Short Stature

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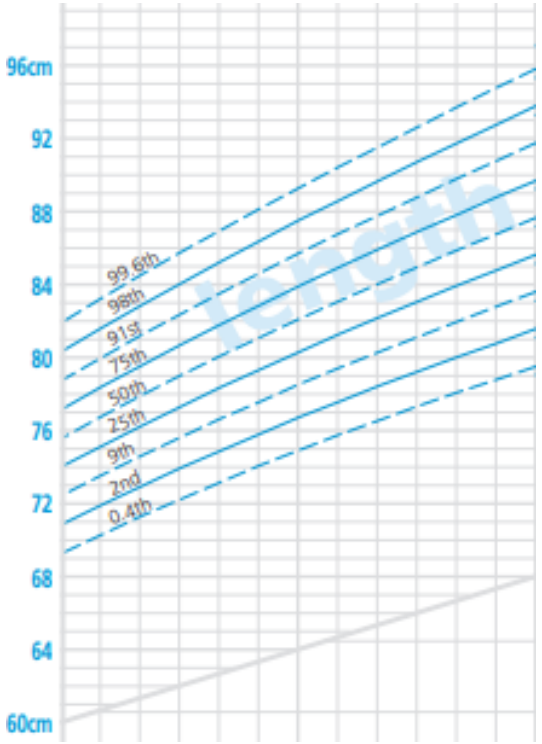
Aims/Objectives

- By the end of this session, you should be able to…
- Recognize what short stature is
- Describe what normal growth is
- Categorize the different causes of short stature
- Discuss the important aspects of the history of a child with short stature
- Explain the important parts of the examination of a child with short stature
- Demonstrate the investigations that are needed to aid diagnosis of short stature

Recognize What Short Stature Is

What is it?

- Height ≤ -2 SD below mean for age
- Height < 0.4th centile
- Height significantly below genetic potentials (-2SD below mid-parental target)
- Downwardly crossing centile channels on growth chart e.g. ≤ -2 (> 18 months age)



Describe What Normal Growth Is

Normal Growth

- Average height velocity at different phases:

  Prenatal growth: 1.2-1.5 cm/week

  Infancy: 23-28 cm/year

  Childhood: 5-6.5 cm/year

  Puberty: 8.3 cm/year (girls), 9.5 cm/year (boys)

<u>Prenatal Growth:</u>

- Uterine size, placental function, maternal nutrition, insulin, insulin-like growth factors (IGFs), and IGF-binding proteins (IGFBPs)

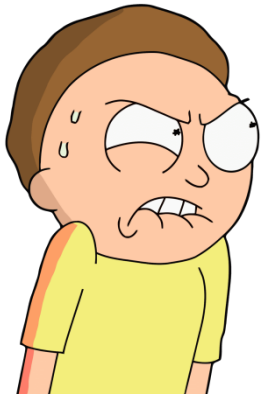
Normal Growth

Infantile Phase

Nutrition

Childhood Phase

Growth Hormone
Thyroid
Nutrition



Puberty Phase

Growth Hormone
Sex Hormones

Normal Growth

Infantile Phase

- <u>Infantile Growth:</u>
- Birth to 2-3 years of age
- Characterized by initial rapid growth rate (up to 2.5cm/month) that declines progressively
- Babies born large or small for their genetic potential will "channel" to their correct percentile in their first 2 years.
- Predominantly under nutritional control

