Short stature

Rasha Odeh

MB,BS.MRCPCH

Assistant professor of pediatric endocrinology

University of Jordan

Growth

Growth in childhood, one of the most fascinating, complex and dynamic biological processes, is tightly controlled and regulated.

remains one of the most useful of all indices of public health and economic well being, specifically in developing countries and countries in transition

Outline

- Normal Growth and puberty
- Causes of short stature
- Approach to a short child

Growth Parameters

- Weight for age and sex
- Height (length) for age and sex
- Weight for length
- Body mass index for age and sex
- Head circumference for age and sex

Early phase of rapid growth weight

- Weight gain in children <2 years

- Term neonates may lose up to 10 percent of their birth weight in the first few days of life and typically regain their birth weight by 10 to 14 days
- Newborns gain approximately 30 g per day until three months of age
- Infants gain approximately 20 g per day between three and six months of age and approximately 10 g per day between 6 and 12 months
- Infants double their birth weight by four months of age and triple their birth weight by one year

Length/height

- The average length at birth for a term infant is 50 cm
- Infants grow 25 cm during the first year of life
- Toddlers grow 10 cm between 12 and 24 months, 7.5 cm between 24 and 36 months, and 7.5 cm between 36 and 48 months
- Children reach one-half of their adult height by 24 to 30 months
- Children grow 5 cm per year between age four years and puberty
- There is a normal deceleration of height velocity before the pubertal growth spurt

Head circumference

- The average head circumference at birth is 35 cm
- Head circumference increases approximately 1 cm per month during the first year of life, with the most rapid growth occurring during the first six months, with an increase of 2 cm in the first month and 6 cm in the first four months
- Brain weight doubles by four to six months of age and triples by one year of age
- Most head growth is complete by four years of age

2 to 20 years: Boys
Stature-for-age and Weight-for-age percentiles

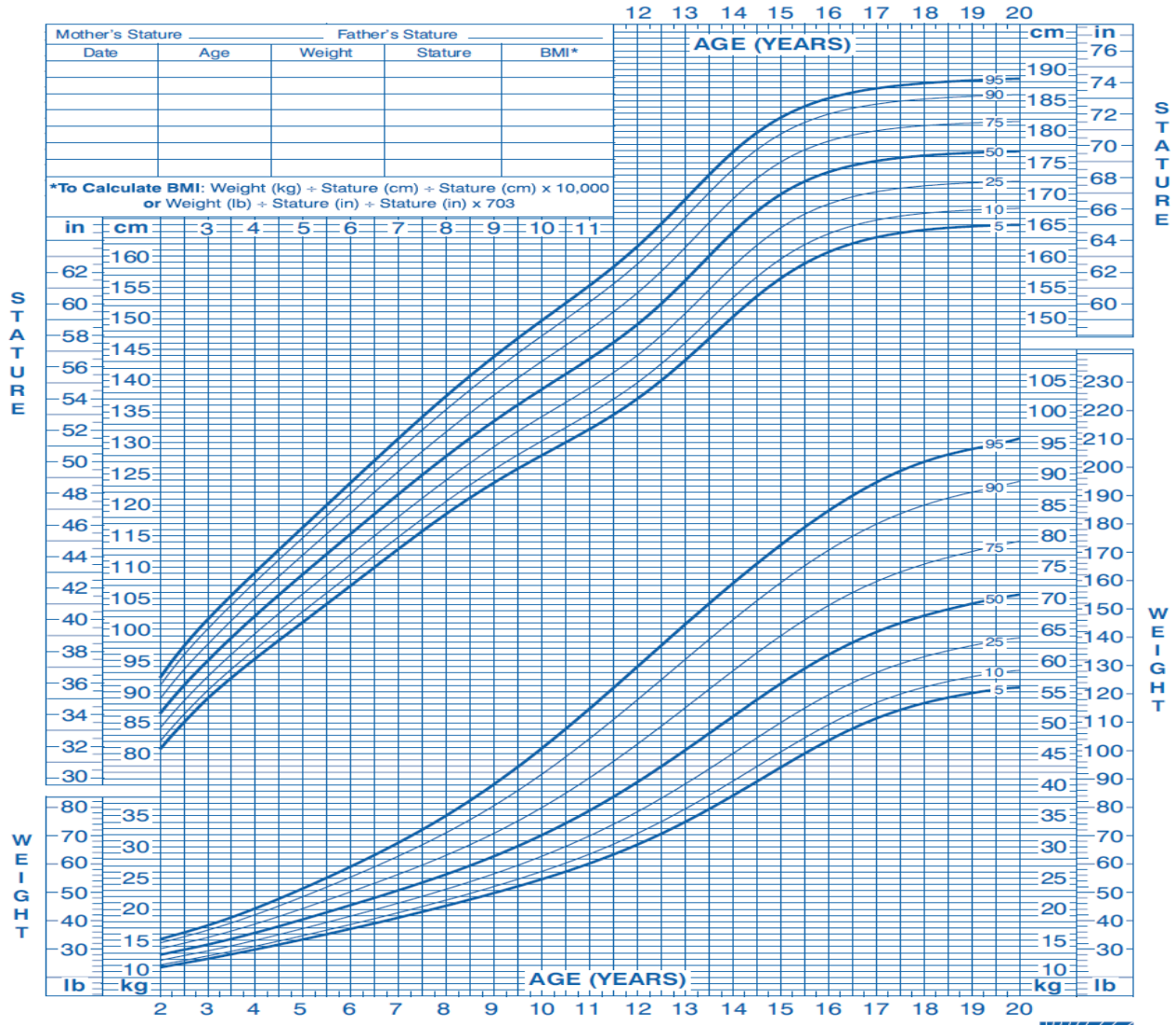
NAME _____

RECORD # _____

Mother's Stature _____ Father's Stature _____

Date	Age	Weight	Stature	BMI*

***To Calculate BMI**: Weight (kg) ÷ Stature (cm) ÷ Stature (cm) x 10,000
or Weight (lb) ÷ Stature (in) ÷ Stature (in) x 703



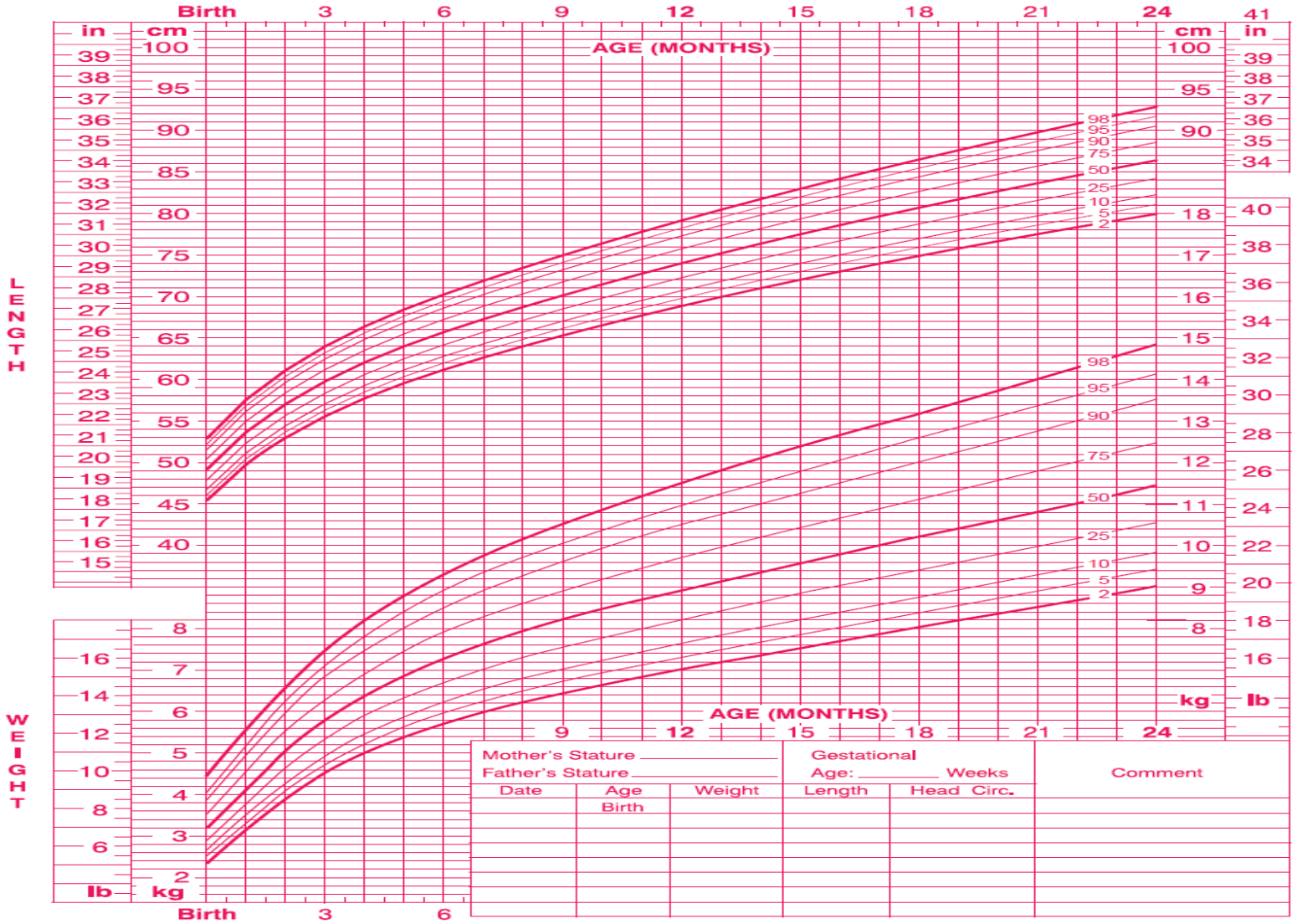
Published May 30, 2000 (modified 11/21/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
http://www.cdc.gov/growthcharts

SAFER · HEALTHIER · PEOPLE™

Birth to 24 months: Girls
Length-for-age and Weight-for-age percentiles

NAME _____

RECORD # _____



Mother's Stature _____

Father's Stature _____

Gestational Age: _____ Weeks

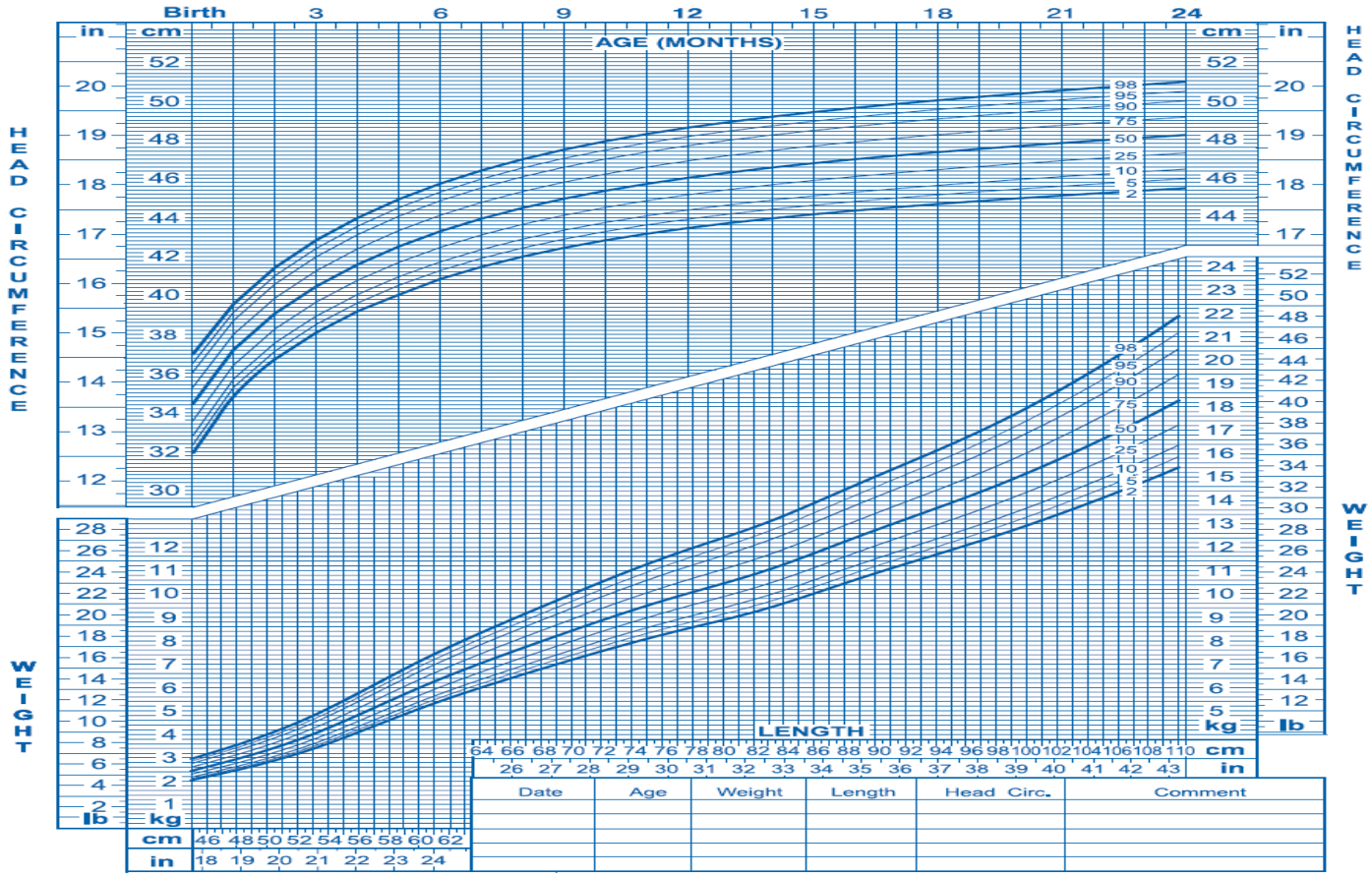
Date	Age	Weight	Length	Head Circ.	Comment
	Birth				

