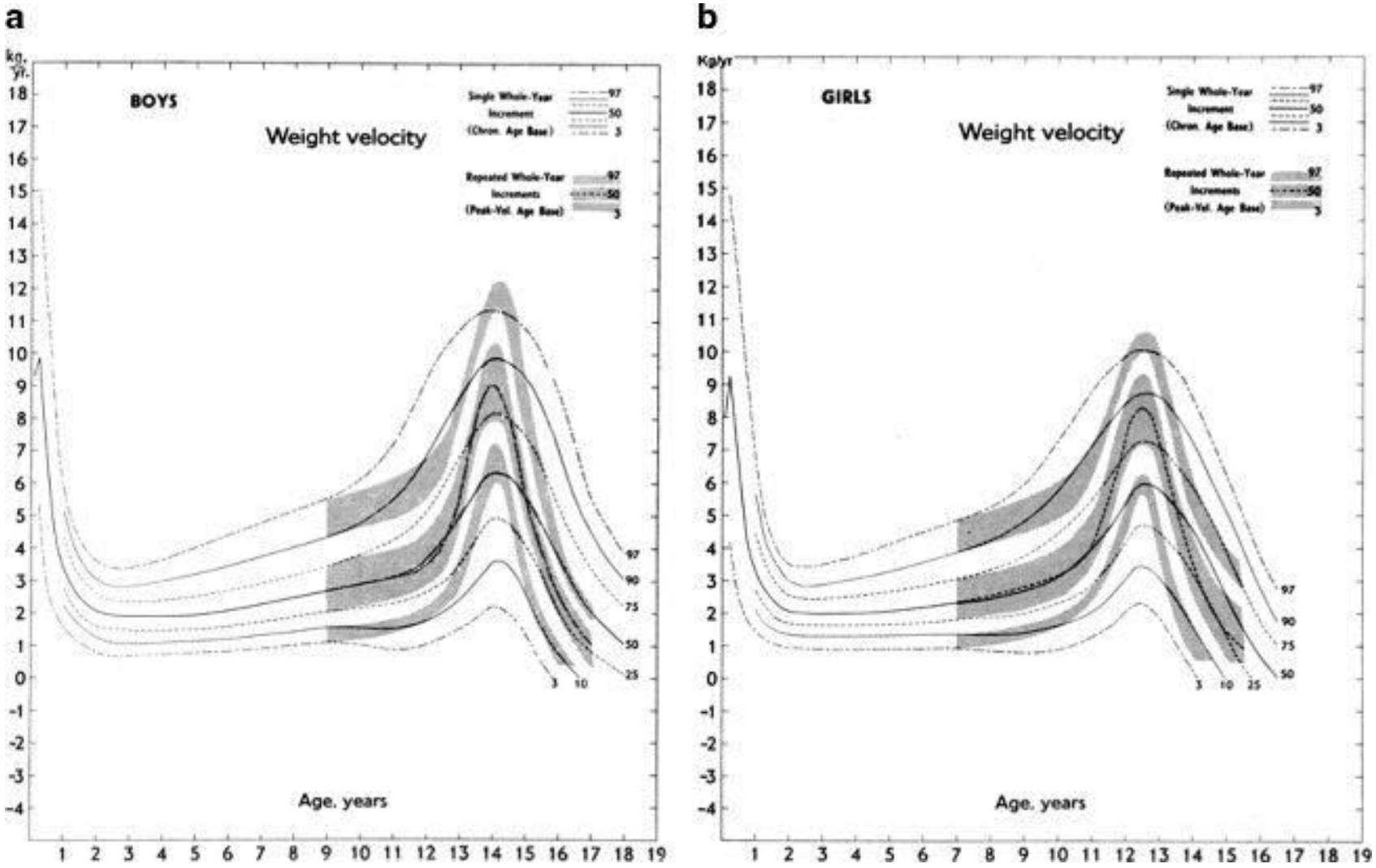
Information from references 1 and 9.

Boys


cm/y
Growth Velocity
97%
90%
75%
50%
25%
10%
3%
Early Maturer (+2 SD)
Late Maturer (-2 SD)
Age (years)

Girls


cm/y
Growth Velocity
97%
90%
75%
50%
25%
10%
3%
Early Maturer (+2 SD)
Late Maturer (-2 SD)
Age (years)


a
kg.
yr.
BOYS
Weight velocity
Single Whole-Year Increment (Chron. Age Base)
Repeated Whole-Year Increments (Peak-Vel. Age Base)
97
50
3
97
90
75
50
25
3
10
Age, years
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
b
Kg/yr
GIRLS
Weight velocity
Single Whole-Year Increment (Chron. Age Base)
Repeated Whole-Year Increments (Peak-Vel. Age Base)
97
50
3
97
90
75
50
3
10
25
Age, years
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

Midparental Height

Definition: estimated adult height of a child calculated on the basis of parental height.

Formula:

For a girl, midparental height is calculated as follows:

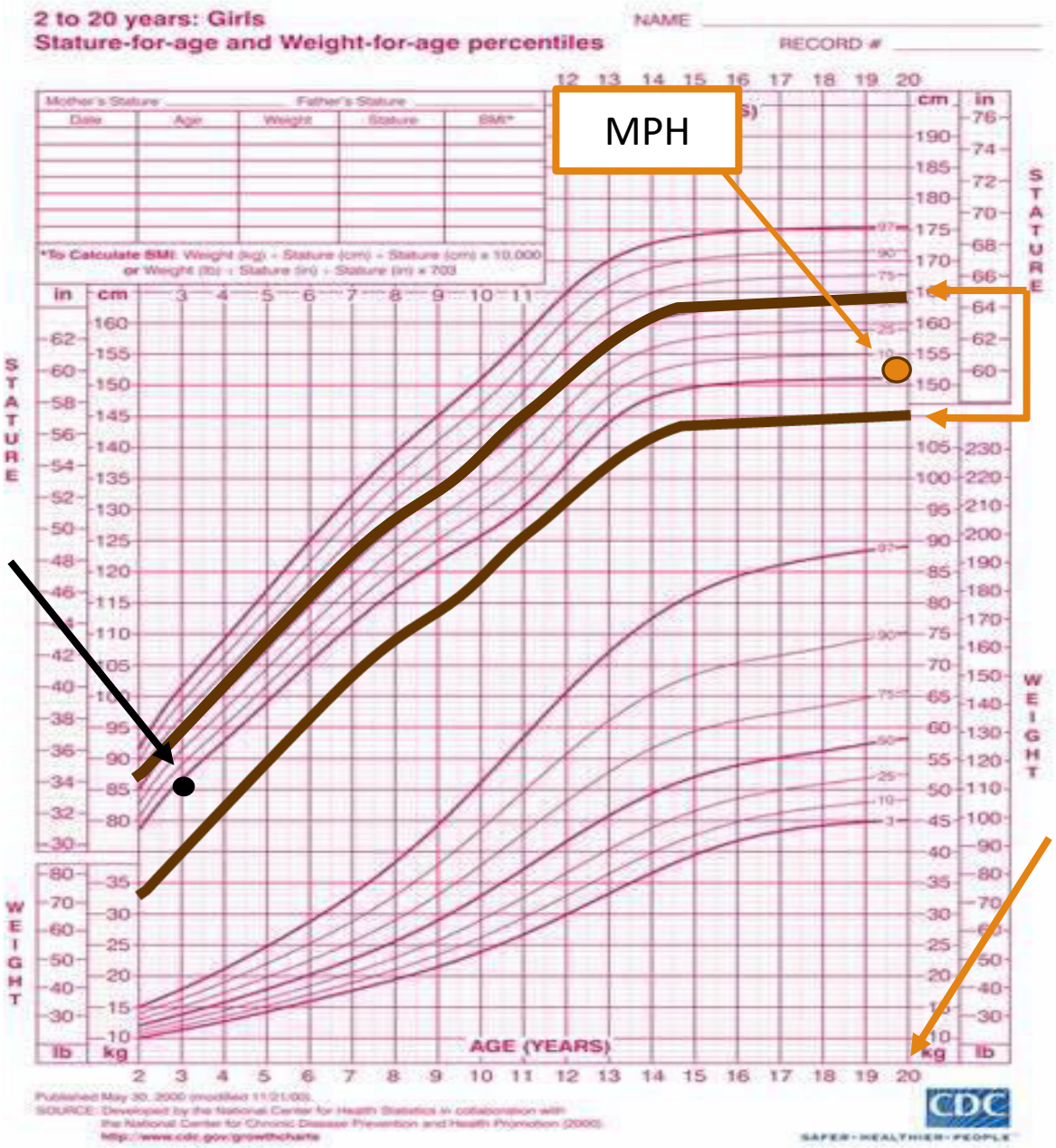
$$\frac{\text{Paternal height (inches)} + \text{Maternal height (inches)}}{2} - 2.5$$