Normal Growth

Childhood Phase

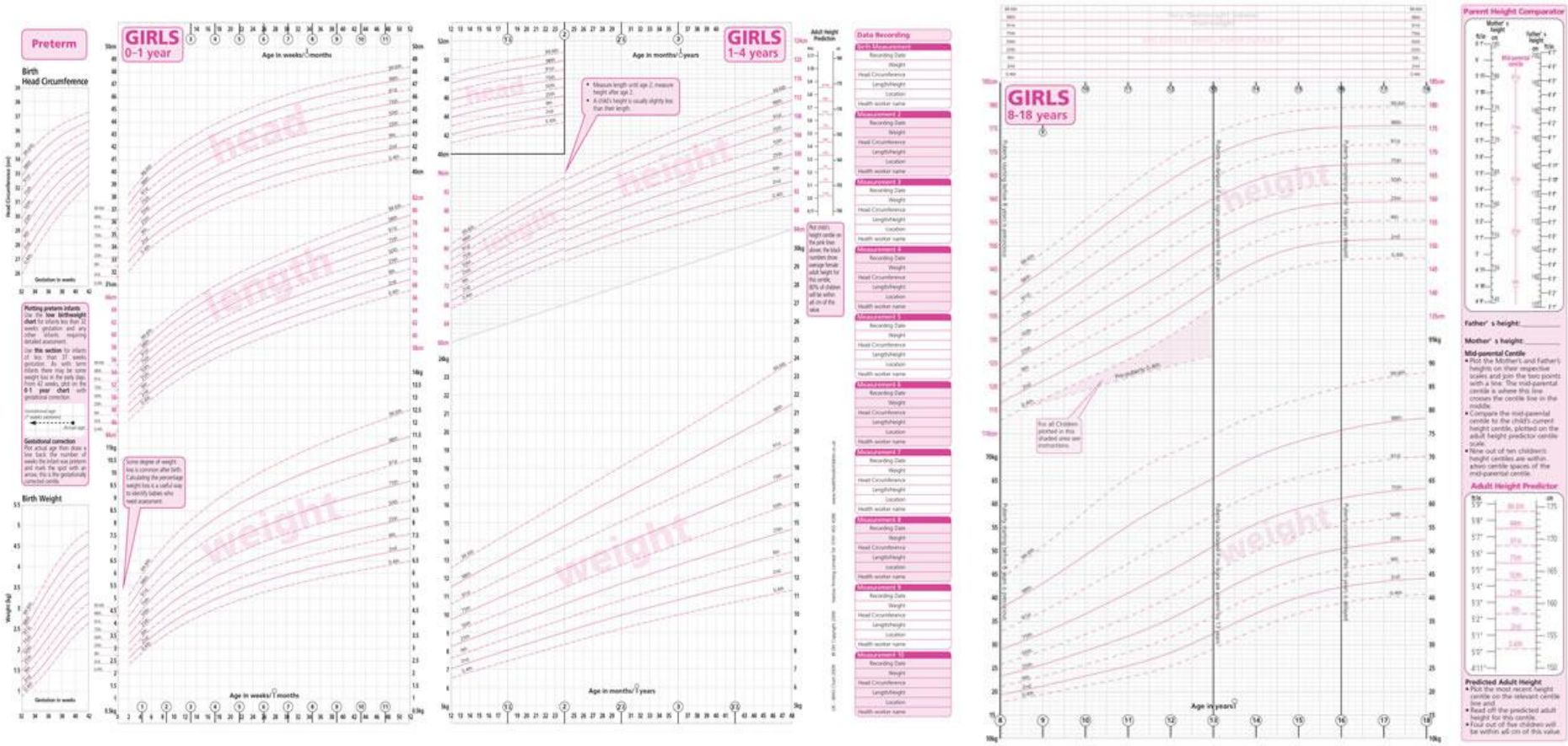
- <u>Childhood Growth:</u>
- Starts 2-3 years of age
- Steady and slowly decelerating growth curve
- Growth hormone, thyroid hormones, nutrition, and insulin play major roles at this time.

Normal Growth

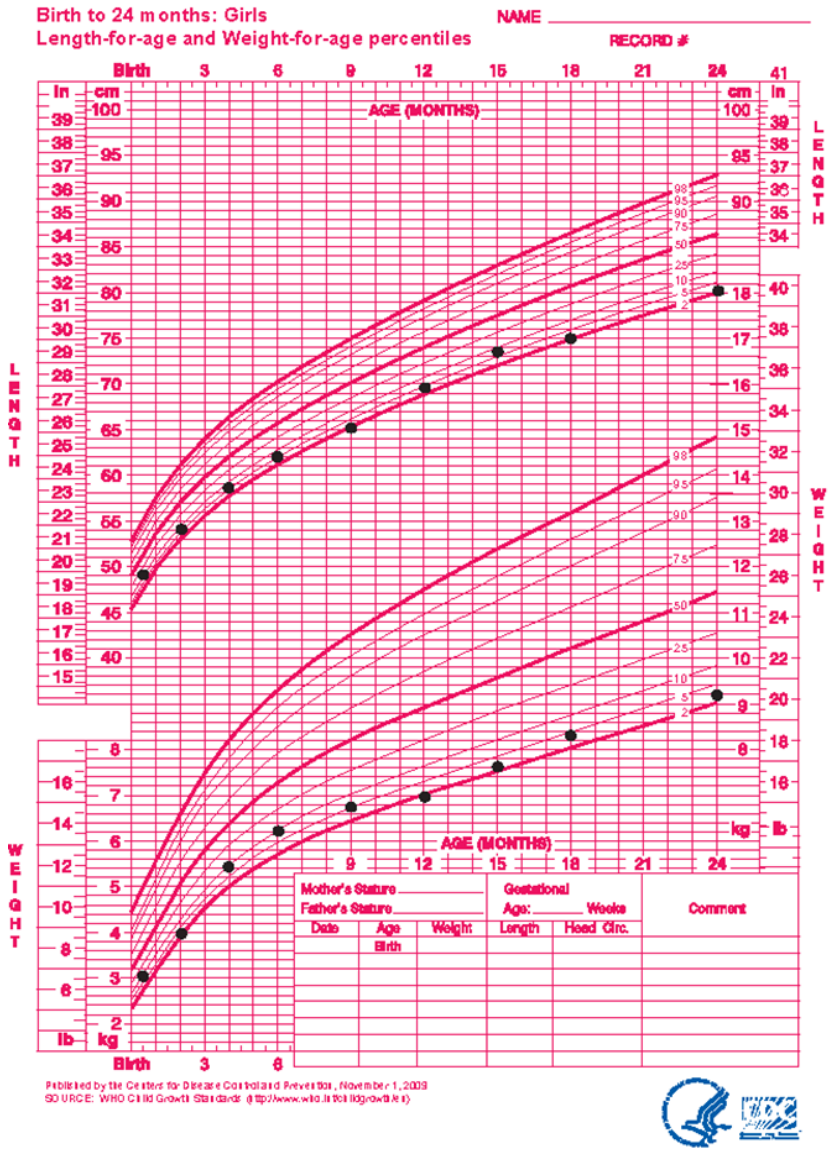
Puberty Phase

- <u>Pubertal Growth:</u>
- Immediately prior to puberty, growth usually slows down ("prepubertal dip"), only to be followed by the pubertal growth spurt
- Sex hormones exert important growth effects during puberty, in addition to other factors such as growth hormone, thyroid hormones, nutrition, and insulin
- Girls have their growth spurt early in puberty
- Boys experience their growth spurt toward the end of puberty