Published by the Centers for Disease Control and Prevention, November 1, 2009
SOURCE: WHO Child Growth Standards (http://www.who.int/childgrowth/en)

Birth to 24 months: Boys
Head circumference-for-age and Weight-for-length percentiles

NAME _____

RECORD # _____

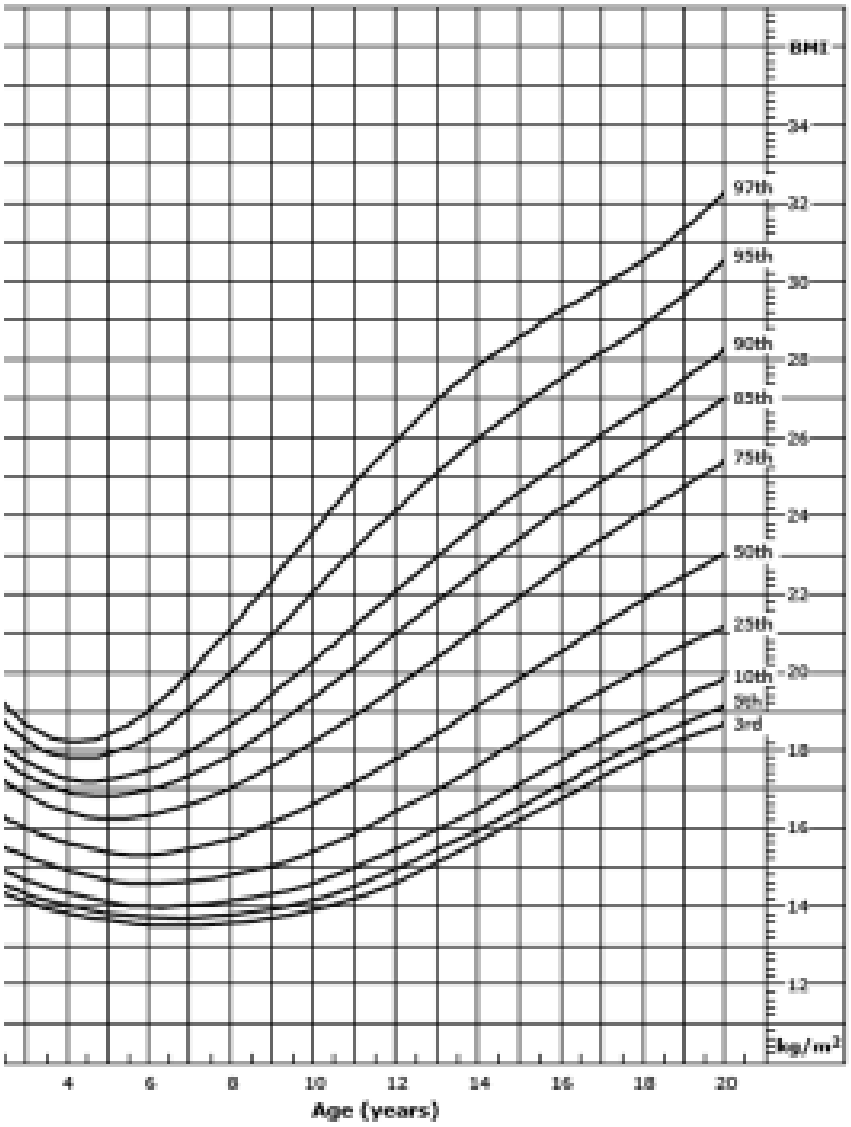


Date	Age	Weight	Length	Head Circ.	Comment

Published by the Centers for Disease Control and Prevention, November 1, 2009
SOURCE: WHO Child Growth Standards (http://www.who.int/childgrowth/en)

overweight: BMI>85th<95th percentile

Obese: BMI>95th percentile



The ICP concept of growth:

Infancy

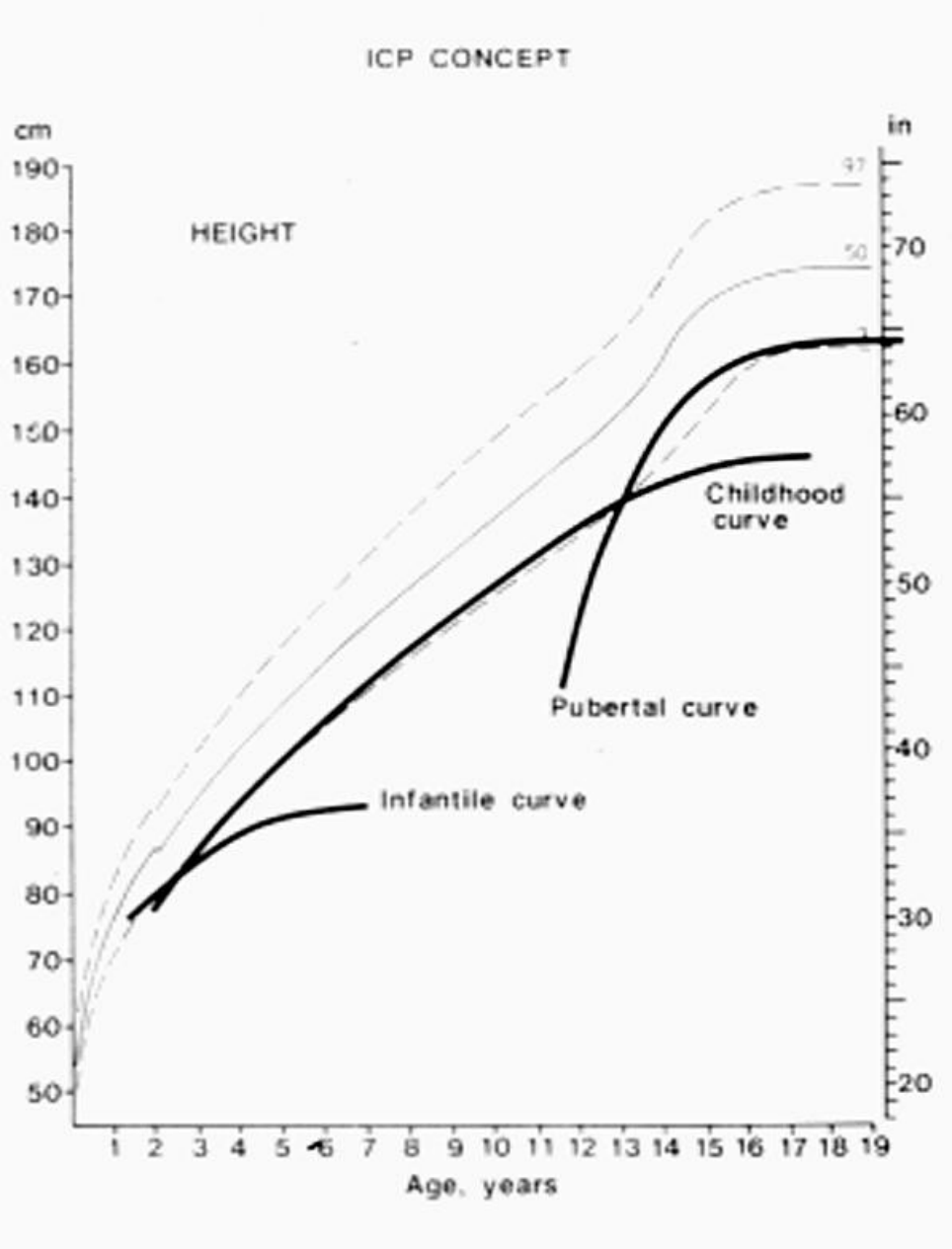
Childhood

Puberty

A mathematical model breaking down linear growth from birth to adulthood into 3 components that reflect the different hormonal phases of the growth process.

Karlberg J. Acta Paediatr Suppl 1989; 350: 70-94

ICP Concept


ICP CONCEPT
cm
in
HEIGHT
97
50
3
Childhood curve
Pubertal curve
Infantile curve
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
70
60
50
40
30
20
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
Age, years

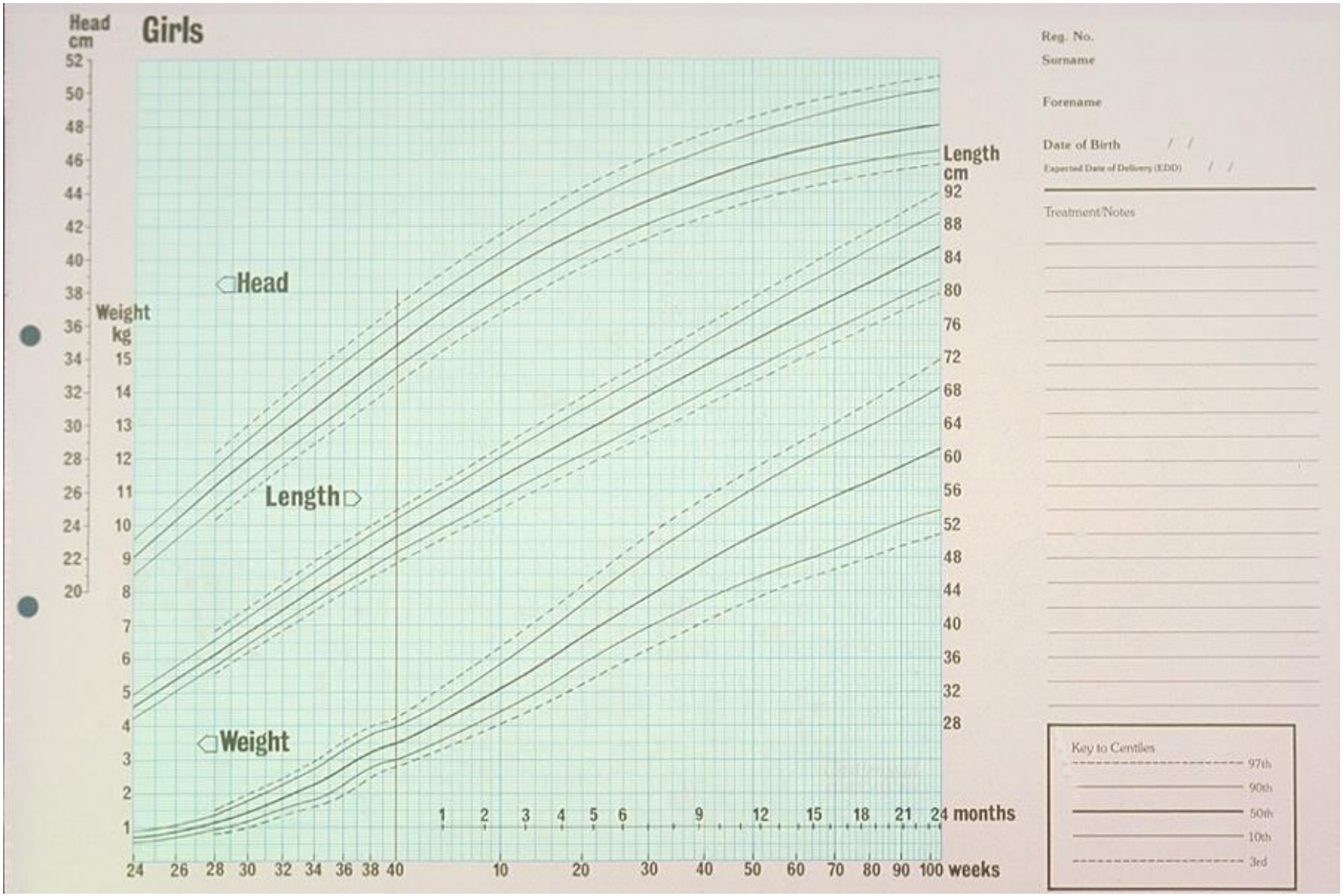
ICP Concept - Infantile Phase

- Rapid period of growth from 0 - 2 years
- Continuation of the rapid but decelerating intra-uterine growth phase
- Depends on factors such as nutrition, insulin and the insulin-like growth factors.
- Largely independent of growth hormone

ICP Concept - Infantile Phase

- In general, birth size reflects intra-uterine environment, e.g. nutrition
- Birth size, therefore, has relatively poor correlation with final height.
- From birth to age 2, infant “tracks” on to his/her genetic centile, related to parental heights

Healy Mj etal. Aberdeen growth study.. Arch Dis Child. 1956;31(159):372.



Reg. No.