For a boy, midparental height is calculated as follows:

$$\frac{\text{Paternal height (inches)} + \text{Maternal height (inches)}}{2} + 2.5$$

MBH

- EXAMPLE:3Y-GIRL
- Ht:85 CM
- Father Ht:165cm
- Mother Ht:155cm
- MPH: (165+155)-13/2= 153.5cm
- Plot on age 20Y
- 153.5±8.5cm
- 145cm-162cm



Bone Age

Definition: The maturity of a child's bone development. It is determined by comparing anterior posterior X-ray images of the nondominant, usually left, hand and wrist to images of bones in an atlas of skeletal development. It's useful for estimation of a child's future growth and adult height if put into relation with the chronological age.

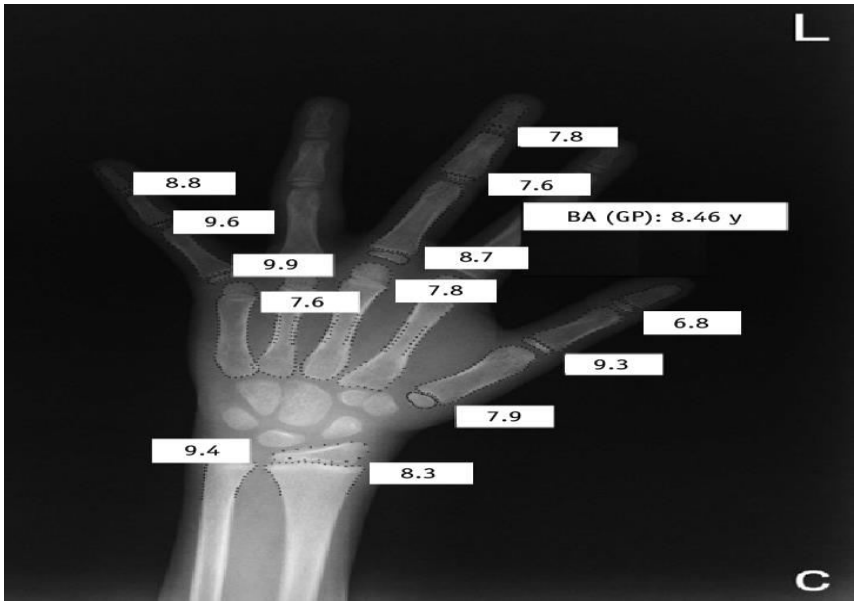


TABLE **173.1** Hormonal Effects on Growth

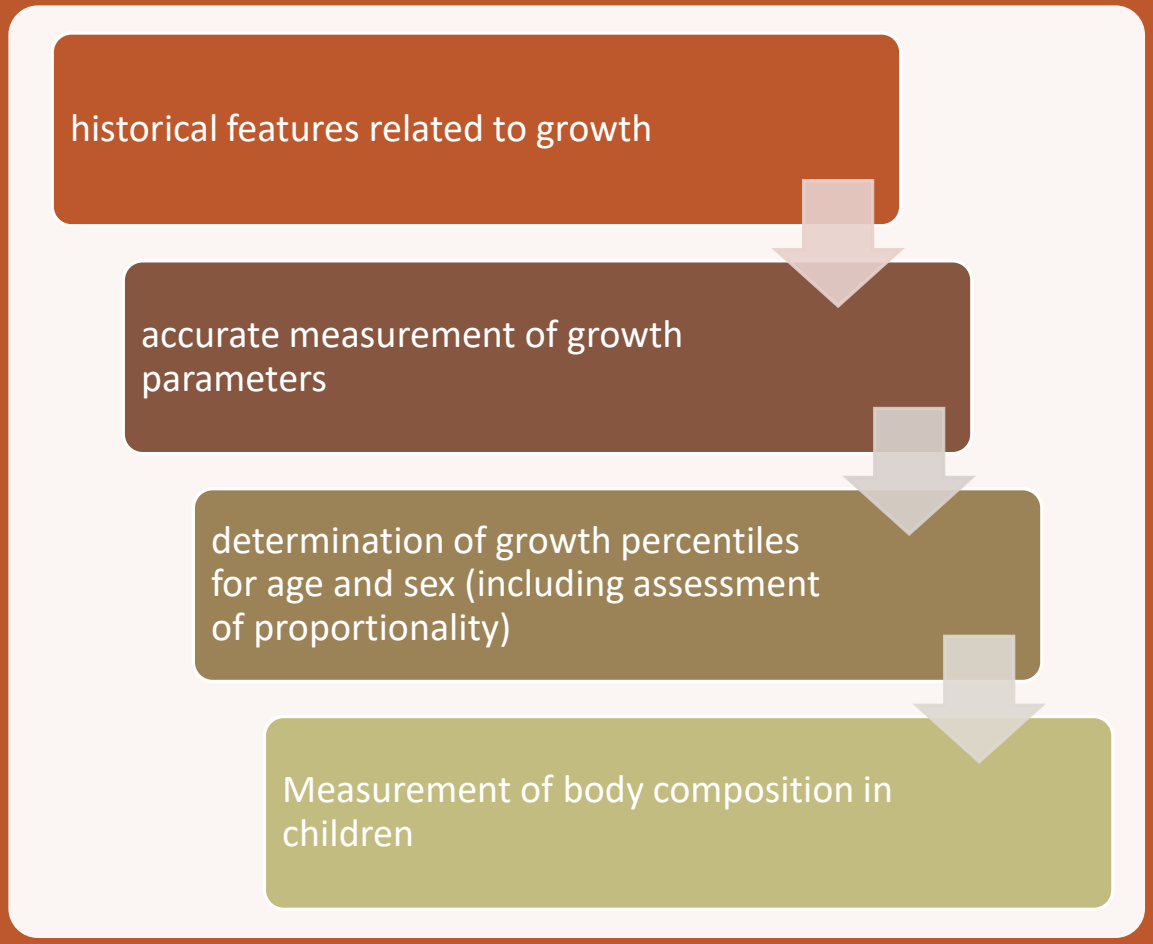
HORMONE	BONE AGE	GROWTH RATE	ADULT HEIGHT*
Androgen excess	Advanced	Increased	Diminished
Androgen deficiency	Normal or delayed	Normal or decreased	Increased slightly or normal
Thyroxine excess	Advanced	Increased	Normal or diminished
Thyroxine deficiency	Retarded	Decreased	Diminished
Growth hormone excess	Normal or advanced	Increased	Excessive
Growth hormone deficiency	Retarded	Decreased	Diminished
Cortisol excess	Retarded	Decreased	Diminished
Cortisol deficiency	Normal	Normal	Normal