Normal Growth



Normal Growth



Categorize The Different Causes of Short Stature

Causes

- Normal variant:
  - Familial short stature (genetic short stature)
  - Constitutional delay
- Genetic:
  - Turners/Noonans/Russell Silver/Di George/Prader Willi
- Chronic Illness
- Musculoskeletal:
  - Skeletal dysplasia, Ricketts
- Psychosocial:
  - Anorexia/Bulimia, Psychosocial deprivation, Fetal Alcohol Syndrome

Causes

- Endocrine –
  - Growth Hormone Deficiency
  - Hypothyroid
  - Hypopituitary
  - Glucocorticoid excess
    - Cushing syndrome, exogenous steroids
  - Poorly controlled Diabetes Mellitus
  - Precocious puberty
  - Pseudohypoparathyroidism
  - Pseudopseudohypoparathyroidism

Discuss The Important Aspects of The History of a Child With Short Stature

History

- Birth history:
  - Birth weight, length and gestation will identify whether the child was born small for gestational age
  - Perinatal complications, such as hypoglycemia or micropenis, are suggestive of growth hormone (GH) deficiency
  - Maternal history e.g. alcohol intake, social concerns
- Development:
  - Delayed in genetic causes and cases of psychosocial deprivation

History

- Medical:
  - Dyspnea may suggest a cardiac or pulmonary cause
  - Diarrhoea may suggest coeliac disease or other malabsorption syndromes
  - Blood in stools may indicate Inflammatory Bowel Disease
  - Joint pains and rash may indicate a systemic inflammatory condition such as Juvenile Idiopathic Arthritis
  - Recurrent respiratory infections with diarrhoea may raise suspicion of Cystic Fibrosis
  - Polyuria, polydipsia and weight loss may suggest Diabetes

History

- Medical:
  - Headache or diplopia, suggestive of a Craniopharyngioma
  - Recent weight gain, acne, mood swings, and headaches may be present with Cushing syndrome
  - Fatigue, cold intolerance, dry skin, hair loss, constipation, lethargy, and weight gain suggest Hypothyroidism

Explain The Important Parts of The Examination of a Child With Short Stature

Examination

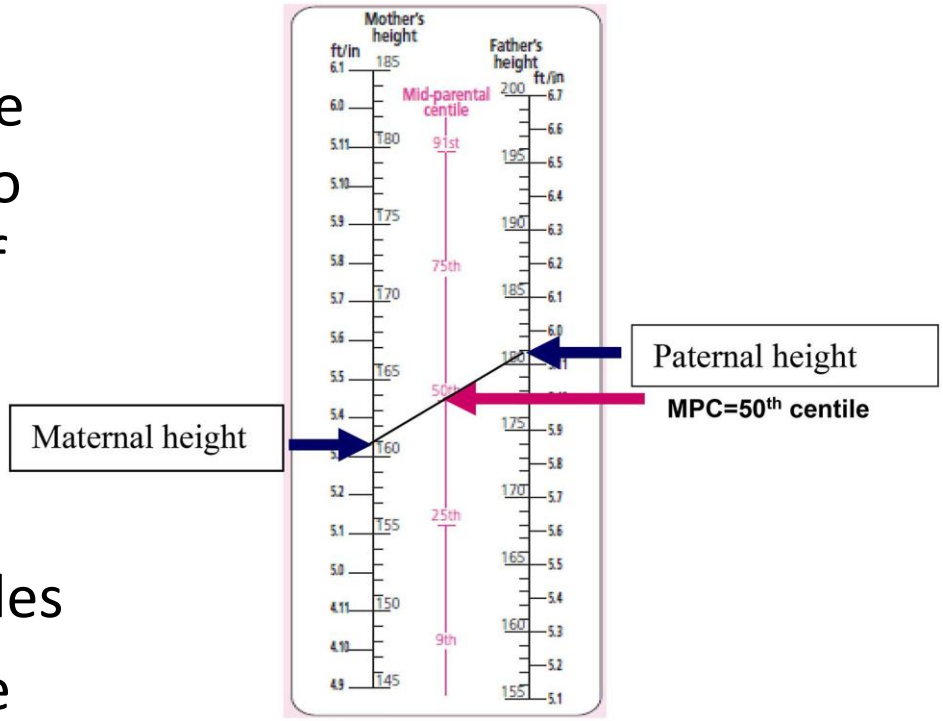
- Plot: Length/Height, weight, OFC (under 3y)
- Growth is strongly related to the genetic potential – always measure the parents' heights
- Target Height-
  - The mid parental height is calculated in males, by adding 7cm to the mean of parental heights; in females by subtracting 7cm
- A short child who is growing close to his/her target height percentile is likely to have familial short stature