Surname

Forename

Date of Birth / /

Expected Date of Delivery (EDD) / /

Treatment/Notes

Key to Centiles

97th

90th

50th

10th

3rd

ICP Concept - Childhood Phase

- Long phase of growth from 2 ~ 12 years (onset of pubertal growth)
- Slower, slightly decelerating curve
- Dependent on growth hormone & thyroxine
- Healthy child will stay on childhood (genetic) centile until puberty

ICP Concept - Pubertal Phase

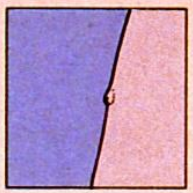
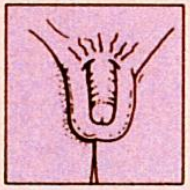
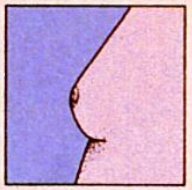
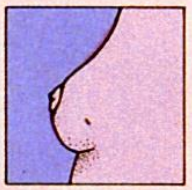
- From around age 12 (time of puberty) to final height
- Dependent on the sex steroid estrogen which is aromatised from testosterone and which causes an increase in growth hormone secretion
- Resulting growth acceleration is limited by fusion of the epiphyses (due to strogen in both sexes)

ICP Concept - Pubertal Phase

- Variable growth phase in terms of :
  age of onset • *duration* • *intensity*

- 95% of normal individuals will attain final heights within 2 standard deviations of mid-parental height (± 8.5 cm)

Pubertal (Tanner) staging

Genitals Tanner stage	Boys	Girls		Pubic hair Tanner stage (Boys and girls)	
Testes < 2.0 cm max. length			No mammary tissue	P1	No pubic hair
Testes > 2.0 cm max. length			Small nubbin mammary tissue behind areola	P2	Sparse growth, slightly pigmented downy hair at base of penis or along labia
Penis lengthening, testes increasing in size			Distinct breast contour	P3	Sparse growth, darker, curled pubic hair at base of penis or along labia
Penis broadening, glans develops, testes increasing in size			Double contour of breast	P4	Small adult configuration
Adult male genitals, testes average 5–6 cm max. length			Single adult breast contour	P5	Adult configuration

G1 G2 G3 G4 G5

.

Tanner Stage	Breasts	Pubic Hair	Growth	Other
1	Elevation of papilla only	Villus hair only	2-2.4 inches per year	Adrenarche and ovarian growth
2	Breast bud under the areola, areola enlargement	Sparse hair along the labia	2.8-3.2 inches per year	Clitoral enlargement, labia pigmentation, growth of uterus
3	Breast tissue grows but has no contour or separation	Coarser hair curled pigmented covers the pubes	3.2 inches per year	Axillary hair, acne
4	Projection of areola and papilla, secondary mound formation	Adult hair, does not spread to the thigh	2.8 inches per year	Menarche and development of menses
5	Adult-type contour, projection of papilla only	Adult hair, spreads to the medial thigh	Cessation of linear growth	Adult genitalia

Tanner Stage	Genitalia	Pubic Hair	Growth	Other
1	Testes <2.5 cm	Villus hair only	2.0-2.4 inches per year	Adrenarche
2	Testes 2.5-3.2 cm Thinning and reddening of the scrotum	Sparse hair at penis base	2.0-2.4 inches per year	Decreases in body fat
3	Testes 3.3-4.0 cm Increase of penis length	Thicker curly hair spreads to the pubis	2.8-3.2 inches per year	Gynecomastia, voice break, increased muscle mass
4	Testes 4.1-4.5 cm, penis growth darkening of scrotum	Adult hair does not spread to thighs	4.0 inches per year	Axillary hair, voice change, acne
5	Testes >4.5cm, adult genitalia	Adult hair spreads to medial thigh	Deceleration, cessation	Facial hair, muscle mass increases

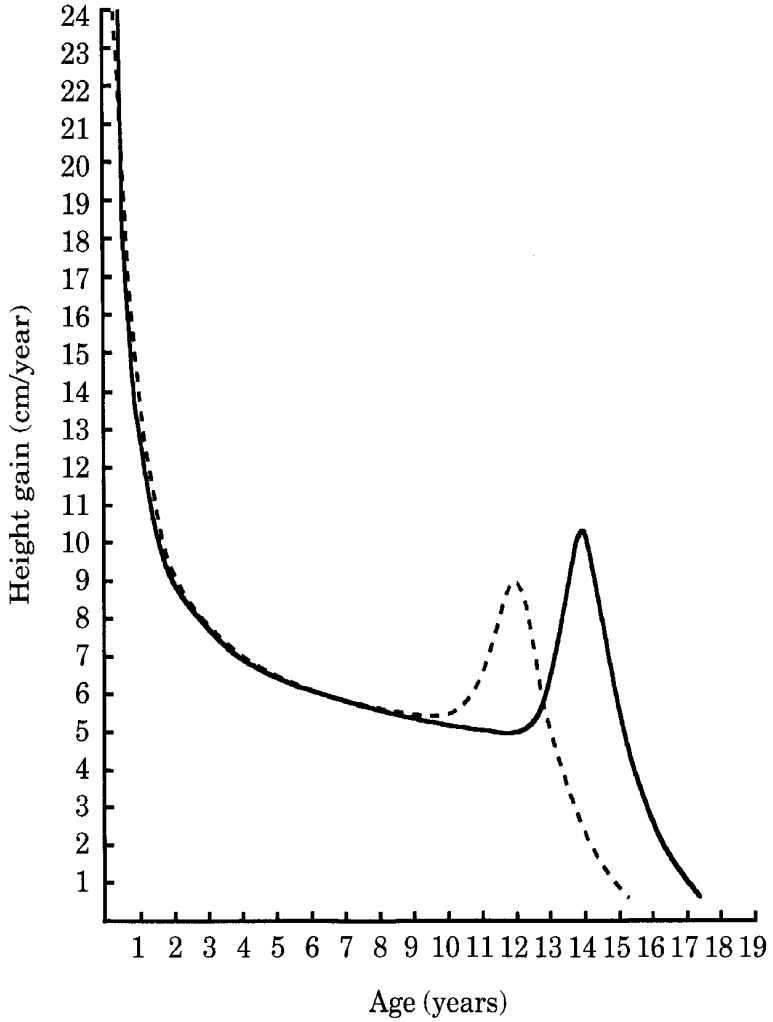
Stages of breast development versus height velocity in girls

B1 – prepubertal	Prepubertal (childhood phase)
B2 – breast budding	Increase in height velocity
B3 – breast mound	Peak height velocity B2-3
B4 – angle between areola and breast mound	Slowing of height velocity; onset of periods (menarche)
B5 – adult breast shape	Adult height

Genital stages versus height velocity in boys

G1 – prepubertal scrotum and penis, testicular volume <4 ml	Prepubertal – childhood phase
G2 – prepubertal penis, enlargement of scrotum, testes ≥ 4 ml	Still in childhood phase, therefore height velocity slower than in G1
G3 – penis begins to enlarge	Increase in height velocity
G4 – penis lengthens and broadens, testes ~12-15 ml	Peak height velocity
G5 – adult, testes ~ 15-20 ml	Significant further growth followed by final height

Height velocity graph showing different growth patterns in boys (solid line) and girls (dotted line)



Mid-parental height and target range - girls

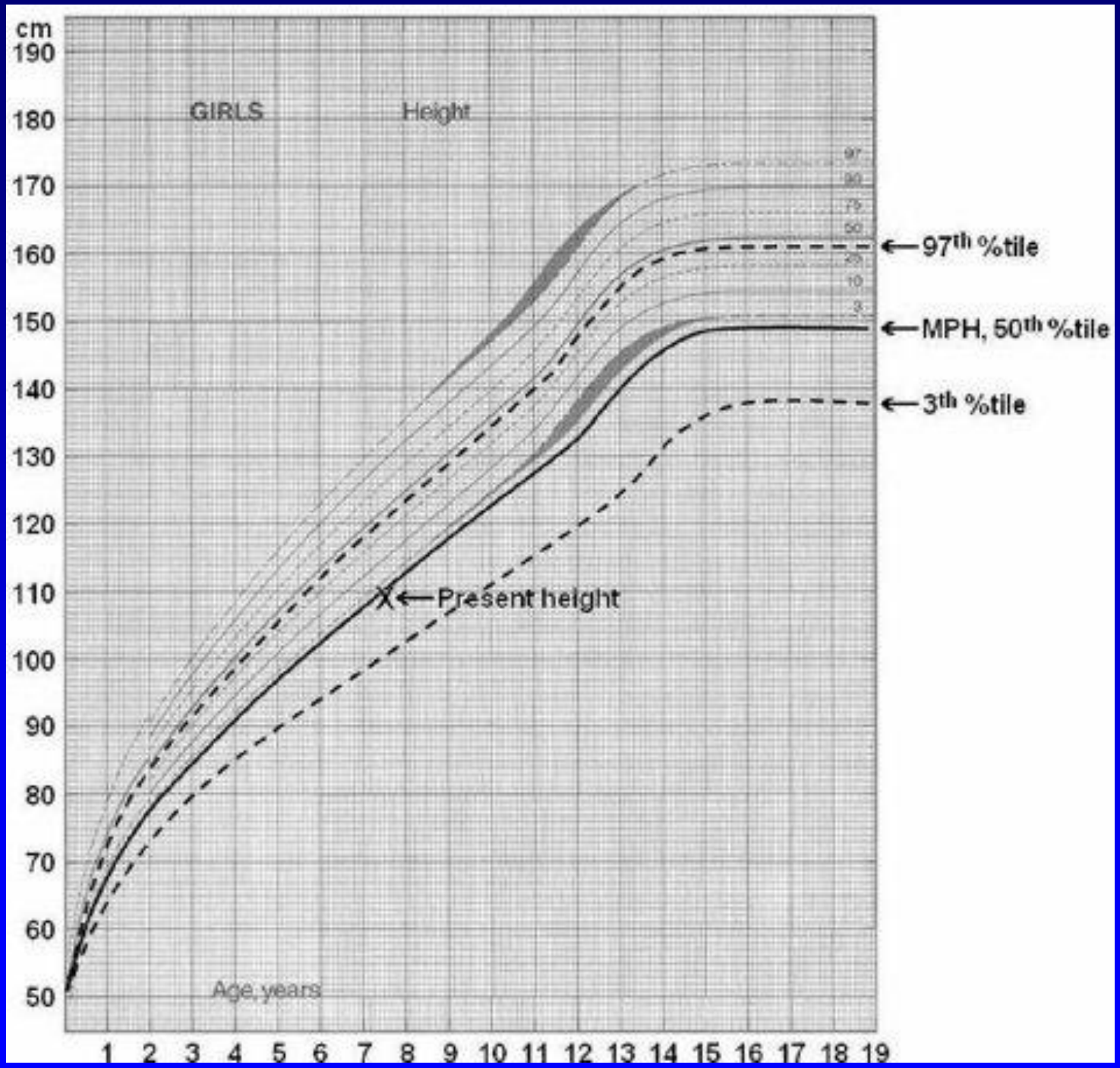
- Plot Mother's height on growth chart
- Plot Father's height *minus 13* cm
- Plot the mid-parental height (MPH)

  (the mean of these two measurements)
- Plot the target range (MPH $\pm$ 8.5 cm)

Mid-parental height and target range - boys

- Plot Father's height on growth chart
- Plot Mother's height *plus* 13 cm
- Plot the mid-parental height (MPH)

  (the mean of these two measurements)
- Plot the target range (MPH $\pm$ 8.5 cm)

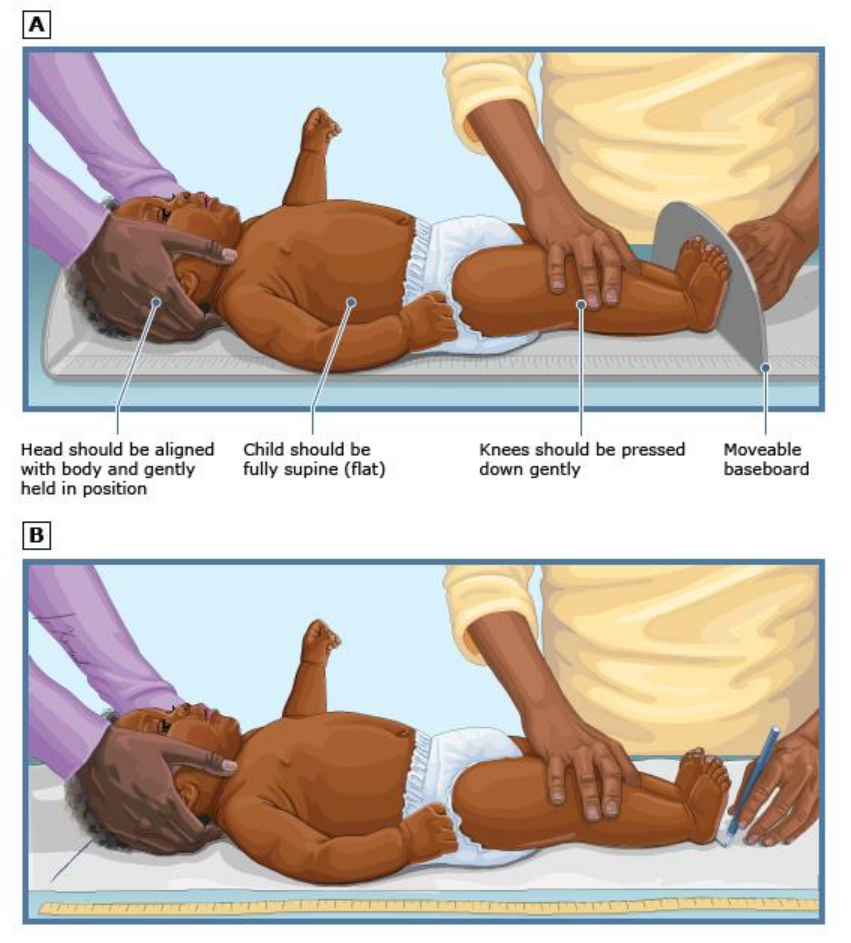

cm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
GIRLS
Height
97
90
75
50
25
10
3
←97th %tile
←MPH, 50th %tile
←3th %tile
X←Present height
Age, years
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