**Effect in most patients with treatment.*

Modified from Underwood LE, Van Wyk JJ. Normal and aberrant growth. In: Wilson JD, Foster DW, eds. Textbook of Endocrinology. *8th ed. Philadelphia: WB Saunders; 1992.*

EVALUATION OF GROWTH

Evaluation of growth in children focuses on:



History The history should include:

- The weight, length, and head circumference at birth
- Prenatal history: maternal infection, intrauterine exposures (cigarettes, drugs, alcohol, and other toxins)
- Interval growth scan
- Past medical history
- Dietary history
- Developmental history
- Review of systems for symptoms (particularly vomiting or diarrhea)
- Family history, including parental heights, parental growth patterns, and timing of pubertal onset in parents (delayed growth and/or puberty in a parent suggests constitutional delay of growth)

Measurement

The physical examination should include careful measurements of weight, length, and head circumference.

The accurate measurement and charting of growth may **prevent** unnecessary evaluation or intervention in a child who has a **normal pattern of growth** or **who has a normal variant of growth**

Growth charts

Comparison	WHO Growth Chart	CDC Growth Chart
Studied population	Breastfed infants and toddlers	Breastfed and formula fed infants and toddlers
Growth pattern	How healthy children SHOULD GROW in ideal conditions	How certain groups of children HAVE GROWN in the past

Correcting for prematurity

It is important to correct growth parameters for gestational age (by subtracting the number of weeks the child was preterm from the child's postnatal age at the time of evaluation)

2009 United Kingdom-WHO growth charts suggest correction of all three parameters until age two years for children born before 32 weeks' gestation, and at least until age 12 months for children born between 32 - 36-weeks' gestation

Growth charts for special populations

- Down syndrome
- Turner syndrome
- Williams syndrome
- Achondroplasia
- Prader-Willi syndrome

Proportionality

Proportionality is the degree to which individual growth parameters correlate with each other.

1. **Weight-for-length**
2. **Body mass index:** proportion between the child's weight and the height squared. 15th – 85th />95th
3. **Ideal body weight -** The percent of ideal body weight (IBW) is another method to assess proportionality and nutritional status

Ideal body weight
The percent of ideal body weight (IBW)

Sex	IBW (kg)
Male	50+ (0.91×height (cm) -152.4)
Female	45.5+ (0.91×height (cm) -152.4)

IBW: Ideal body weight

$$\%IBW = \frac{Wt \times 100}{IBW}$$

- >120 – Obese
- 110 to 120 – Overweight
- 90 to 110 – Normal variation
- 80 to 90 – Mild wasting
- 70 to 80 – Moderate wasting
- <70 – Severe wasting

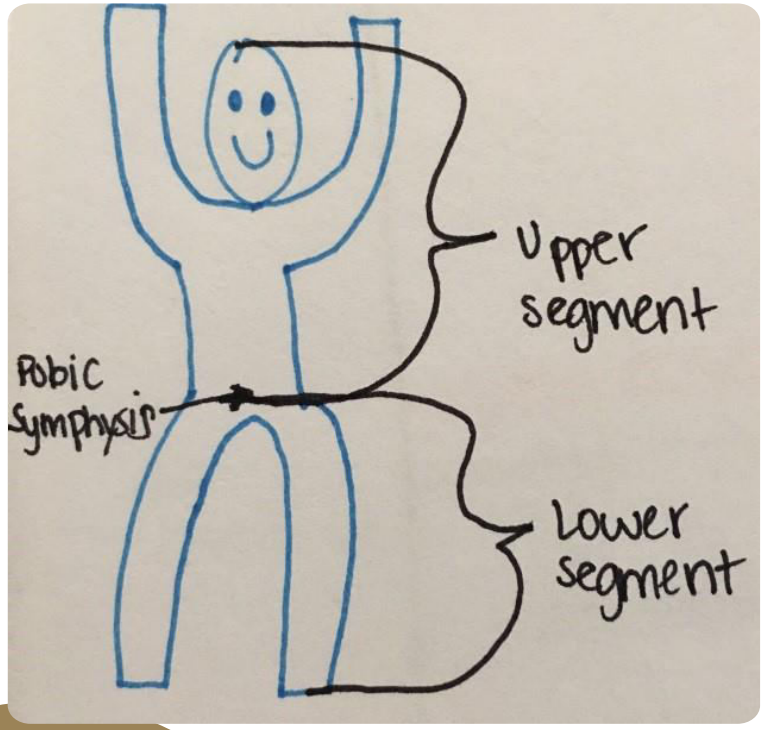
Body proportions

The proportions of the body change during fetal and postnatal growth.

The most commonly used descriptors of body proportions:

1. the ratio of the upper body segment to the lower body segment
2. the ratio of arm span to height.