Examination

- Decreased or normal weight-to-height ratio suggests inadequate caloric intake or chronic illness
- A high weight-to-height ratio suggests an endocrine etiology, e.g. GH deficiency/insensitivity, hypothyroidism or glucocorticoid excess

Examination - Mid-Parental Centile

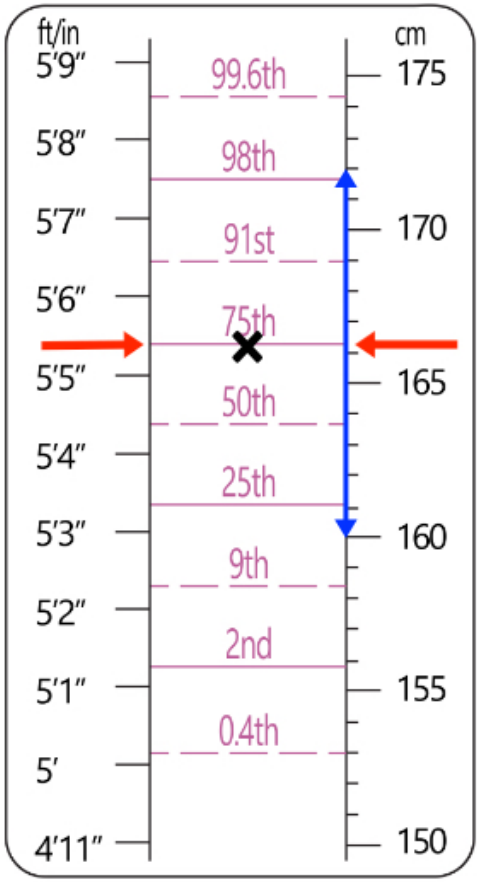
- The mid-parental centile is the average adult height centile to be expected for all children of these particular parents
- Measure both the parent's heights
- Mark their heights on the scales
- Join the two points with a line between them
- The mid parental centile is where this line crosses the centile line in the middle



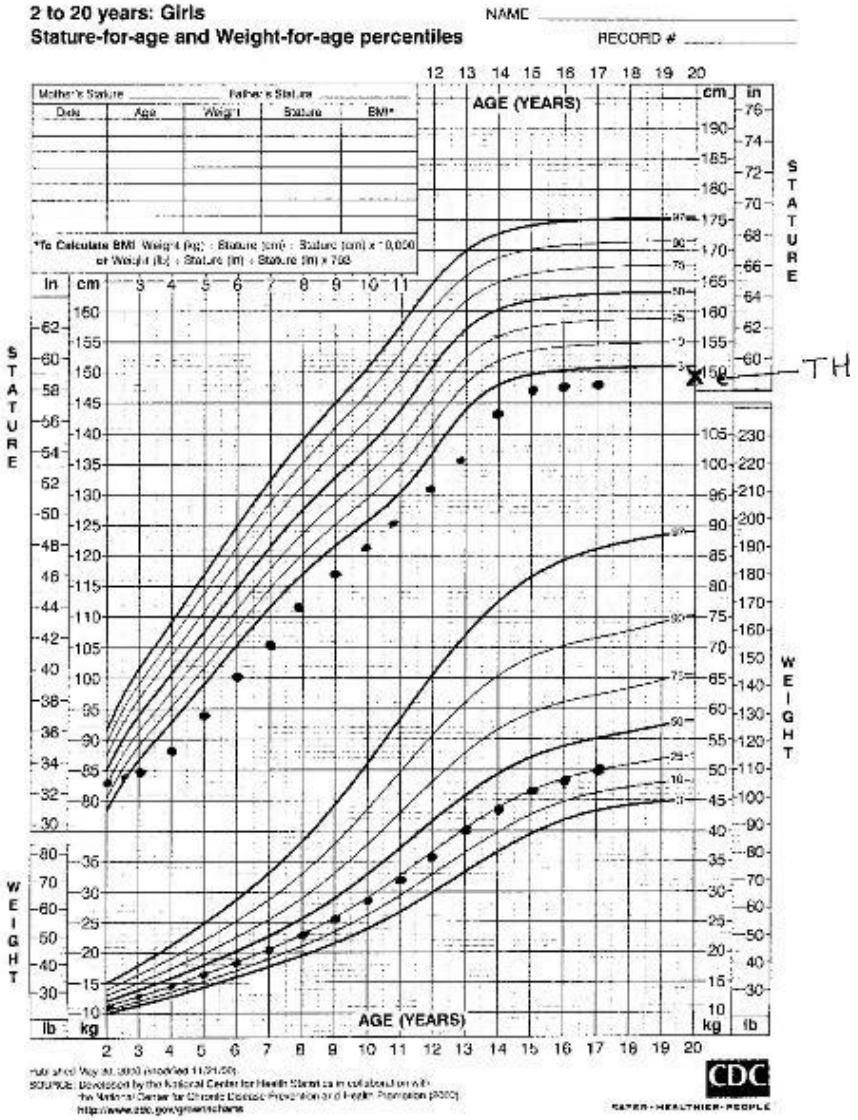
- 9/10 children's height centiles are within ±2 centile spaces of the mid-parental centile