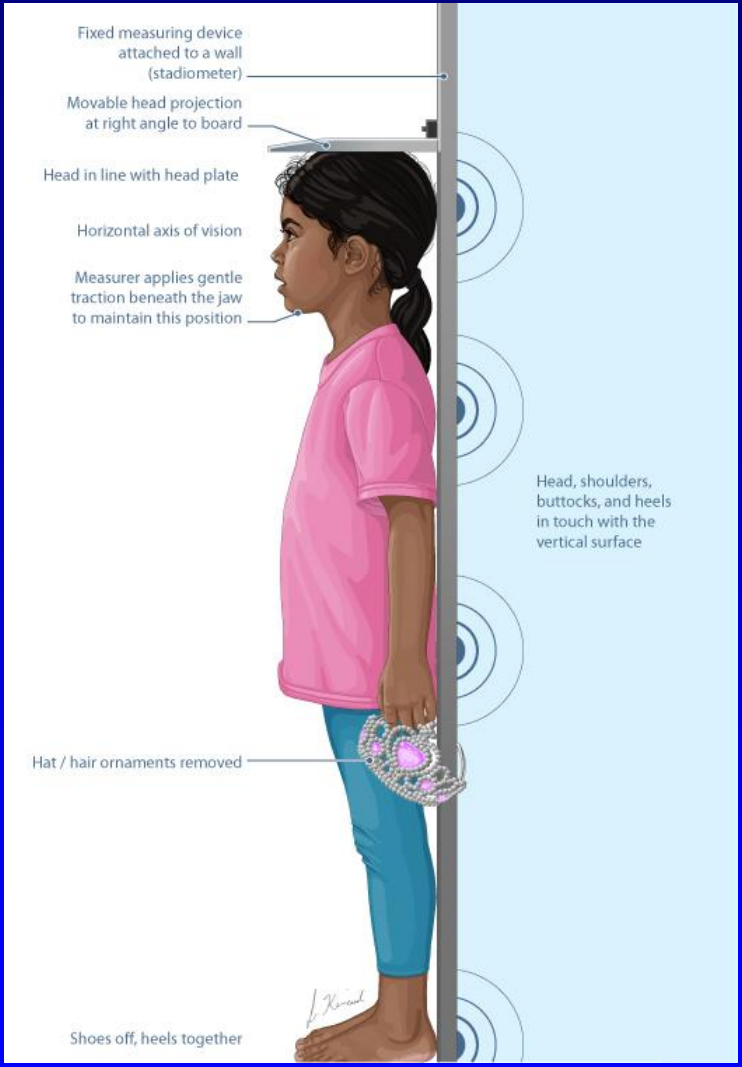
Essentials for growth assessment

- Reliable, accurate measuring equipment
- Accurate measurement of child & parents (standing height/supine length)
- Calculation of decimal age and height velocity
- Careful plotting of growth chart
- Calculation of mid-parental height (MPH) and target range
- Pubertal staging
- Bone age assessment

Measurement of Height

- Reliable, accurate measuring equipment
- Accurate measurement of child & parents !
- Frankfurt plane
- Stretched height
- Measurement of sitting height in selected cases


A
Head should be aligned with body and gently held in position
Child should be fully supine (flat)
Knees should be pressed down gently
Moveable baseboard
B

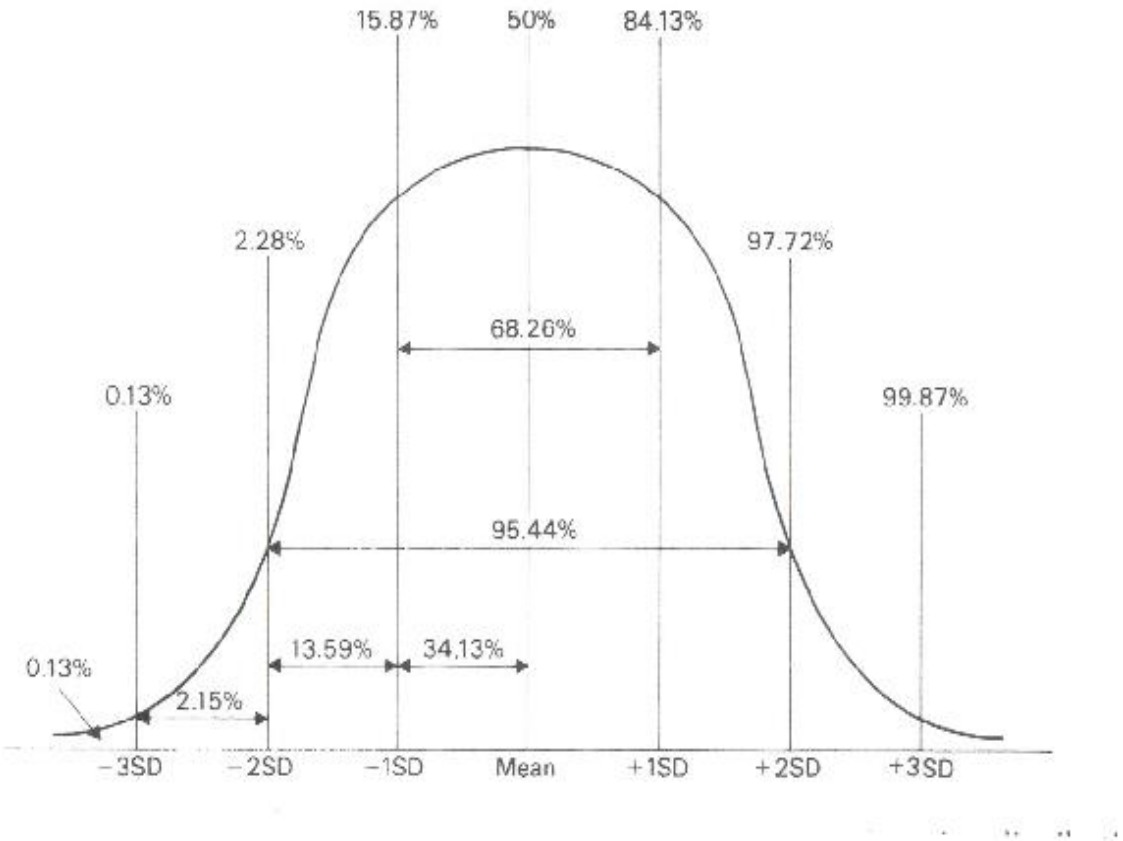

Fixed measuring device attached to a wall (stadiometer)
Movable head projection at right angle to board
Head in line with head plate
Horizontal axis of vision
Measurer applies gentle traction beneath the jaw to maintain this position
Head, shoulders, buttocks, and heels in touch with the vertical surface
Hat / hair ornaments removed
Shoes off, heels together

Evaluation of Growth

- IS/How short is the child?
- Is the child's height velocity (HV) impaired?
- What is the child's likely adult height?
- Is the child growing on a centile appropriate for the genetic target height?

Is the child short?

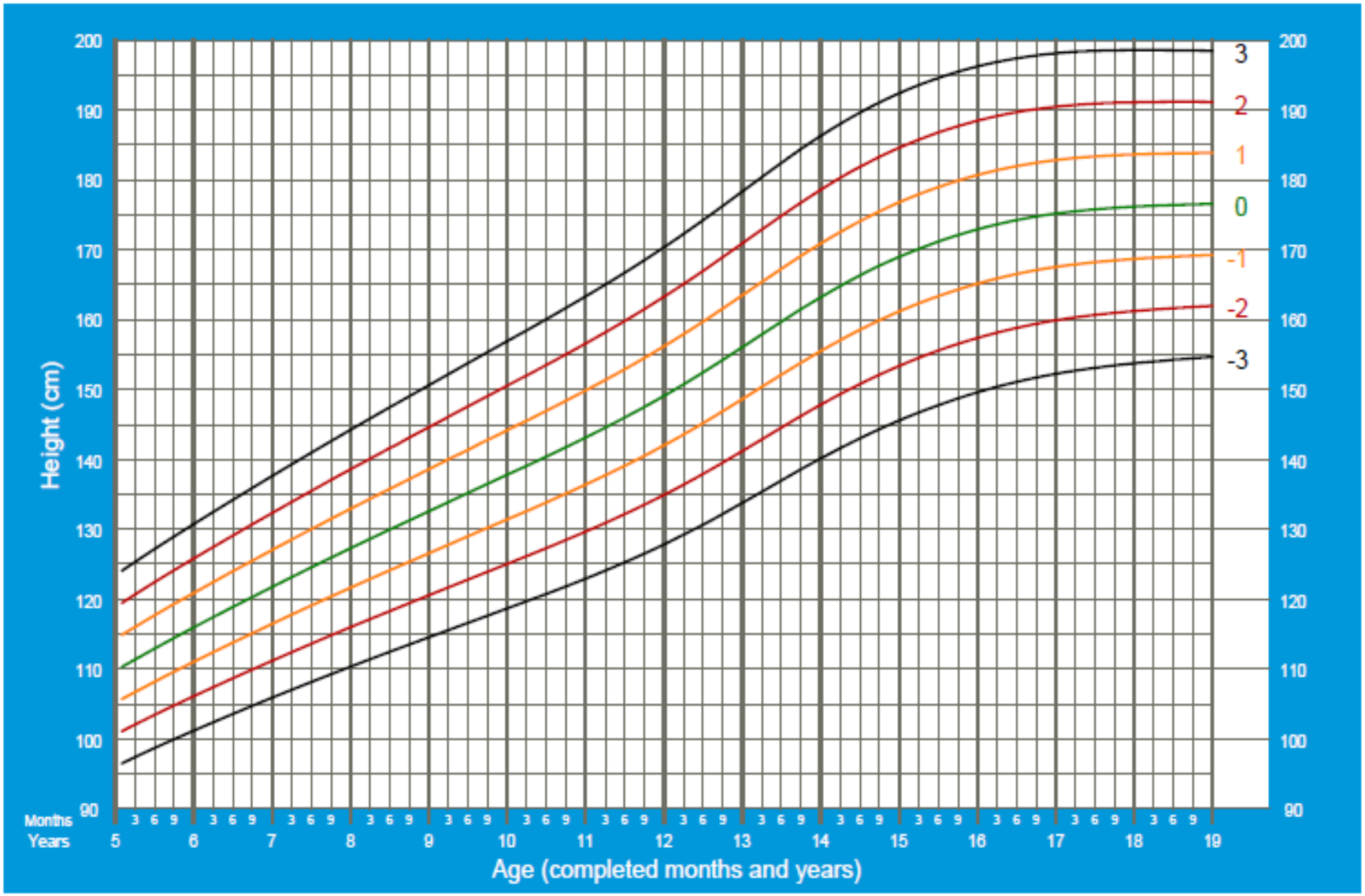
Relationship between centiles and standard deviations for values with a Gaussian distribution



Height-for-age BOYS

5 to 19 years (z-scores)

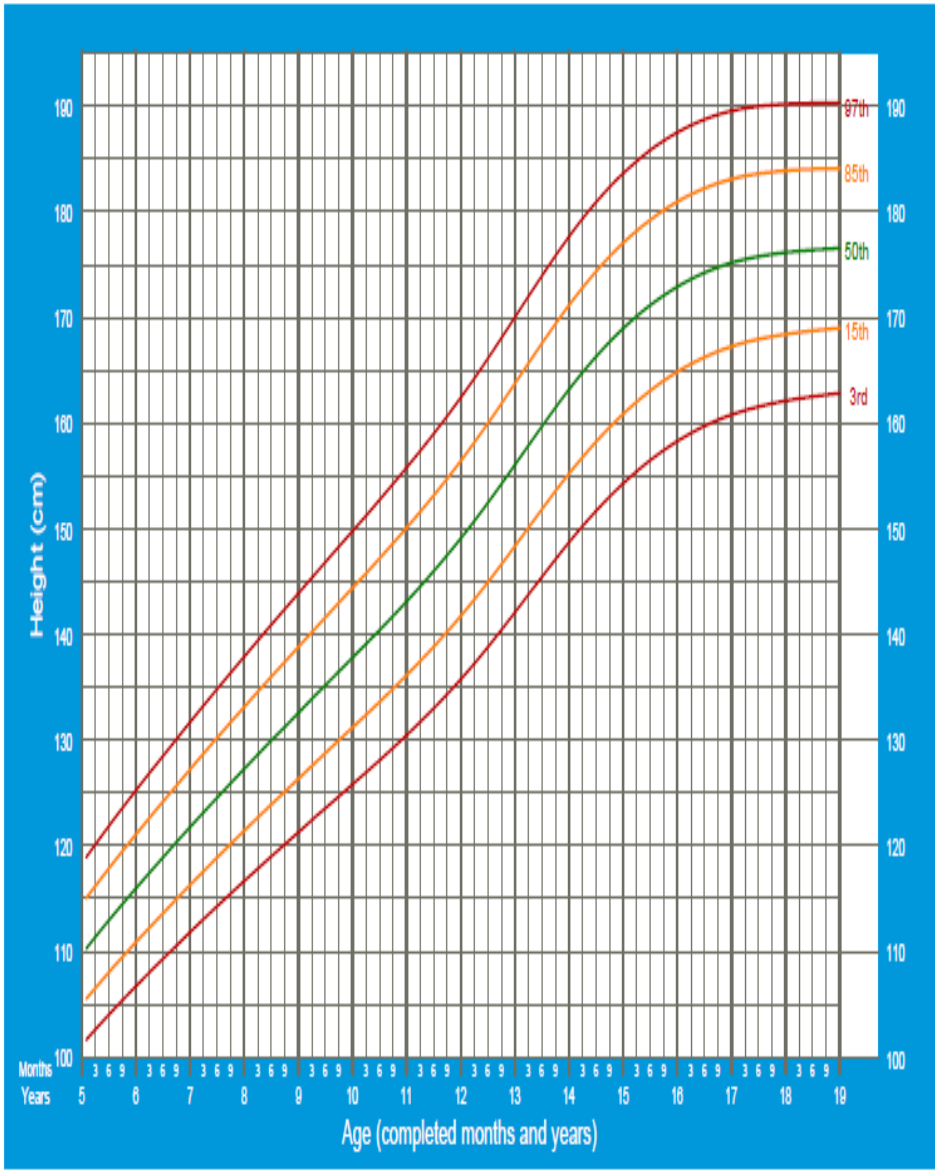
World Health Organization



2007 WHO Reference

Height-for-age BOYS

5 to 19 years (percentiles)