Upper segment to lower segment

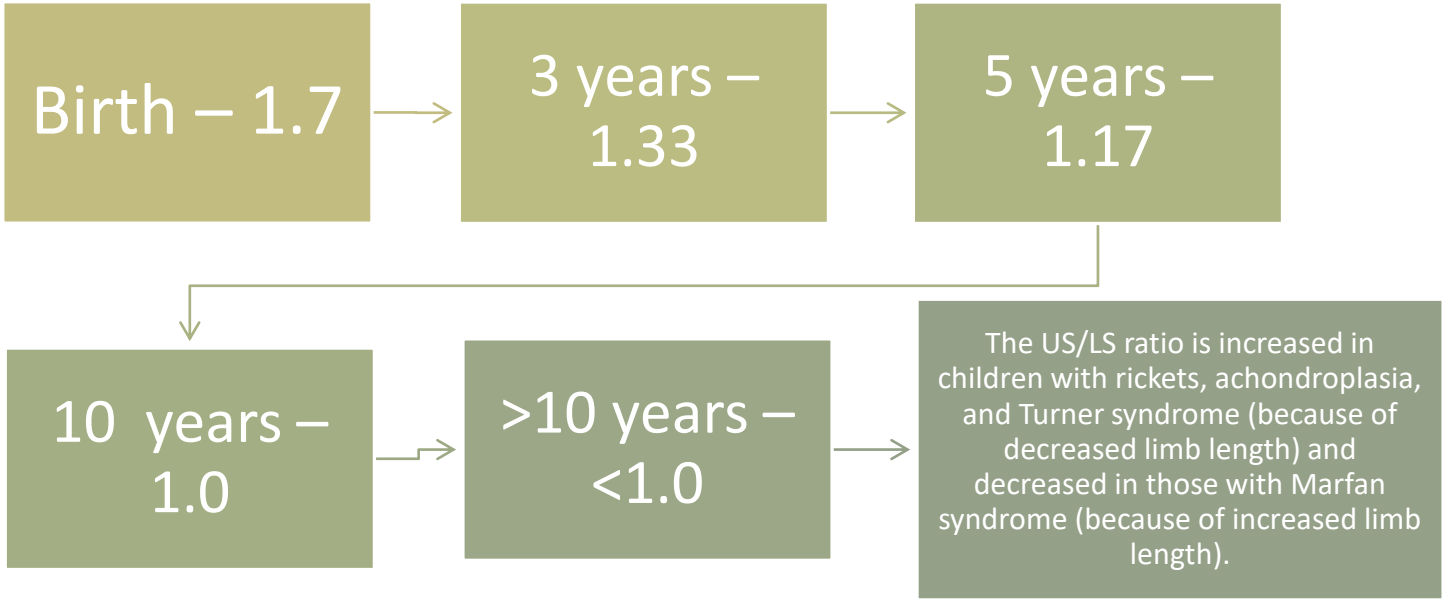


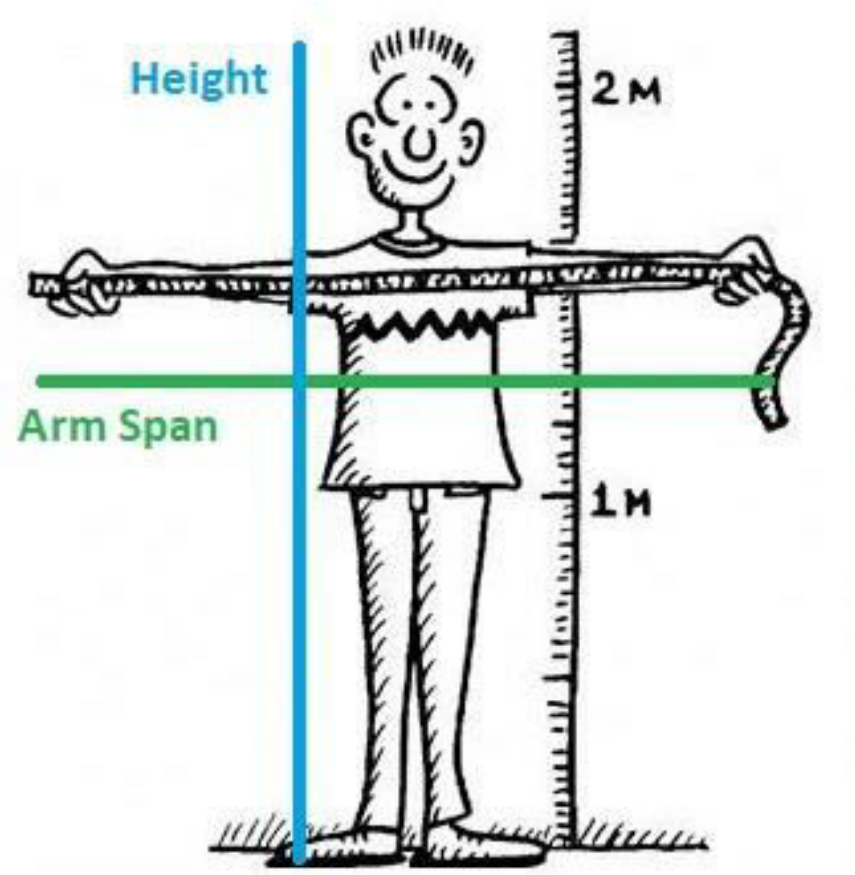
The upper segment to lower segment ratio (US/LS ratio) is helpful in distinguishing among causes of short or tall stature and in distinguishing disproportionate growth from immaturity

The lower segment is measured from the top of the symphysis pubis to the plantar surface of the foot.

The upper segment is calculated by subtracting the lower segment from the child's height.

Upper segment to lower segment





Arm span to height

The arm span is the distance between the tips of the middle fingers when the arms are raised to a horizontal position

The arm span-to height ratio is helpful in identifying conditions with a disproportion between the limbs and the trunk (eg, Marfan syndrome, in which the arm span usually exceeds height by at least 5 cm)

Arm span to height

At birth, the arm span is typically less than length (by at least 2.5 cm)
By approximately 10 years of age in males and 12 years of age in females, the arm span exceeds height
0 to 5 cm greater than height in approximately three-fourths of healthy children
5 to 10 cm greater in approximately one-fourth
≥10 cm greater in approximately 1 percent

Causes of short stature

1) Non-pathological :

- Constitutional delay of growth
- Familial short stature
- Idiopathic short stature

2) Pathological

- Nutrition
- Endocrine
- Syndromes
- Chronic diseases
- Skeletal
- Small for gestational age

Costitutional delay of growth

- results in childhood short stature but relatively normal adult height.
- Children with Constitutional delay are usually of normal size at birth. However, a downward shift in growth begins at three to six months of age that is parallel to that seen in most normally growing children in this age group but tends to be more severe and prolonged. By three or four years of age, children with Constitutional delay usually are growing at a lower limits of normal normal rate.
- In addition to a low preadolescent height velocity, they tend to have delayed development of secondary sexual characteristics.

- The hallmark of constitutional delay is delayed skeletal age ; it is more closely related to the height age (age at which one's height would be average) than the chronologic age, height data should be interpreted according to bone age rather than chronologic age to accurately reflect height potential.
- Because the bone age is delayed, growth typically continues longer than normal, often resulting in adult stature within the normal range.
- In many cases, there is a family history of delayed growth and puberty in one or both parents

Familial or genetic short stature

- refers to the stature of a child of short parents, who is expected to reach a lower than average height and yet normal for these parents
- Their bone age is consistent with their chronologic age, which helps distinguish them from children with constitutional delay of growth
- Individuals with familial short stature usually have low-normal height velocity throughout life. The otherwise normal height velocity generally distinguishes these children from those with pathologic causes of short stature.