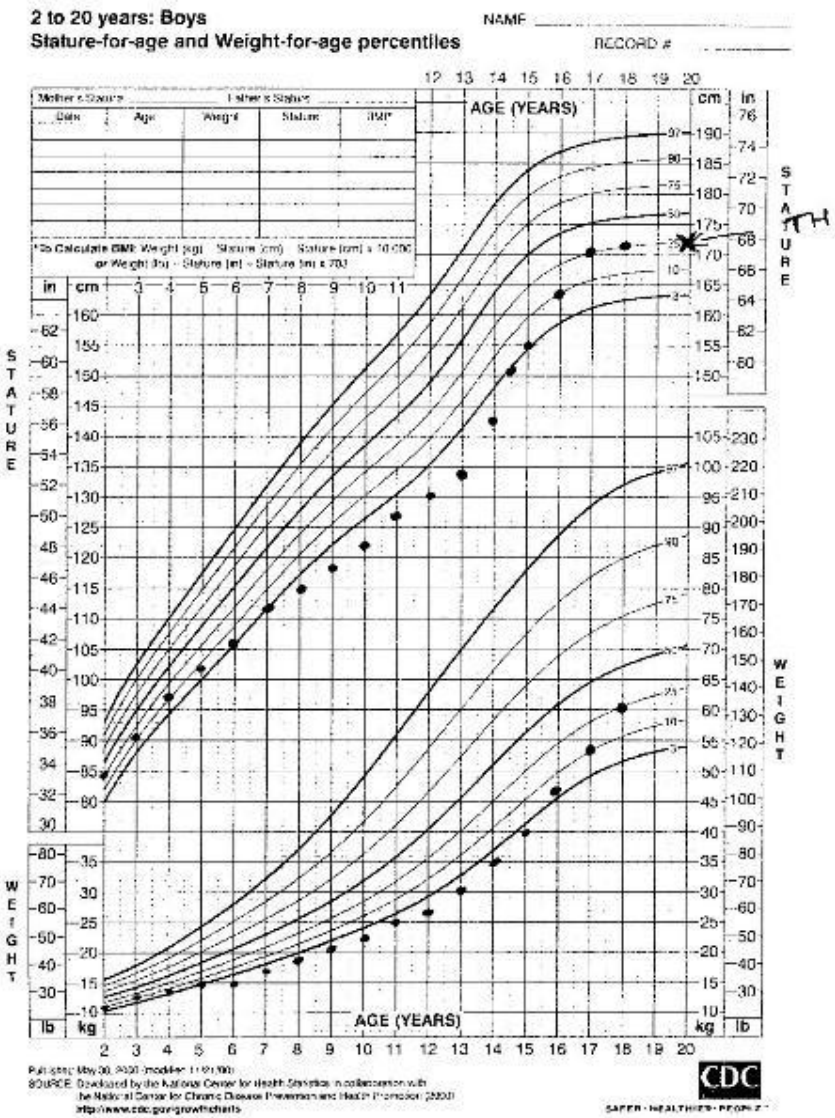
Examination – Adult Height Predictor

- Adult height predictor chart allows for a prediction of the child's adult height based on their current height
- Plot the most recent height centile on the centre line and read off the predicted adult height for this centile.
- 80% of children will be within +/- 6cm of this value as adults



Examination





Examination

- Dysmorphic features:

Table 1 Syndromes and conditions commonly associated with short stature

Condition	Associated features
Turner syndrome	Webbed neck, shield shaped chest, low posterior hairline, wide carrying angle, low set ears, cardiac lesions, hypogonadism
Growth hormone deficiency	Midface hypoplasia, micropenis, truncal obesity
Noonan syndrome	Low hairline, webbed neck, hypertelorism, low set posteriorly rotated ears, cardiac defects, pectus deformities
Russell Silver syndrome	Prominent forehead, triangular facies, micrognathia, thin upper lip
Prader–Willi syndrome	Obesity, hypogonadism, almond shaped eyes, narrow bridge of nose, thin upper lip
Achondroplasia/ hypochondroplasia	Short arms and legs, macrocephaly, prominent forehead, lumbar lordosis

Demonstrate The Investigations That Are Needed to Aid Diagnosis of Short Stature

Investigations

Cause	Test
GH Deficiency	Insulin-like growth factor 1 (IGF-1) and IGF-binding protein 3 (IGFBP-3) and Glucagon Stimulation tests
Hypothyroidism	TFTs
Turners, SHOX	Karyotype and Genetics
Rickets	Vitamin D
DiGeorge	Calcium
Chronic illness	FBC/ESR/UE/LFT/FBC
Coeliac disease	Tissue transglutaminase
Precocious Puberty	FSH/LH