2007 WHO Reference

World Health Organization

2 to 20 years: Boys
Stature-for-age and Weight-for-age percentiles

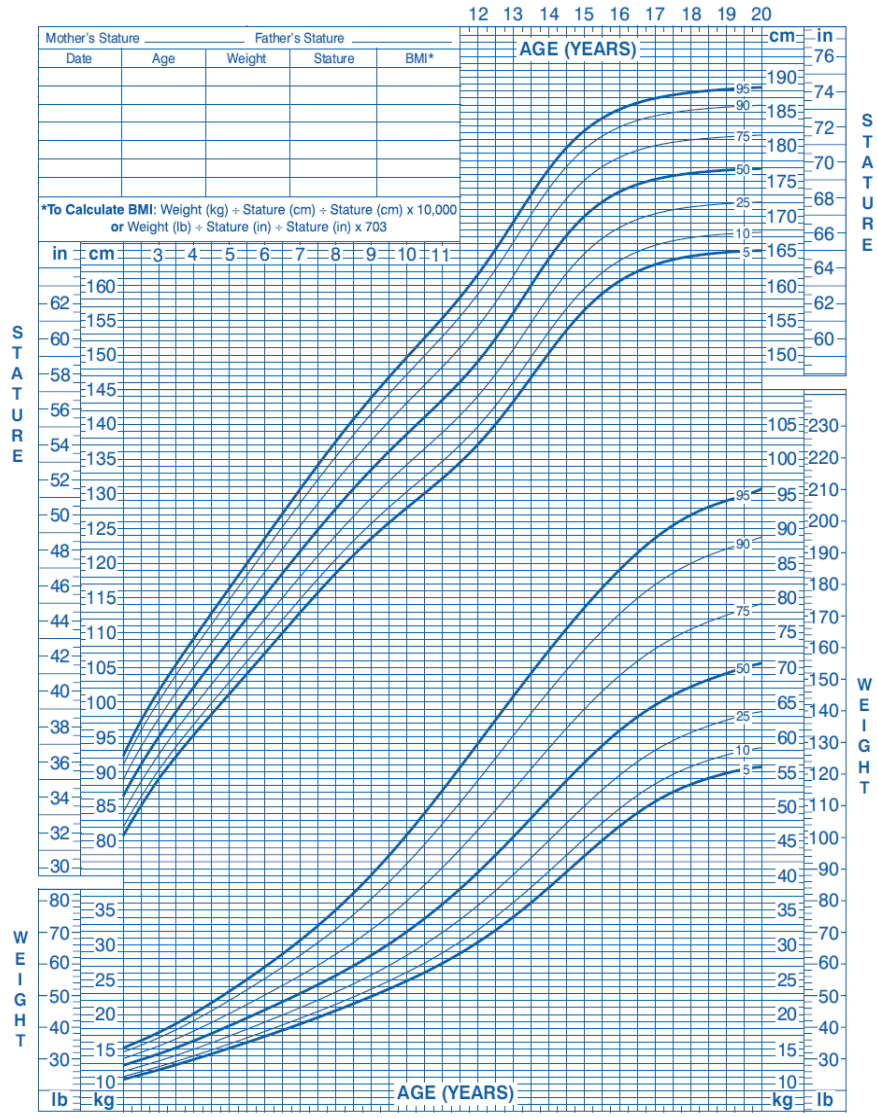
NAME _____

RECORD # _____

Mother's Stature _____ Father's Stature _____

Date	Age	Weight	Stature	BMI*

*To Calculate BMI: Weight (kg) ÷ Stature (cm) ÷ Stature (cm) x 10,000
or Weight (lb) ÷ Stature (in) ÷ Stature (in) x 703

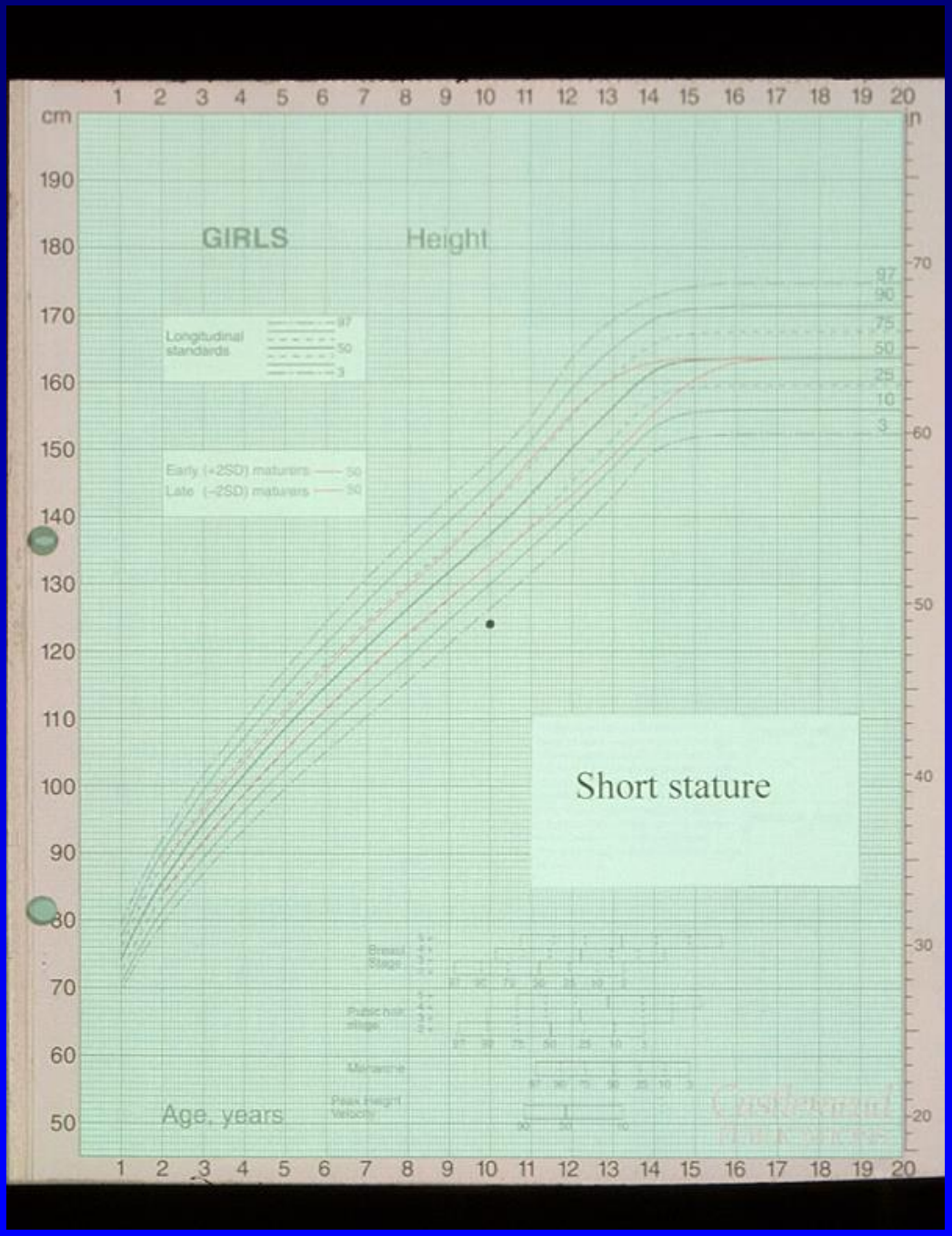


Published May 30, 2000 (modified 11/21/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
http://www.cdc.gov/growthcharts

CDC SAFER · HEALTHIER · PEOPLE™

Short stature:

Height below 2 standard deviations from the mean. (3rd centile)

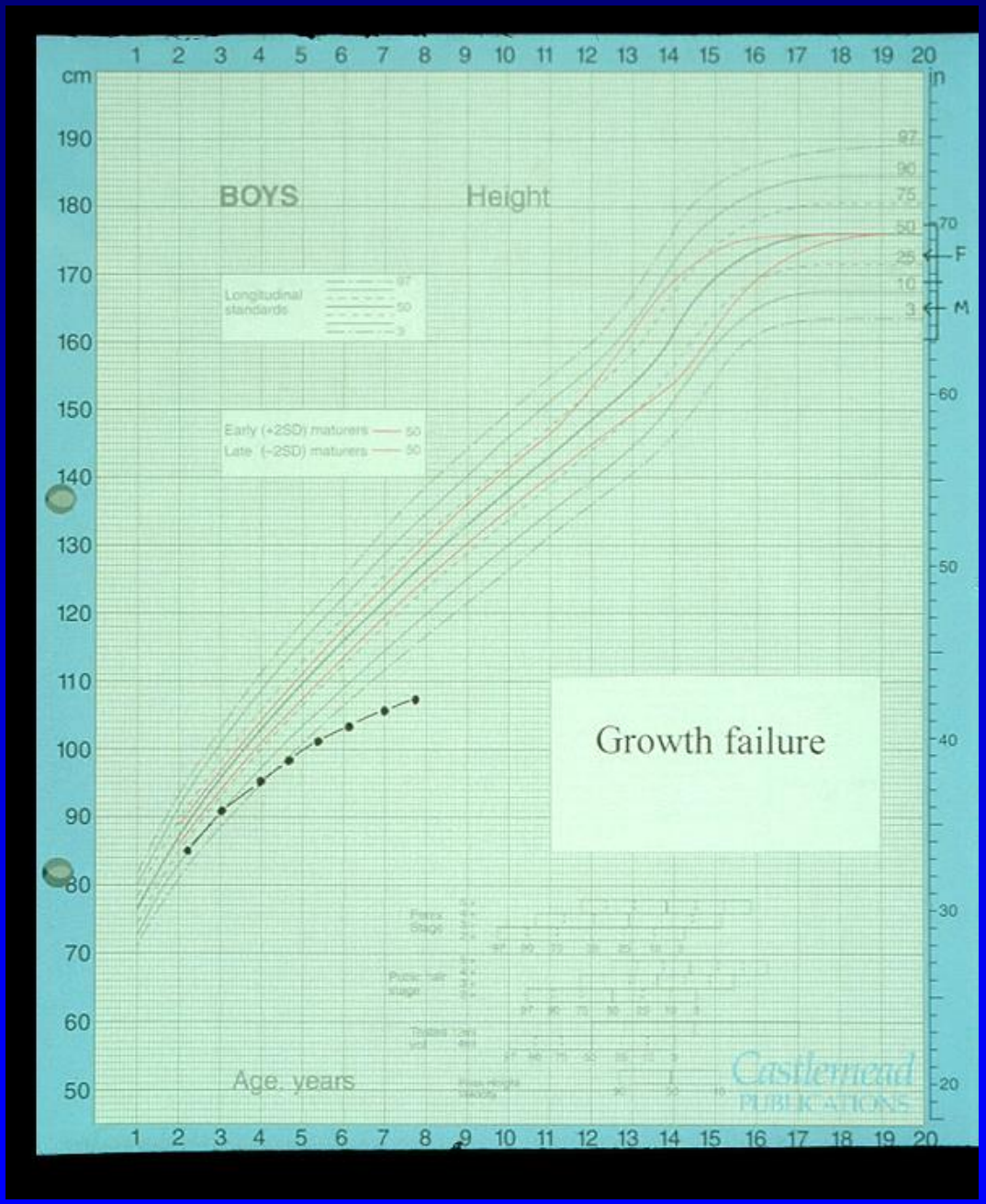

GIRLS
Height
cm
in
Longitudinal standards
97
50
3
Early (+2SD) maturers
Late (–2SD) maturers
Short stature
Age, years

Is the child's height velocity (HV) impaired?