Idiopathic short stature

- Definition : is a height below 2 standard deviations (SD) of the mean for age, in the absence of any endocrine, metabolic, or other diagnosis.
- These children have normal (often at the lower limit) height velocity and no biochemical or other evidence for a specific growth-retarding condition, which implies normal results for endocrine screening tests.
- ISS is a diagnosis of exclusion. The child's height percentile is below the range predicted by the mid-parental height and the bone age is not delayed, but there is no evidence of underlying genetic, systemic, or endocrine disease

Undernutrition

- Undernutrition is the most common cause of poor growth globally.
- In many cases, undernutrition is isolated, caused by inadequate food supply (due to poverty) or self-imposed restriction (due to fear of obesity).
- In other cases, undernutrition is related to an underlying systemic disease that interferes with food intake or absorption or increases energy needs.

Endocrine causes of short stature

1) Growth hormone deficiency

- **Idiopathic** : most common cause of both congenital and acquired GH deficiency.

- **Congenital** : could be isolated GH deficiency , with other pituitary hormone deficiencies , with pituitary agenesis or gene deficiencies .Affected children present with pronounced postnatal growth failure, delayed bone age, and very low serum concentrations of growth hormone, IGF-1, and IGF-binding protein-3 (IGFBP-3; the major circulating binding protein for IGF-1). Additional findings are hypoglycemia, prolonged conjugated hyperbilirubinemia, midface hypoplasia, hypotonia, high-pitched voice .

- **Acquired** : intracranial tumor , cranial irradiation and head trauma.

(2) Hypothyroidism — Growth failure is a well-recognized consequence of hypothyroidism during childhood and may be the presenting feature.

- The bone age is delayed
- many children with hypothyroidism have a reasonably normal growth potential once the disorder is identified and treated.
- The evaluation should include measurements of both TSH and free thyroxine to allow detection of both primary and central hypothyroidism.

(3) Precious puberty : increased secretion of gonadal steroids (estradiol in girls and testosterone in boys), which have two consequences :

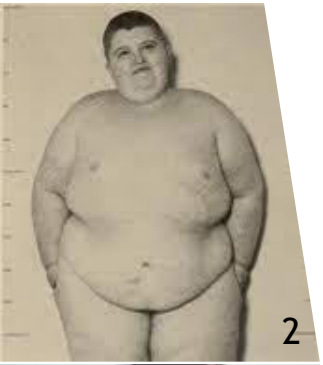
1. One is sexual precocity.
2. The other is accelerated epiphyseal maturation, which causes rapid childhood growth but more rapid advancement of bone age (tall as a child , short as an adult)

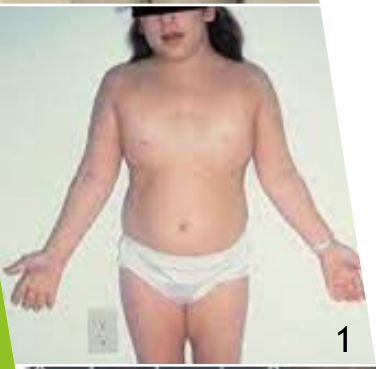
(4) Cushing syndrome : Cushing syndrome is caused by excessive glucocorticoids and is characterized by the combination of weight gain and growth retardation, resulting in excessive weight-for-height

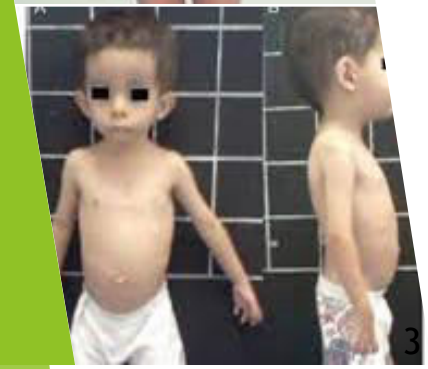
(5) Diabetes mellitus under poor control

(6) Diabetes insipidus (untreated)

(7) Hypophosphatemic vitamin D-resistant rickets







Syndromes of short stature

- **Turner syndrome** -- Virtually all girls with Turner syndrome have short stature, with an average adult height approximately 20 cm shorter than predicted by the mid-parental height. In addition, affected patients usually have absent or very delayed pubertal maturation and may have a square "shield" chest and webbed neck.(1)
- **Prader-Willi syndrome** — Prader-Willi is the most common syndromic form of obesity. Obesity and hyperphagia typically develop during early childhood and can be severe. Other common clinical characteristics are hypotonia and feeding problems during infancy, developmental delay, and hypogonadism. Short stature is common but may not develop until late childhood when the child fails to undergo a pubertal growth spurt.(2)
- **Silver-Russell syndrome** —is characterized by severe intrauterine growth restriction and postnatal growth retardation with a prominent forehead, triangular face, downturned corners of the mouth, and body asymmetry (hemihypertrophy).(3)
- **Laurence-Moon-Bardet-Biedl syndrome** -- is characterized by retinitis pigmentosa, hypogonadism, and developmental delay with an autosomal dominant inheritance pattern. Laurence-Moon syndrome is associated with spastic paraplegia
- **Noonan syndrome**
- **Trisomy 13 , 18 , 21**

Chronic diseases

- **Cardiac disease** — Growth failure is common in children with severe heart disease of any cause. The major pathogenetic factors are thought to be hypoxia, anorexia, and increased basal energy requirements .
- **Pulmonary disease** — Cystic fibrosis is predominantly a pulmonary and gastrointestinal disease. Growth failure in children with this disorder may be caused by multiple mechanisms, including poor food intake, maldigestion or malabsorption, chronic infection, and increased energy requirements (work of breathing) . Asthma (sever steroid dependent)
- **Gastrointestinal** -- celiac disease , crohn disease , IBD Hepatic disorders
- **Hematological disorders** -- sickle cell anemia , fanconi anemia and thalassemia
- **Renal diseases** (Chronic kidney disease) — Growth failure is seen in at least one-third of children with chronic kidney disease. The primary causes of growth faltering in children with chronic kidney disease are disturbances of growth hormone metabolism and its main mediator, insulin-like growth factor 1 (IGF-1). Other factors may include metabolic acidosis, uremia, poor nutrition secondary to dietary restrictions.

- **Immunologic disease** — immune deficiency disorders , Human immunodeficiency virus (HIV) infection is associated with growth failure.