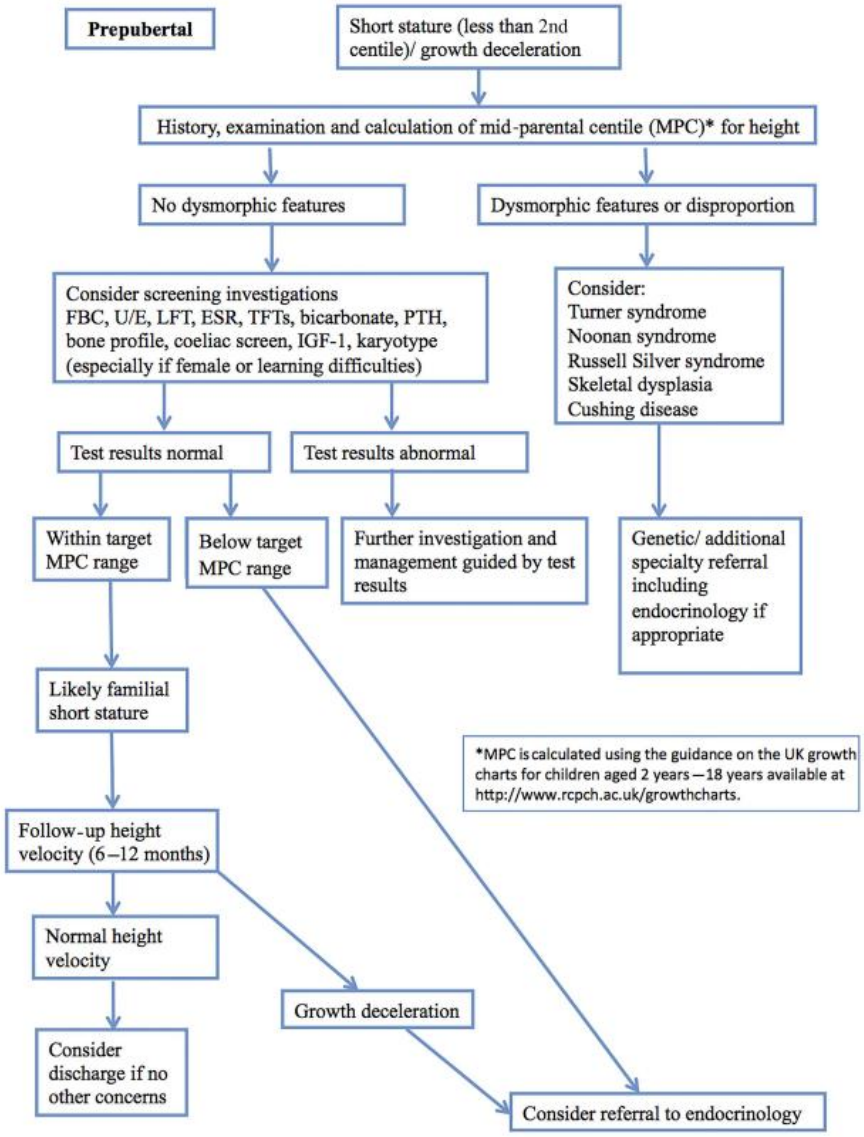
Investigations

- X-ray wrist - Rickets
- X-ray - Bone age (anteroposterior radiograph of left hand and wrist)
- Echo – Congenital heart disease
- Urinary cortisol levels, Dexamethasone suppression test - Cushing syndrome

Investigations

- Bone age reflects skeletal maturity and can be useful in the evaluation of growth disorders
- In children with normal growth, the bone age is usually equal to the chronological age, but an advance or delay of up to 18 months can be within the normal range
- Large bone age discrepancies are not diagnostic, but can indicate a pathological cause
- Significant bone age delays may be found in delayed puberty or an underlying chronic illness
- Conditions of rapid growth, such as precocious puberty, can result in an advancement of bone age