Growth failure:

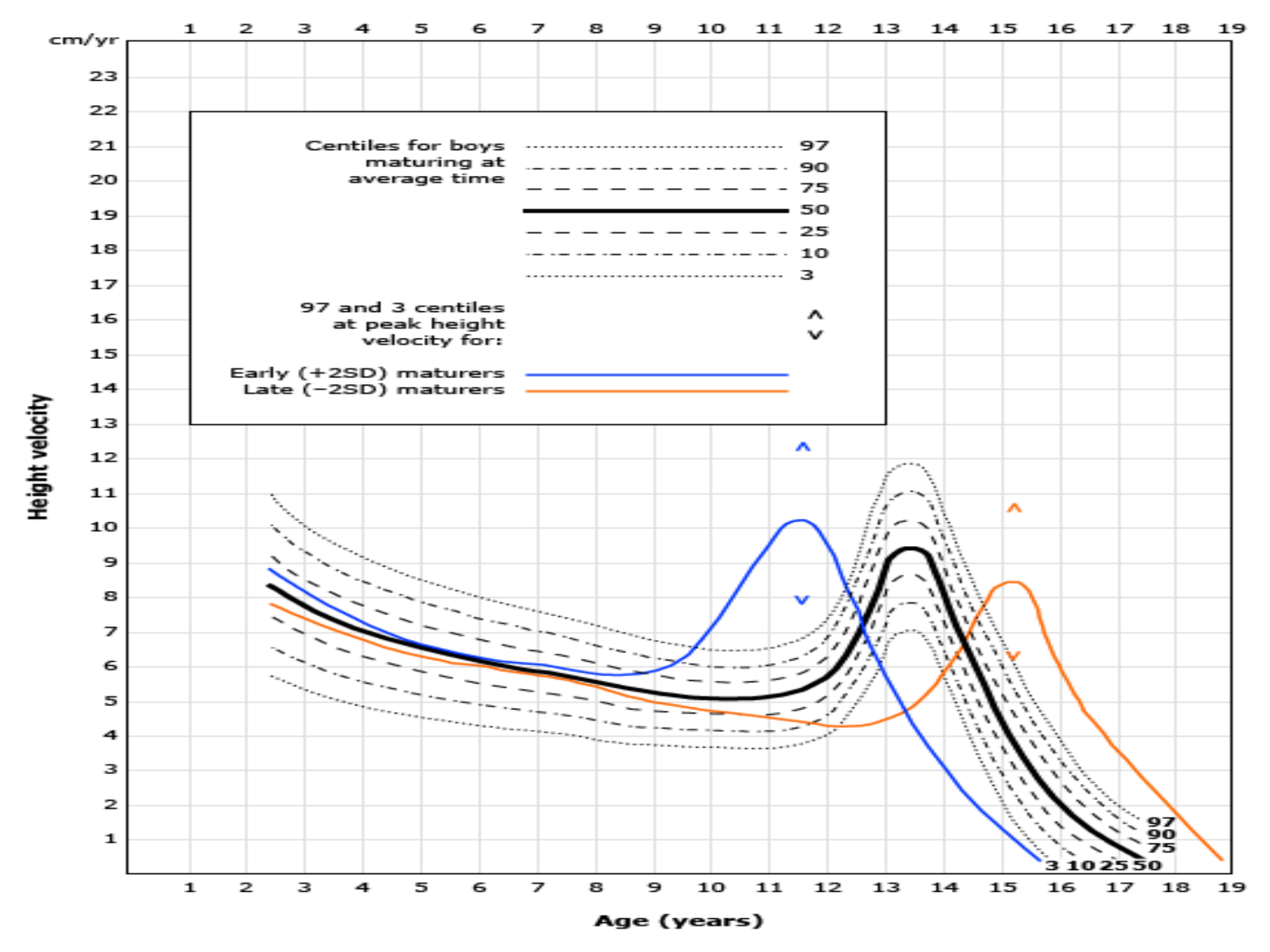
•Failure to maintain a HV that is appropriate for age and maturity.

• HV should be calculated in (cm/year) using accurate measurements of height and an interval between measurements of at least six months


BOYS
Height
cm
in
Age, years
Longitudinal standards
Early (+2SD) maturers
Late (-2SD) maturers
Growth failure
Castlereagh PUBLICATIONS

For children two years and older, **growth failure is likely** if:

- The height-for-age curve has deviated downwards across two major height percentile curves.
- Or, if the child is growing slower than :
- Age 2-4 years: HV less than 5.5 cm/year
- Age 4-6: HV less than 5 cm/year
- Age 6 years to puberty:
- HV less than 4 cm/year for boys
- HV less than 4.5 cm/year for girls


cm/yr
Centiles for boys maturing at average time
97
90
75
50
25
10
3
97 and 3 centiles at peak height velocity for:
Early (+2SD) maturers
Late (−2SD) maturers
Height velocity
Age (years)
97
90
75
3 10 25 50

Failure to thrive/weight faltering:

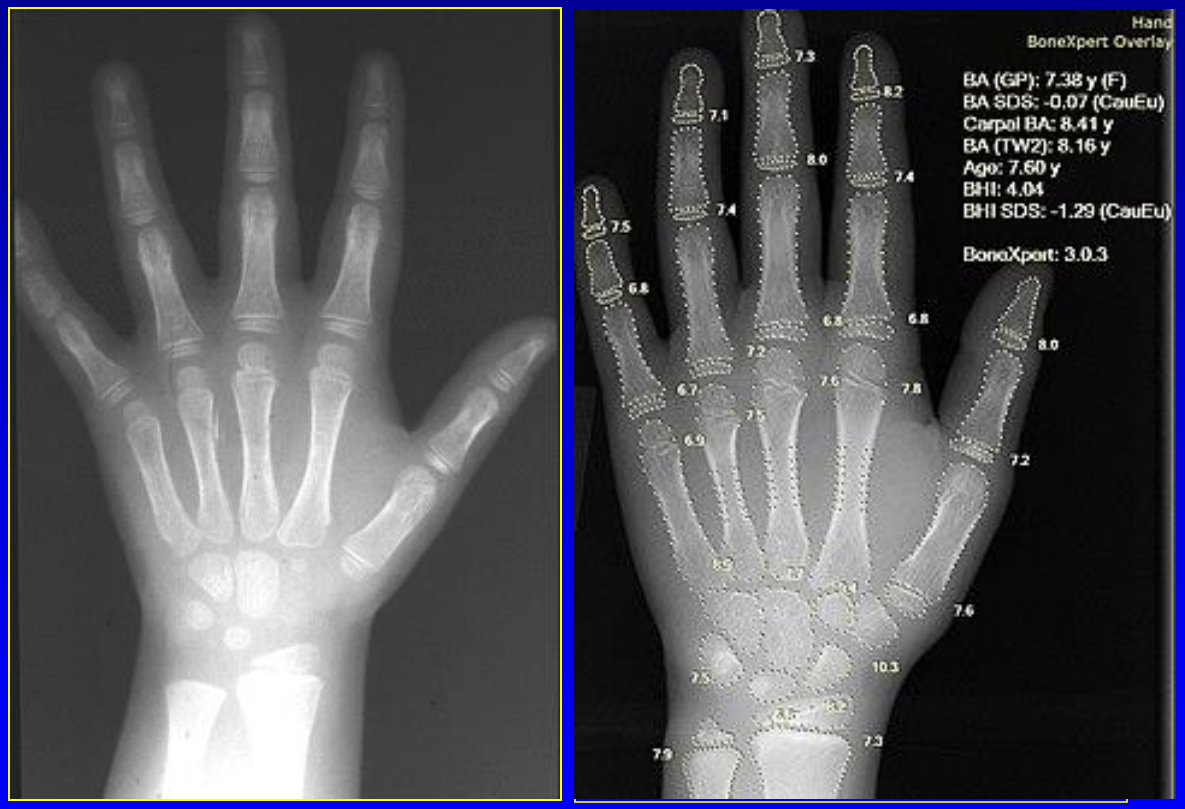
Term usually applied to infants and pre-school children, denoting failure to gain weight at an appropriate rate

What is the child's likely adult height?

- Many methods, different accuracies but in general it depends on:

1. Mid parental height (target height)
2. Bone age : Greulich & Pyle, Tanner Whitehouse…

X-ray of left hand and wrist for bone age assessment



Causes of Short Stature

- Normal (genetic and constitutional delay)
- Small for gestational age
- Dysmorphic syndromes
- Skeletal dysplasias
- Chronic disease
- Endocrine
- Dire social circumstances!
- Idiopathic short stature

Table 1. Causes of short stature according to the ESPE classification

A Primary growth disorders

A1 Clinically defined syndromes
- Turner syndrome
- Cornelia de Lange syndrome
- DiDeorge syndrome (velocardiofacial syndrome)
- Down syndrome
- Noonan syndrome
- Prader-Willi-Labhart syndrome
- Von Recklinghausen's disease (neurofibromatosis type 1)
- Silver-Russell syndrome

A2 Small for gestational age with failure of catch-up growth
- IGF-I deficiency, IGF resistance
- Due to known cause, e.g. prenatal infections, drugs, smoking, alcohol
- Idiopathic

A3 Skeletal dysplasias
- Achondroplasia
- Hypochondroplasia
- Dyschondrosteosis (Leri-Weill and other defects in the SHOX gene)
- Osteogenesis imperfecta I–VI
- Mucopolysaccharidosis (type IH, IS, II–VII)
- Mucolipidosis (type II and III)

A4 Dysplasias with defective mineralization

B Secondary growth disorders

B1 Insufficient nutrient intake (malnutrition)

B2 Disorders in organ systems
- Cardiac disorders
- Pulmonary disorders, e.g. cystic fibrosis
- Liver disorders
- Intestinal disorders, e.g. Crohn's disease, malabsorption syndromes
- Short bowel syndrome
- Renal disorders, e.g. Fanconi syndrome, renal acidosis
- Chronic anemia

B3 Growth hormone deficiency (secondary IGF-I deficiency)
- Idiopathic
- Genetic (HESX1, PROP1, POU1F1, LHX3, LHX4, GHRHR, GH)
- Associated with syndromes or cerebral or facial malformations, e.g. septo-optic dysplasia, empty sella syndrome
- Associated with prenatal infections, e.g. rubella
- Acquired (craniopharyngioma, other pituitary tumors, e.g. germinoma, hamartoma)
- Head trauma
- Central nervous system infections
- Granulomatous diseases, e.g. histiocytosis

B4 Other disorders of the growth hormone-IGF axis (primary IGF-I deficiency and resistance)
- Bioinactive growth hormone
- Abnormalities of the growth hormone receptor (growth hormone insensitivity syndrome, Laron syndrome)
- Abnormalities of GH signal transduction, e.g. STAT5B defect
- ALS (acid-labile subunit) deficiency
- IGF-I deficiency
- IGF resistance (IGF1R defects, postreceptor defects)

B5 Other endocrine disorders
- Cushing syndrome
- Hypothyroidism
- Leprechaunism
- Diabetes mellitus (poorly controlled)
- Short adult stature caused by accelerated bone maturation, e.g. precocious puberty, hyperthyroidism, congenital adrenal hyperplasia, exogenous estrogens or androgens

B6 Metabolic disorders
- Disorders of calcium and phosphorus metabolism
- Disorders of carbohydrate metabolism
- Disorders of lipid metabolism
- Disorders of protein metabolism

B7 Psychosocial
- Emotional deprivation
- Anorexia nervosa
- Depression

B8 Iatrogenic
- Systemic glucocorticoid therapy
- Local glucocorticoid therapy (inhalation, intestinal, other)
- Other medication
- Treatment of childhood malignancy
- Total body irradiation
- Chemotherapy
- Other specified iatrogenic causes

C Idiopathic short stature

C1 Familial (idiopathic) short stature

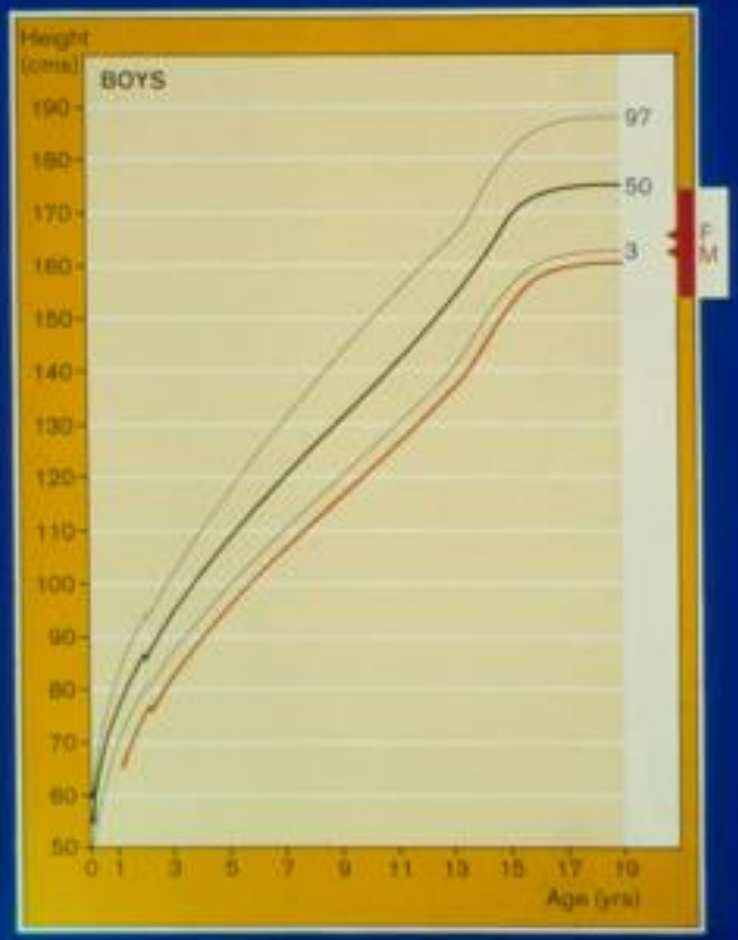
C2 Non-familial (idiopathic) short stature

Classification according to the ESPE classification [19].