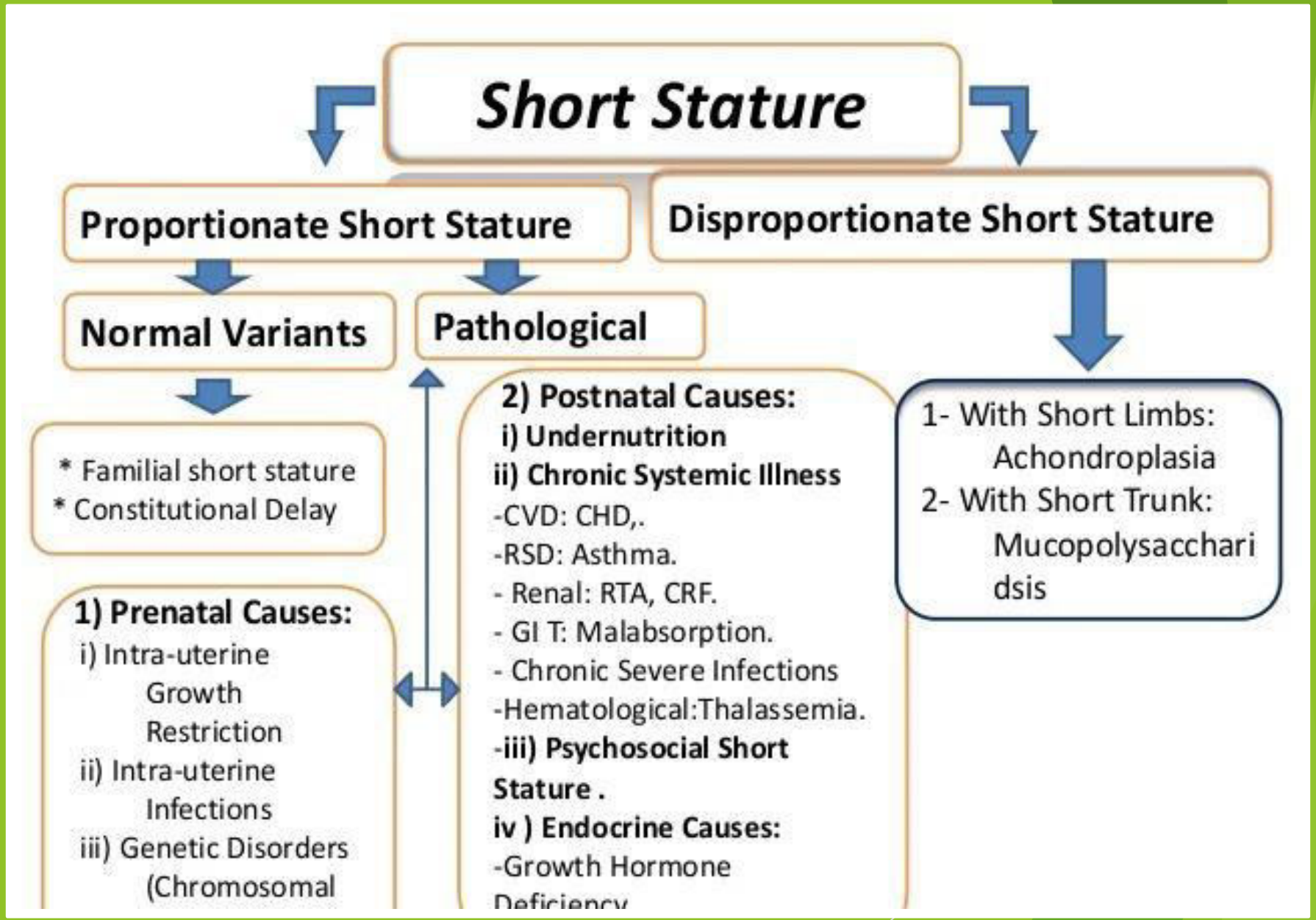
- **Cancer** — Children with cancer may grow poorly before diagnosis because of poor food intake, nausea, vomiting, and increased caloric utilization. After diagnosis, anorexia, nausea, and vomiting induced by chemotherapy and radiotherapy also can contribute to impaired growth.
- **Rheumatologic disease** — Childhood rheumatologic diseases, especially systemic juvenile idiopathic arthritis, are frequently associated with growth retardation. This may be a consequence of the proinflammatory cytokines associated with disease activity and is also caused by the high-dose glucocorticoids that are often used for treatment .

Skeletal , skeletal dysplasias /growth plate abnormalities

- Scoliosis
- Skeletal dysplasia (osteogenesis imperfecta , osteochondroplasias , achondroplasia) associated with short stature are caused by inherited defects in cartilage/bone development and are often associated with disproportionate short stature (with limbs disproportionately short for the trunk or vice versa). These disorders should be suspected in a child presenting with short stature and bone deformities, recurrent fractures, or abnormal findings on radiographs (eg, enchondromas, bowing or shortening of the long bones, vertebral defects, or rib abnormalities).

Small for gestational age

- Approximately 10 percent of infants born SGA fail to experience catch-up growth sufficient to be within the normal range by two years of age. This growth pattern is more likely in those with severe SGA and can be considered pathologic, although the underlying mechanisms are unclear and likely vary.


Short Stature
Proportionate Short Stature
Disproportionate Short Stature
Normal Variants
Pathological
* Familial short stature
* Constitutional Delay
1) Prenatal Causes:
i) Intra-uterine Growth Restriction
ii) Intra-uterine Infections
iii) Genetic Disorders (Chromosomal
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
1- With Short Limbs: Achondroplasia
2- With Short Trunk: Mucopolysaccharidsis

Diagnostic approach for short stature:

Q : WHICH CHILDREN REQUIRE EVALUATION FOR SHORT STATURE ?

Ans: Any children with short stature should be evaluated with careful serial measurements of length or height and compared with reference of standards curve of hight for age and sex.

The clinical significance of the short stature depends on many factors, especially 1)height velocity, 2)severity of the short stature, and 3)genetic potential.
Many children with moderate short stature and normal growth (eg, height velocity at least 5 cm/year between four and six years of age and at least 4 cm/year between six years and puberty) require only a basic evaluation (including Hx, PEx, and bone age evaluation)

A more comprehensive evaluation is required in children with one or more of the following features:

.Growth failure – This is suggested if a height-for-age curve has deviated downward or stunted, acrossing two major height percentile curves (eg, from above the 25th percentile to below the 10th percentile),

or if the child is growing slower than the following rates:

Age two to four years – Height velocity less than 5.5 cm/year (<2.2 inches/year)

Age four to six years – Height velocity less than 5 cm/year (<2 inches/year)

Age six years to puberty:

-Height velocity less than 4 cm/year for boys (<1.6 inches/year)

-Height velocity less than 4.5 cm/year for girls (<1.8 inches/year)

- Features that raise concerns for hypothalamic-pituitary adrenal axis dysfunction, either congenital (eg, hypoglycemia, microphallus, cryptorchidism, or wandering nystagmus) or acquired (eg, intracranial tumor, cranial irradiation, or head trauma), with decelerating growth, even if the child's height is within the normal range.

DIAGNOSTIC APPROACH:

The first step is to evaluate for other causes of growth failure, which can be established by detailed medical history and physical examination including chronic systemic disease manifestation(celiac, Crohn's, CKD, hypothyroidism symptoms, Turner syndrome feature (in girls), and skeletal disorders.

Laboratory evaluation should be performed when appropriate, including screens for systemic disease, undernutrition, inflammation marker, and thyroid function test, and a karyotype in girls to rule out Turner syndrome.