Investigations



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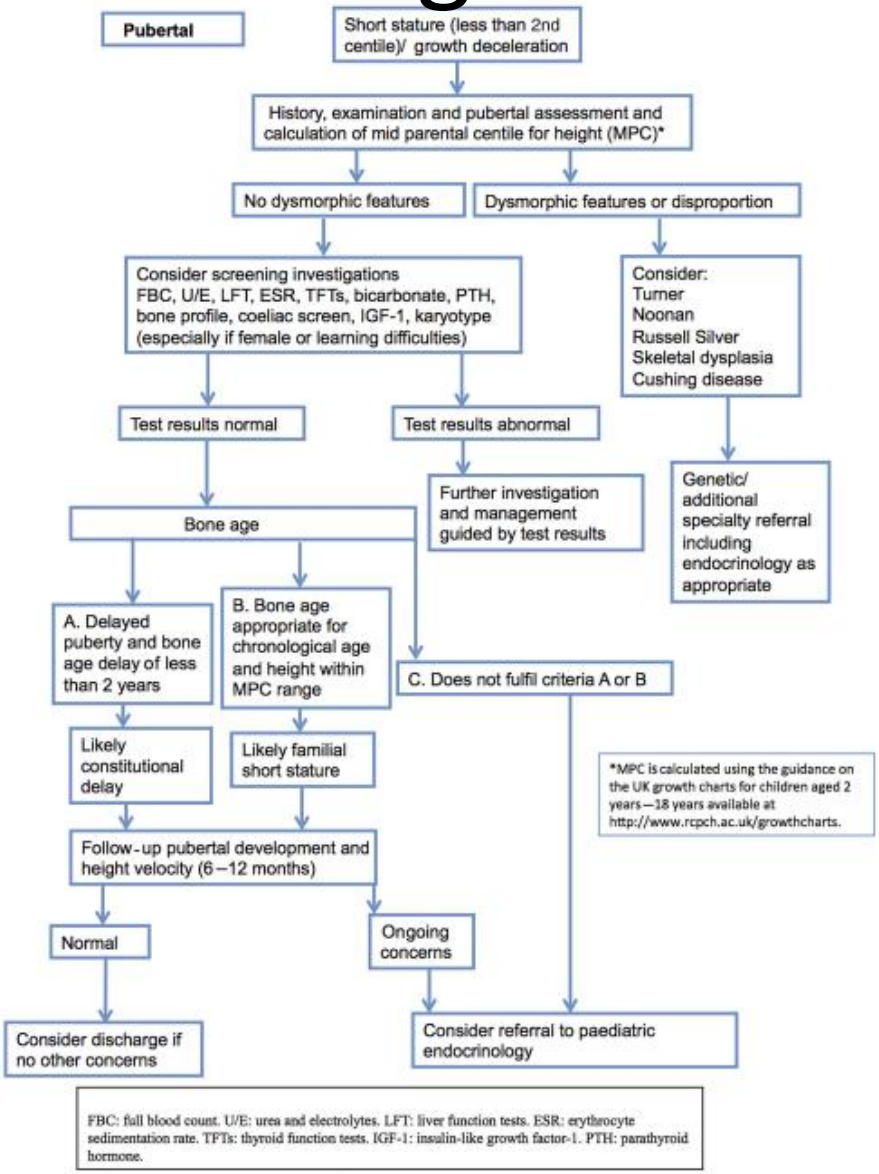

Any Questions?

Aims/Objectives

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References

Amin et al 2015. Fifteen-minute consultation: The child with short stature Amin N, et al. Arch Dis Child Educ Pract Ed 2015;100:180–18.

Cheetham et al 2014. Investigation and management of short stature. Arch Dis Child 2014;99:767–771

NICE 2010. Human growth hormone (somatropin) for

the treatment of growth failure in children (TA188). 2010.

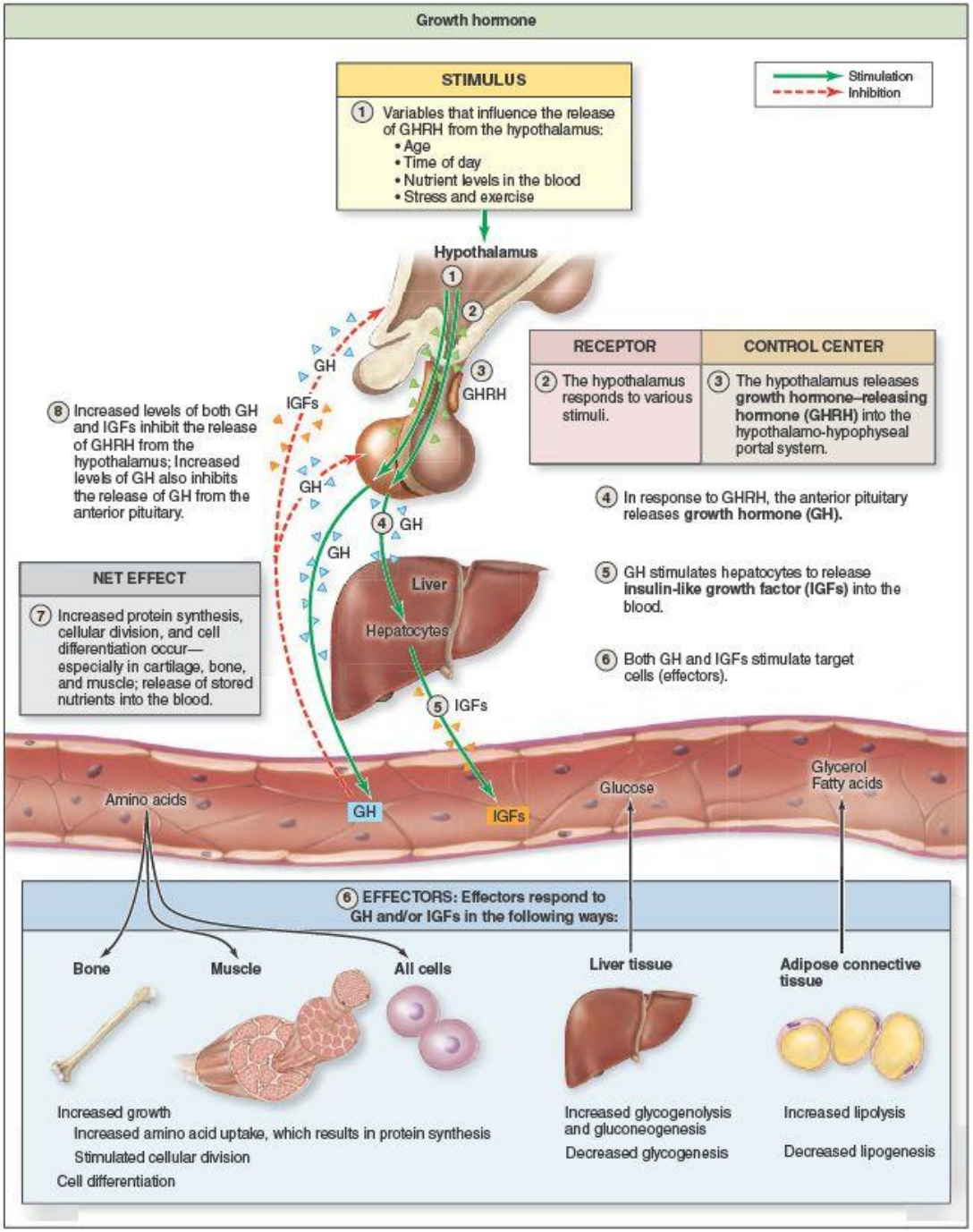
BSPED recommendations for the initial clinical assessment,