Normal genetic short stature

- Child short and normal
- Parent(s) short and normal
- Bone age not delayed
- Child destined to become short adult

Familial (genetic) short stature



Constitutional delay

- Child short, normal but looks younger than chronological age
- Parent(s) not short, but may have been so in childhood
- Bone age delayed
- Late puberty and catch-up growth
- Final height usually in lower half of target range

2 to 20 years: Boys
Stature-for-age and Weight-for-age percentiles

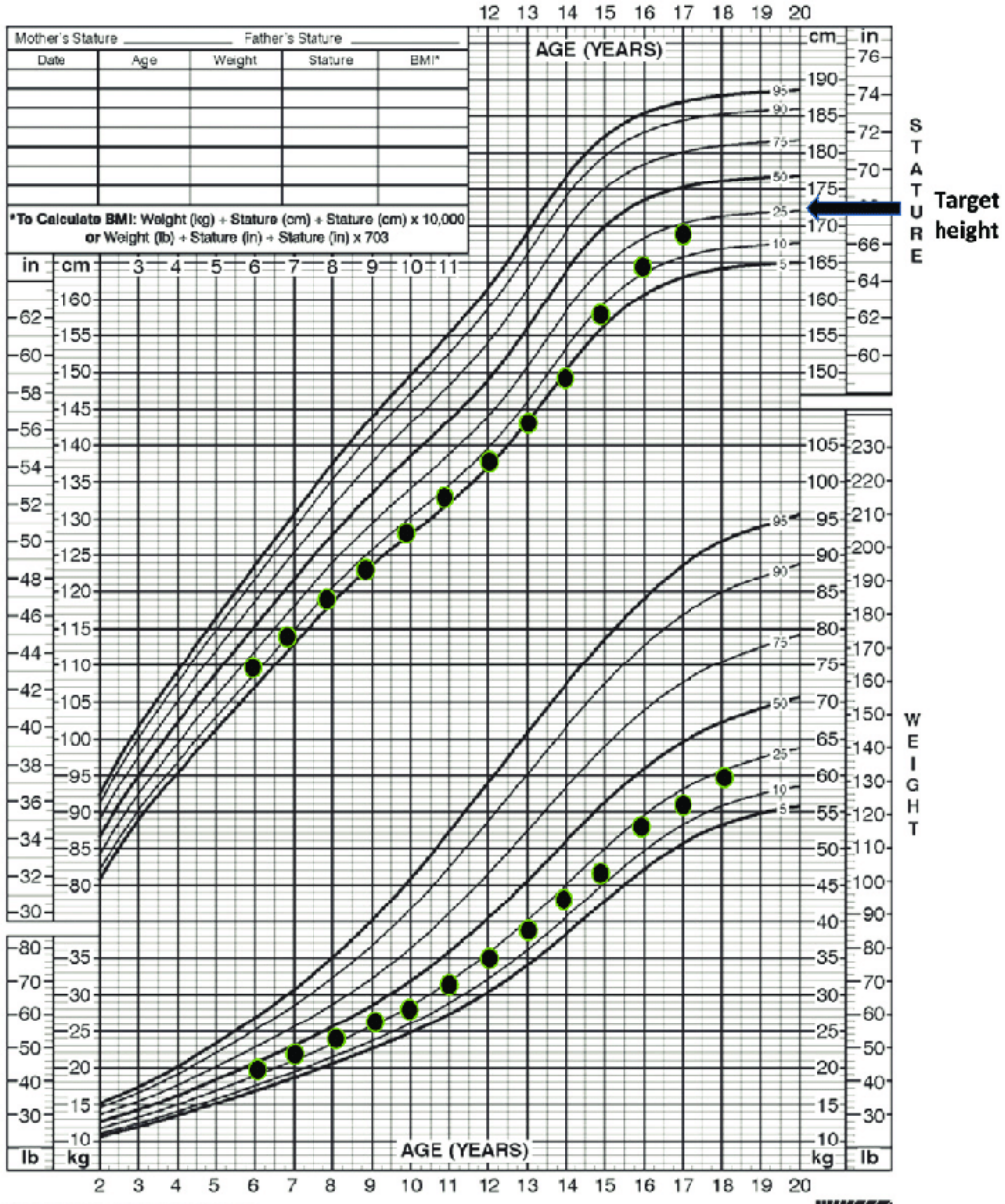
NAME _____

RECORD # _____

Mother's Stature _____ Father's Stature _____

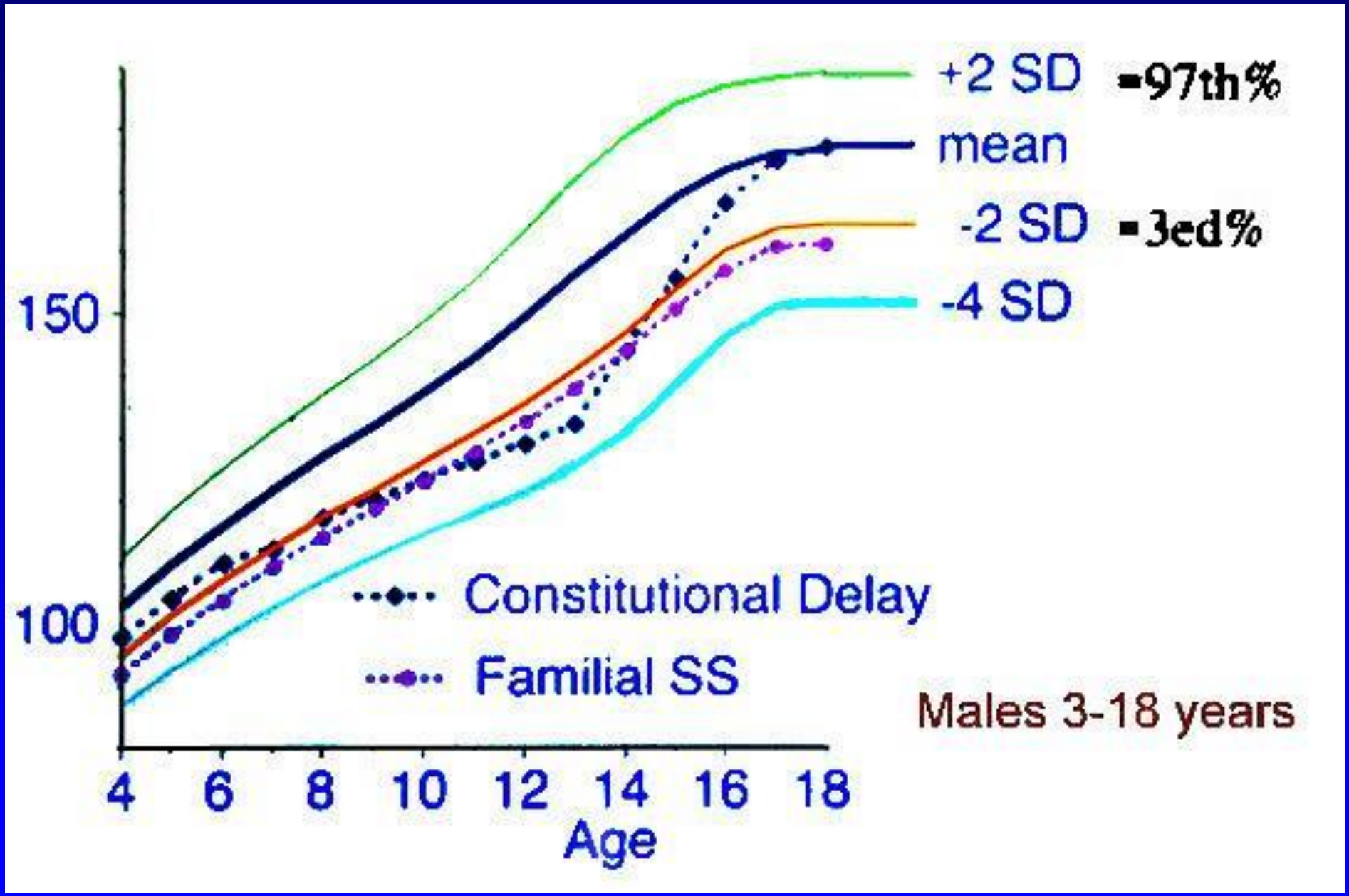
Date	Age	Weight	Stature	BMI*

*To Calculate BMI: Weight (kg) ÷ Stature (cm) ÷ Stature (cm) x 10,000 or Weight (lb) ÷ Stature (in) ÷ Stature (in) x 703



Published May 30, 2000 (modified 11/21/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
http://www.cdc.gov/growthcharts

CDC
SAFER • HEALTHIER • PEOPLE™


+2 SD
=97th%
mean
-2 SD
=3ed%
-4 SD
150
100
Constitutional Delay
Familial SS
Males 3-18 years
4
6
8
10
12
14
16
18
Age

Intrauterine growth retardation (IUGR)

- Asymmetric (HC>L>Wt)

  3rd trimester malnutrition; catch-up growth during infancy; normal childhood growth and final height

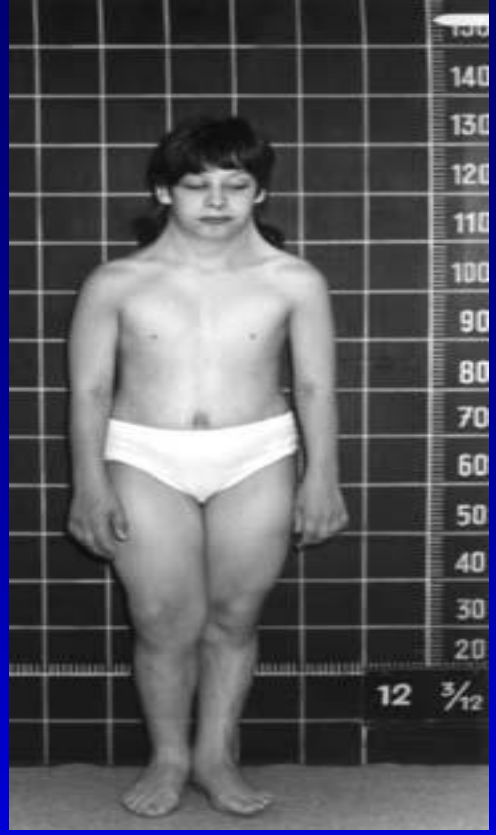
- Symmetric (HC=L=Wt)

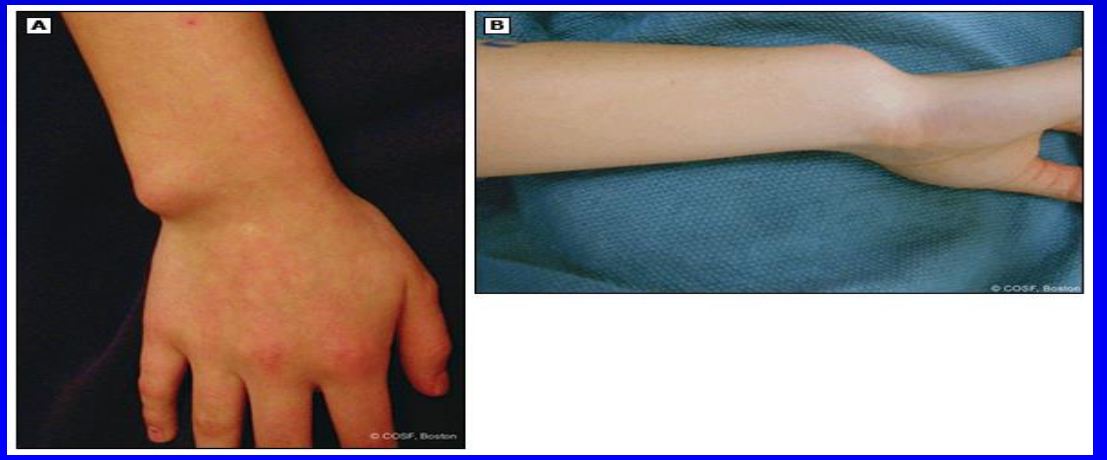
  prolonged intrauterine malnutrition; catch-up growth in infancy partial/absent; short stature in childhood despite normal growth rate; short adult

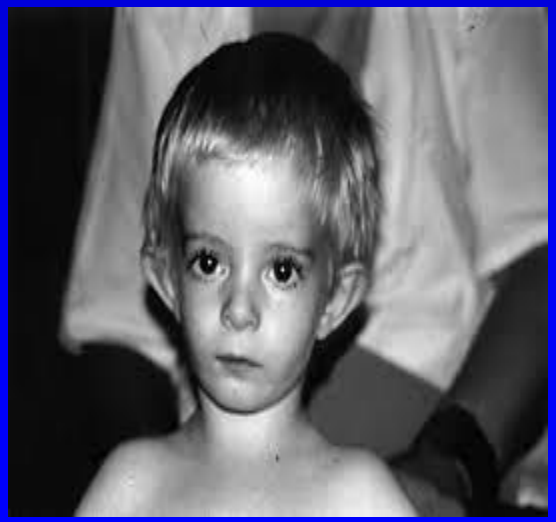
- Most infants born small for gestational age (SGA) experience catch-up growth by two years of age
- About 10 % of SGA infants, particularly those born with more severe SGA, do not experience catch-up growth to reach the normal range by two years of age.