- If there is no evidence of these disorders, then the possibility of GHD should be investigated with the following tests:

- Insulin-like growth factor 1 (IGF-1)
- Insulin-like growth factor binding protein-3 (IGFBP-3)
- provocative testing for GH

Key point: GHD is effectively excluded in children with a normal bone age and height velocity. In this case, provocative testing for GHD is not required.((Familial short stature))

Investigation tests and images for evaluating short stature:

- CBC/BLOOD FILM →
- CRP/ESR/LDH→
- URINANLYSIS→
- STOOL ANALYSIS→
- KFT→
- TFT/PTH→
- LFT→
- CELIAC SERIOLOGY→(Anti tTG, ENDOMYLASE, AND GLIDEN ANTIBODY)
- SWEAT CHLORID TEST→ CF
- FSH/KARYOTYPE→ TURNER SYNDROM
- GENATIC TESTING → SKLETAL DYSPLASIA
- EARLY MORNING CORTISOL LEVEL
- IGF-1/IGFBP-3
- PROVACTIVE GH TEST

- BONE AGE→
- MRI WITH AND W/O CONTRAST →

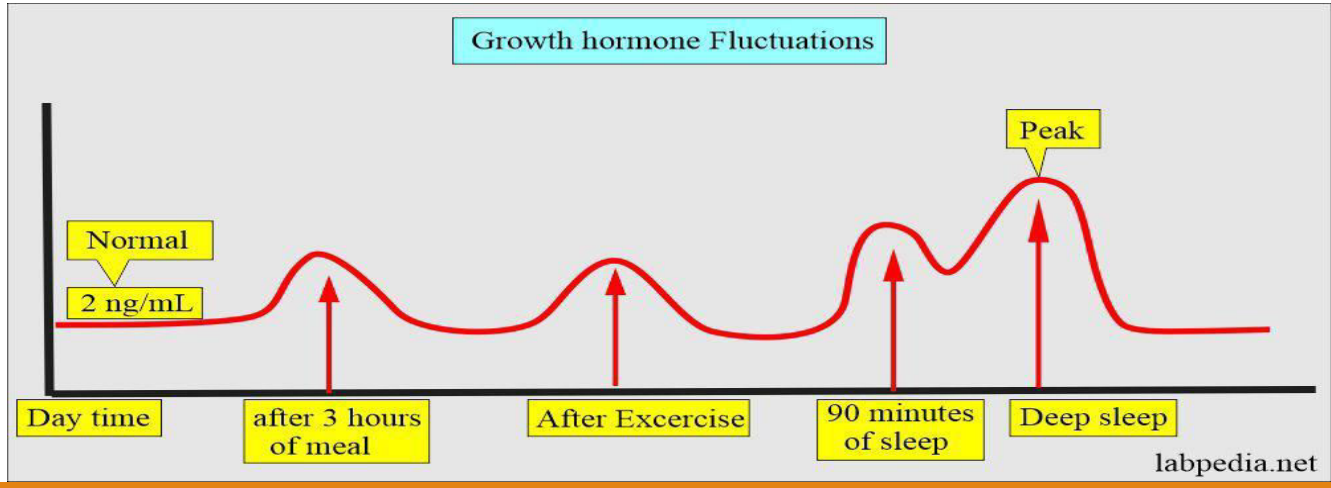
Laboratory tests	Significance
Blood	
Hemoglobin	Chronic anemia
Creatinine, albumin, sodium, potassium, calcium, phosphate, alkaline phosphatase	Renal diseases, rickets and malabsorption
IgA anti-endomysium, IgA anti-transglutaminase, total IgA	Celiac disease
Free-T4, TSH	Hypothyroidism
FSH, karyotype	Turner syndrome in girls
IGF-I, IGFBP-3	First screening for GH deficiency or GH resistance
Acid-base balance (0-2 years)	Renal tubular acidosis
Urine	
pH, glucose, proteins, blood	Renal diseases

T4: thyroxine; TSH: thyrotropin; FSH: follicle stimulating hormone; IGF-I: insulin like growth factor-I; IGFBP-3: IGF binding protein-3, GH: growth hormone

TESTING FOR GROWTH HORMONE DEFICIENCY:

The assessment of pituitary GH production is quite difficult, because GH secretion is pulsatile, with the most consistent surges during stages 3 and 4 of sleep. The regulation of GH secretion involves at least two well-studied hypothalamic factors, GH-releasing hormone (GHRH; stimulatory) and somatostatin (inhibitory).

- Between normal pulses of GH secretion, serum GH levels are often low, below the limits of sensitivity of most conventional assays. Thus, measurement of a random serum GH level is not helpful in diagnosing GHD.



IGF-1 and IGFBP-3: (the mediators of most of the growth-promoting actions of GH)

Advantages:

*Their concentrations often reflect the integrated concentration of secreted GH

*Unlike the pulsatile secretion of GH, IGF-system peptides are stable during the day (serum half-lives of 12 to 16 hours).

Interpretation of test results:

If the IGF-1 and IGFBP-3 (SD ≥0); ie, in the upper one-half of the normal range →GHD is extremely unlikely, and no further testing is required(normal level).

If the IGF-1 and IGFBP-3 (eg, between 0 and -2 SD) →The decision about whether to perform provocative GH testing depends on individual patient characteristics, including the severity of growth failure, degree of bone age delay, and whether the low levels can be explained by other factors, such as poor nutrition(somewhat low).

IGF-1 and IGFBP-3 (eg, <-2 [SD]) with delayed bone age → high possibility of GHD, should be explored by provocative GH testing(moderate to severe low level)(dwarfism).

Growth hormone provocative(stimulation) tests:

Indications — Provocative (stimulation) GH testing is indicated for most patients to confirm a diagnosis of GHD. Because this testing has strong limitations, the results should not be used as the sole diagnostic criterion, and should be interpreted in the context of auxological findings, bone age, and IGF-1 and IGFBP-3 concentrations

- Limitations:

*The tests are non-physiologic.
*The cutoff level of "normal" is arbitrary and may depend on the specific provocative agent used.
*The interpretation of the test results depends upon age and sex hormone concentrations.
*The tests are expensive, uncomfortable, and carry some risks.