investigation and genetic testing of children with growth failure

and/or short stature

Growth Hormone Deficiency

- In many cases cause of Growth Hormone deficiency is idiopathic
- Not inherited
- Can be present at birth or develop later in childhood


Growth hormone
STIMULUS
1 Variables that influence the release of GHRH from the hypothalamus:
• Age
• Time of day
• Nutrient levels in the blood
• Stress and exercise
Stimulation
Inhibition
Hypothalamus
RECEPTOR
2 The hypothalamus responds to various stimuli.
CONTROL CENTER
3 The hypothalamus releases growth hormone–releasing hormone (GHRH) into the hypothalamo-hypophyseal portal system.
GHRH
GH
IGFs
8 Increased levels of both GH and IGFs inhibit the release of GHRH from the hypothalamus; Increased levels of GH also inhibits the release of GH from the anterior pituitary.
4 In response to GHRH, the anterior pituitary releases growth hormone (GH).
5 GH stimulates hepatocytes to release insulin-like growth factor (IGFs) into the blood.
6 Both GH and IGFs stimulate target cells (effectors).
NET EFFECT
7 Increased protein synthesis, cellular division, and cell differentiation occur—especially in cartilage, bone, and muscle; release of stored nutrients into the blood.
Liver
Hepatocytes
Amino acids
Glucose
Glycerol
Fatty acids
6 EFFECTORS: Effectors respond to GH and/or IGFs in the following ways:
Bone
Muscle
All cells
Liver tissue
Adipose connective tissue
Increased growth
Increased amino acid uptake, which results in protein synthesis
Stimulated cellular division
Cell differentiation
Increased glycogenolysis and gluconeogenesis
Decreased glycogenesis
Increased lipolysis
Decreased lipogenesis

Growth Hormone Deficiency - Causes

- Growth Hormone deficiency:
    - Birth injury
    - Craniopharyngioma
    - Brain tumours
    - Midline defects
    - Haemosiderosis
- Hormone insensitivity (Laron syndrome)

Growth Hormone Deficiency – Clinical Features

- Hypoglycemia or micropenis at birth
- Growth deceleration occurs after the age of 2 years
- May be accompanied by other pituitary deficiencies
- “Cherubic" appearance
- Midline defects such as a single incisor, cleft lip/palate, midfacial hypoplasia
- Most do not have any clinical features other then concerns about growth

Growth Hormone Deficiency – Investigations

Cause	Test
GH Deficiency	Insulin-like growth factor 1 (IGF-1) and IGF-binding protein 3 (IGFBP-3) and Glucagon Stimulation tests*
Hypothyroidism	TFTs
Turners, SHOX	Karyotype and Genetics
Rickets	Vitamin D
DiGeorge	Calcium
Chronic illness	ESR/UE/LFT/FBC
Coeliac disease	Tissue transglutaminase
Precocious Puberty	FSH/LH

- Bone age x-ray: delayed
- MRI brain: Craniopharyngioma, Brain tumours

Growth Hormone Deficiency – Treatment

- Who can be given Growth Hormone?

- Growth hormone deficiency
- Turner syndrome
- Prader–Willi syndrome
- Chronic renal insufficiency
- Born small for gestational age with subsequent growth failure at 4 years of age or later
- Short stature homeobox-containing gene (SHOX) deficiency

Growth Hormone Deficiency – Treatment

- The dosage varies according to the condition being treated:

Condition	Dose
GH Deficiency	0.7mg/m² (pre puberty) (daily) 1.0 mg/m² (post puberty) (daily)
Children born small for gestational age	1.0 mg/m² (daily)
Turners Syndrome	1.4mg/m²
SHOX deficiency	45–50 microgram/kg daily

SHOX

- The short stature homeobox-containing gene (SHOX) is located on the distal ends of X and Y chromosomes and plays a role in long bone growth
- Normal growth requires two functional copies of the gene
- Consequently, growth impairment can occur if one copy of the SHOX gene has been inactivated by mutation or deleted (haploinsufficiency)

Any Questions?

- Thank you