Limitations of provocative testing for growth hormone deficiency in children

Pharmacologic testing is not physiologic
Normality is arbitrarily defined, if defined at all
Reproducibility in both normal and abnormal children is poor, even when the same test is performed
Age and sex steroid hormone status affect the response
Nutritional adequacy and body composition (particularly, adiposity) can affect response
There is no standard serum growth hormone assay, and there are large interassay variations among the assays in use
All of the tests are costly

UpToDate

Choice of provocative(stimulus) agent:

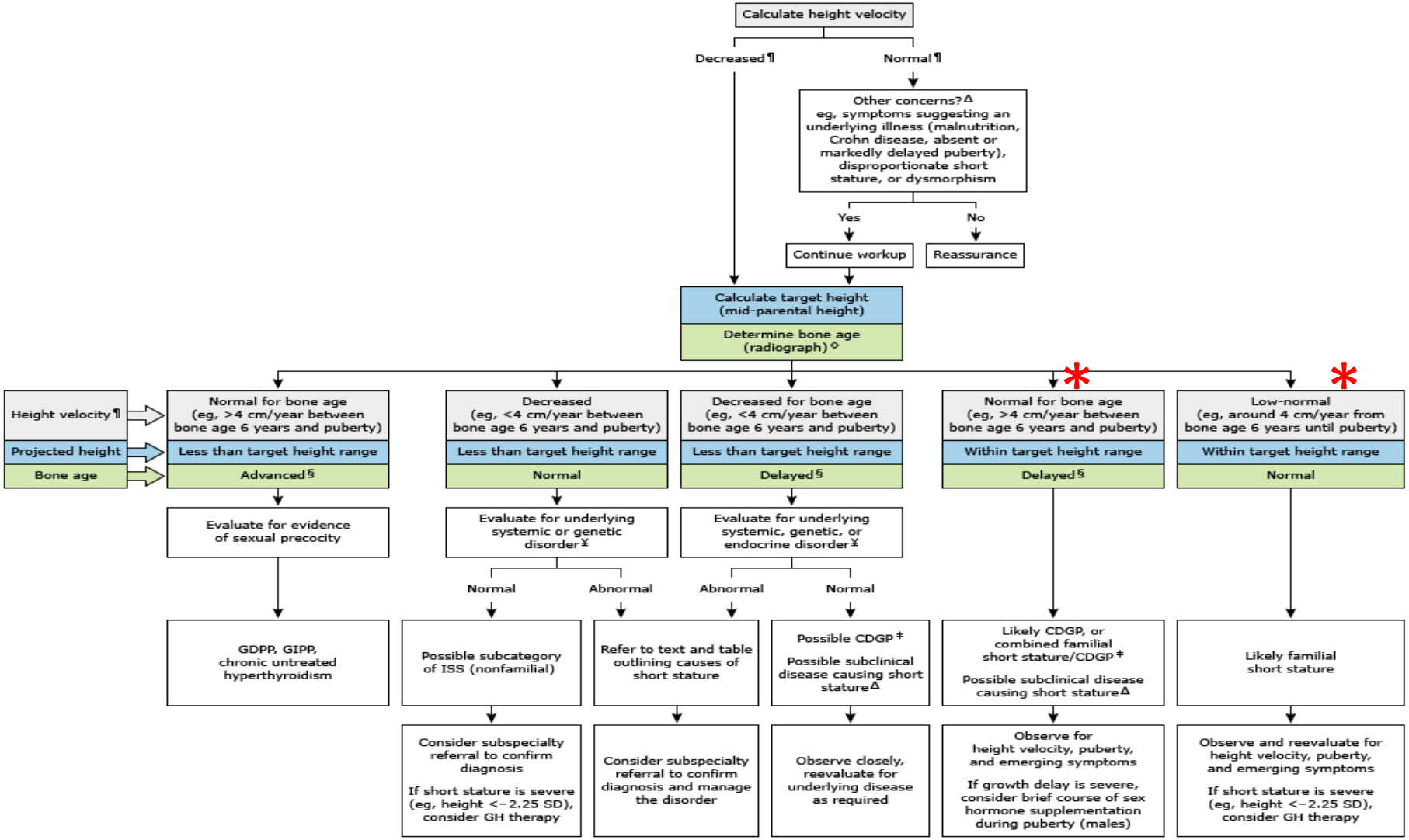
Clonidine: stimulates GH by several mechanisms. administered orally at a dose of 5 mcg/kg (maximum 250 mcg), and serum GH is measured at 0, 30, 60 and 90 minutes; peak GH secretion typically occurs one hour after the stimulus is given. Clonidine may cause modest hypotension and hypoglycemia, so patients should be monitored for these problems during the test. Also, it have a relatively good specificity.

Arginine – An intravenous infusion of 0.5 g/kg body weight (to a maximum of 40 g) is given over 30 minutes, and serum GH is measured at 0, 30, 60, 90, and 120 minutes [64]. The maximum GH peak is expected at approximately 60 minutes. There are no side effects from this test, GH secretion can be enhanced (and therefore false-positive results reduced) by adding a dose of L-Dopa orally just prior to the administration of arginine.

Glucagon – Administration of glucagon causes transient hyperglycemia, which in turn stimulates endogenous insulin secretion, followed by controlled hypoglycemia and consequent GH secretion. It is less risky than insulin-induced hypoglycemia and is a good choice for infants and young children. Glucagon is administered subcutaneously at a dose of 0.03 mg/kg (maximum 1 mg), and serum samples are drawn at intervals between one and three hours after the stimulus. Peak GH secretion occurs between two and three hours after glucagon administration; side effects are mild and transient and include nausea, vomiting, sweating, or headaches.

Insulin-induced hypoglycemia – Insulin-induced hypoglycemia is a potent stimulant of GH release and is therefore among the most specific tests for GHD, However, this test is less commonly used in children because of safety concerns.

Algorithm for the evaluation of a child with short stature*



Treatment of growth hormone deficiency in children:

Recombinant human growth hormone (rhGH)

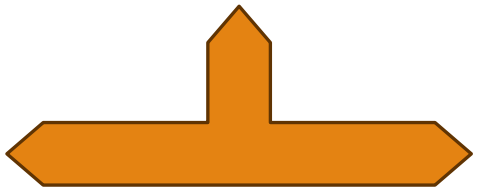
Is the primary treatment for growth hormone (GH) deficiency-induced short stature.

Is appropriate for children with GH deficiency whose epiphyses are still open. The growth response is greater when rhGH is initiated at younger versus older age.

Is also prescribed for short stature associated with small for gestational age (SGA), chronic kidney disease, Turner syndrome, Prader-Willi syndrome, mutations in the SHOX gene, and Noonan syndrome…

Formulations of growth hormone

Once-daily formulations:
Most children with GHD are treated with.
biosynthetic recombinant human growth hormone.
administered by subcutaneous injection.
equally biopotent and have the same natural sequence structure as endogenous human GH.(e.g, somatropin)



Long-acting formulations
two type: sustained-release preparations of rhGH, and analogues of rhGH with additional peptides or fatty acids or bound to larger molecules(e.g, Lonapegsomatropin, Somapacitan)

Laboratory monitoring — For children who achieve IGF-1 levels in the target range (0<IGF-1>+2SD)after initial dose adjustments, we continue rhGH therapy and measure IGF-1 levels every 6 to 12 months.

For patients with multiple pituitary hormone deficiencies, adrenal and thyroid function should be reassessed a few months after initiation of rhGH therapy and periodically by measuring 8 to 9 AM serum cortisol and free T4, respectively. Free T4 should be measured because this type of hypothyroidism is usually central and would not be detectable with thyroid-stimulating hormone (TSH) screening alone

ADVERSE EFFECTS OF GROWTH HORMONE THERAPY

the most common treatment-associated complaint is headaches, which usually are benign.
increased intraocular pressure,
slipped capital femoral epiphysis, and worsening of existing scoliosis

Other rare adverse effects are severe hypersensitivity reactions, pancreatitis, transient gynecomastia

Algorithm for growth hormone therapy in children