Dysmorphic syndromes

- Turner
- Noonan
- Silver Russel
- William
- Prader-Willi


140
130
120
110
100
90
80
70
60
50
40
30
20
12 3/12


A
B
© COSF, Boston
© COSF, Boston

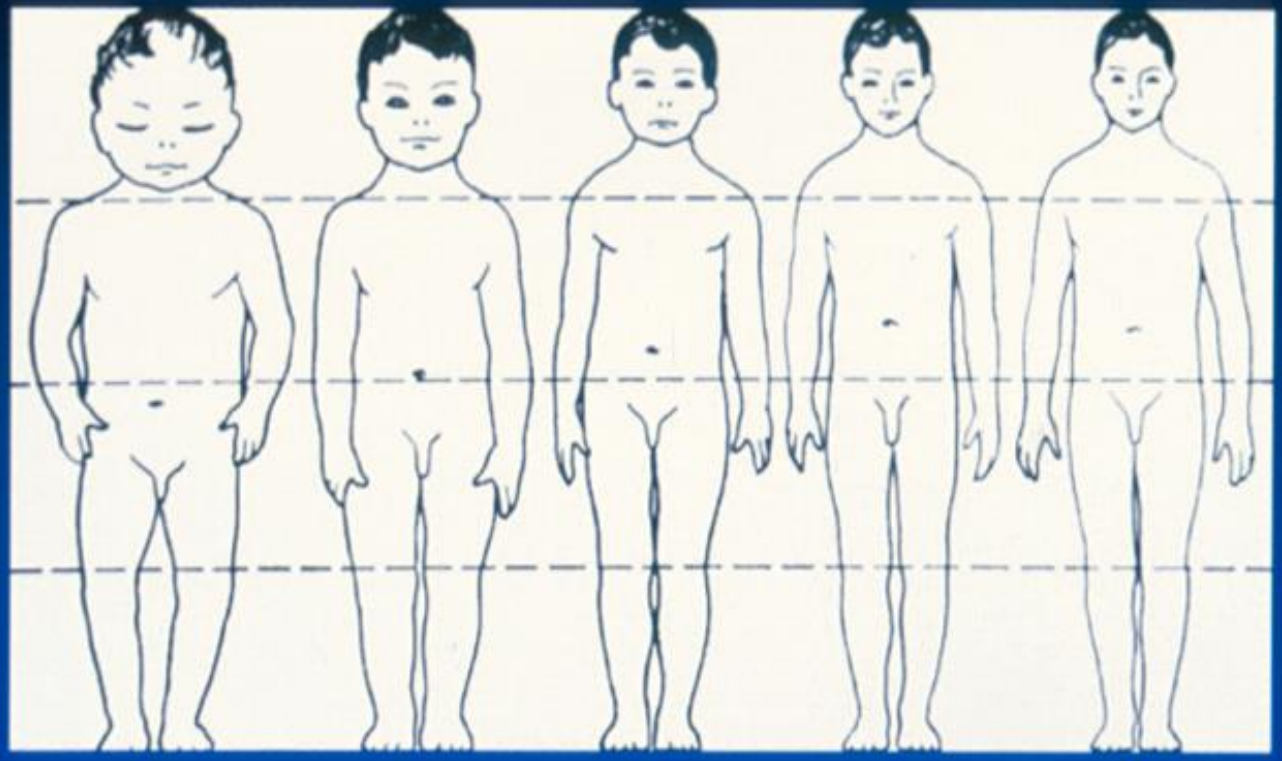


Skeletal dysplasia

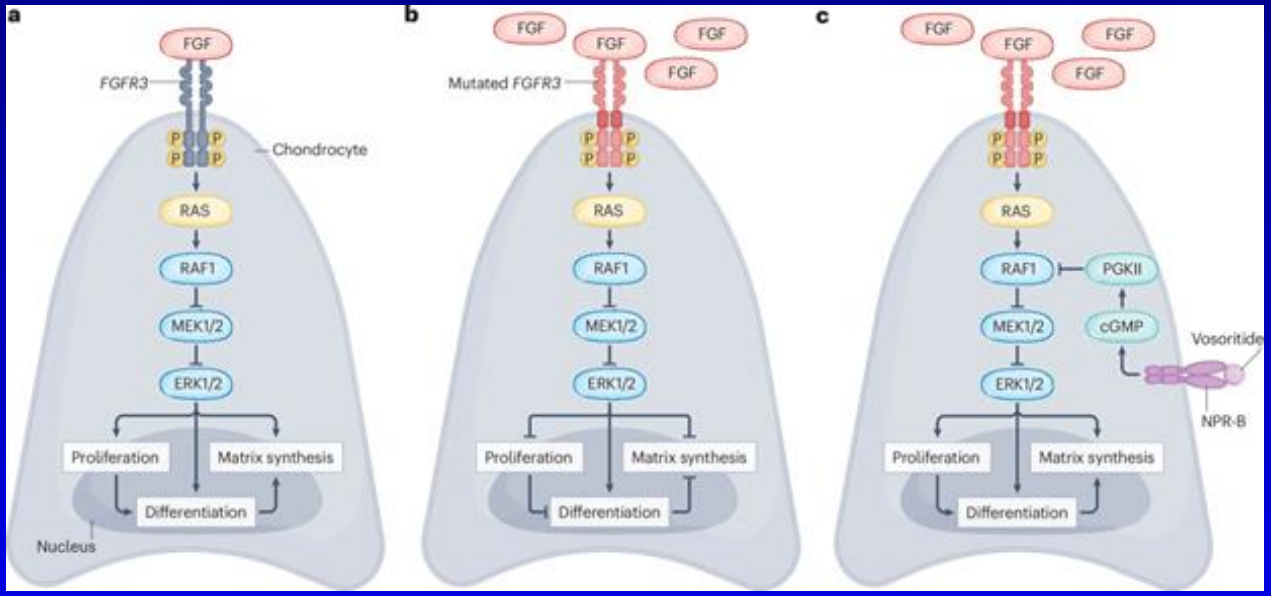
- Frank skeletal abnormality affecting
  - epiphyses (epiphyseal dysplasia)
  - metaphyses (metaphyseal dysplasia)
  - spine (spondyleal dysplasia)

  in various combinations (e.g. spondylo-epiphyseal dysplasia)
- Bone age tends to be advanced
- Adult height SDS < Childhood height SDS

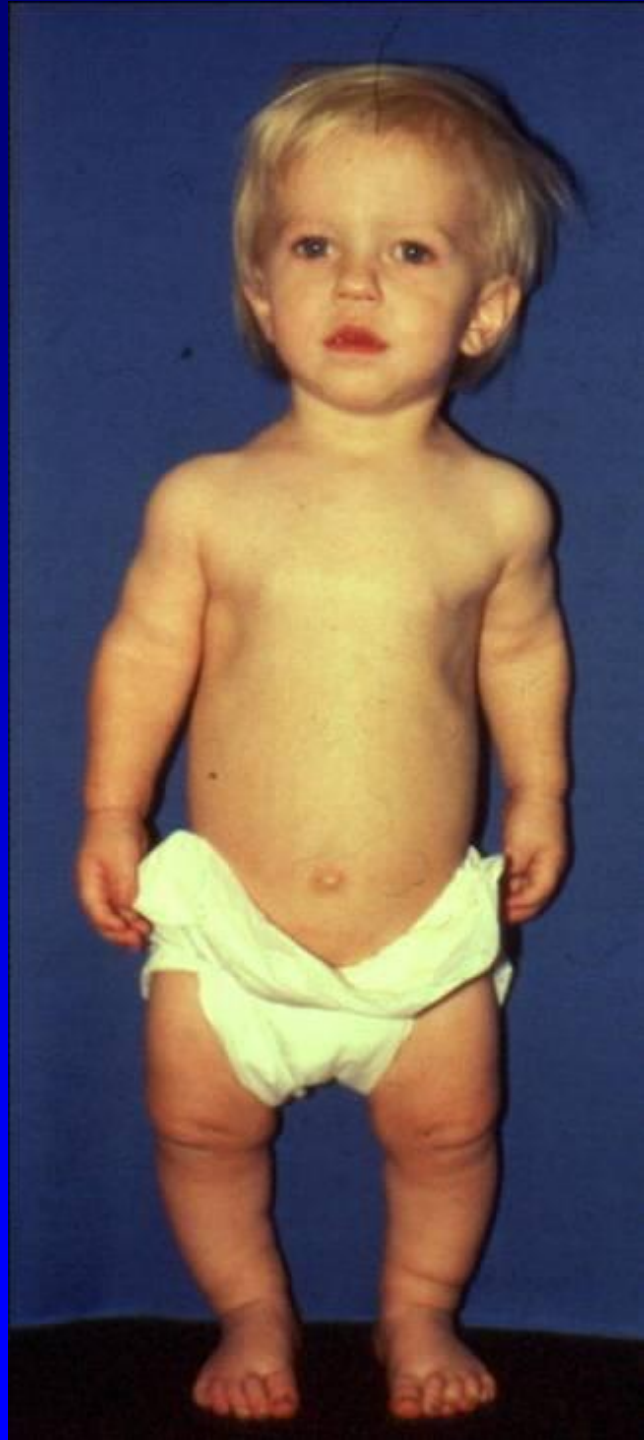
Stature divided into quarters



Achondroplasia



- Gain of function mutation in the fibroblast growth factor receptor 3 (FGFR3) gene. (AD)
- disrupts normal bone growth, in the long bones of the arms and legs by interference with endochondral ossification, the process by which cartilage is replaced by bone, resulting in shortened and abnormally shaped bones.



Chronic systemic disease

Many different types

Any chronic condition (e.g. GI, cardiac, respiratory, renal, metabolic, CNS, joints) can cause short stature and/or slow growth

Chronic renal disease and GI disorders (e.g. coeliac disease) can be silent, and present with short stature.

Social and emotional short stature

- Children from poor communities tend to be shorter than those from affluent areas
- Severe short stature with growth failure may result from emotional abuse/neglect (psychosocial deprivation)

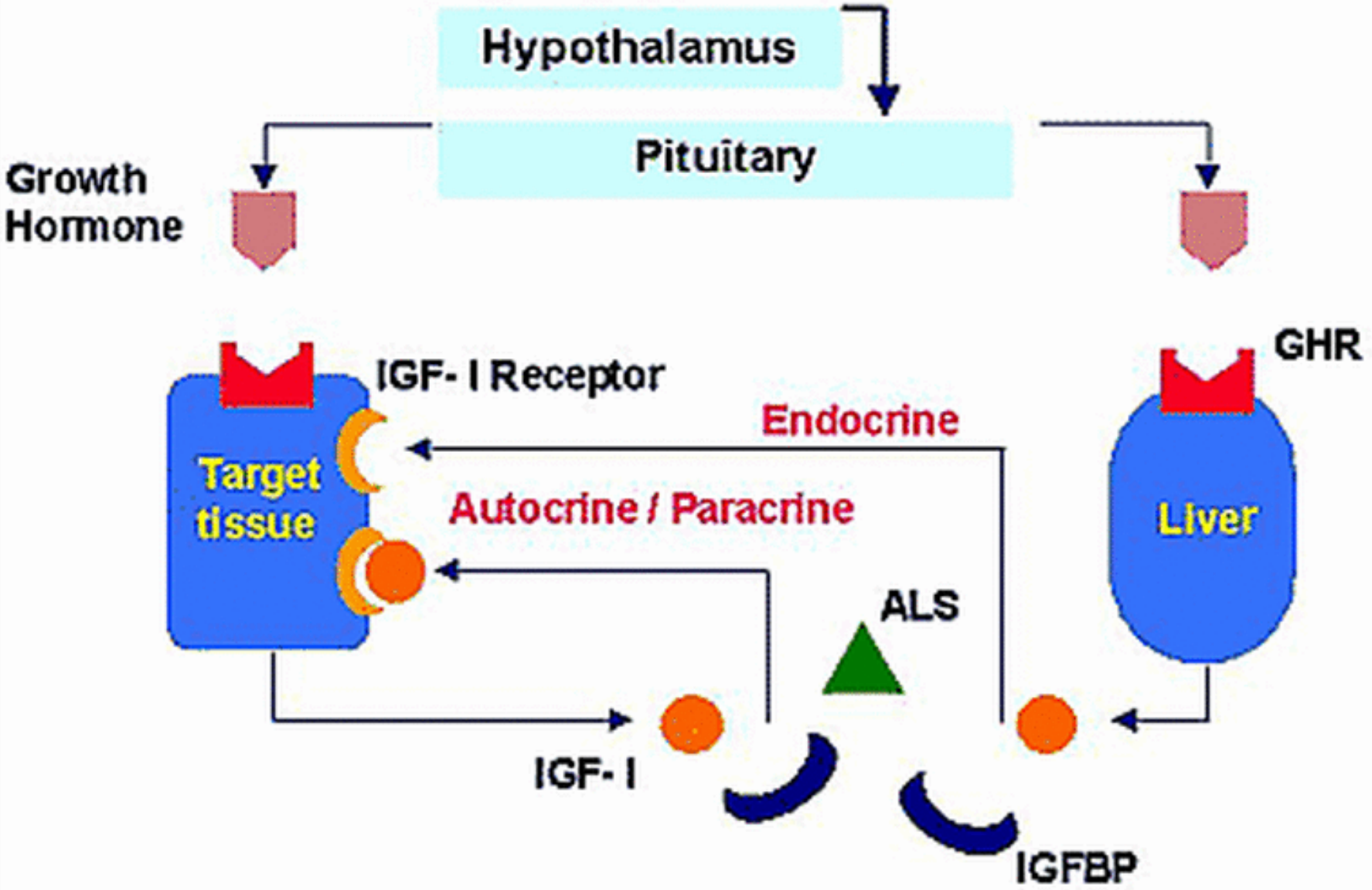
Endocrine disorders

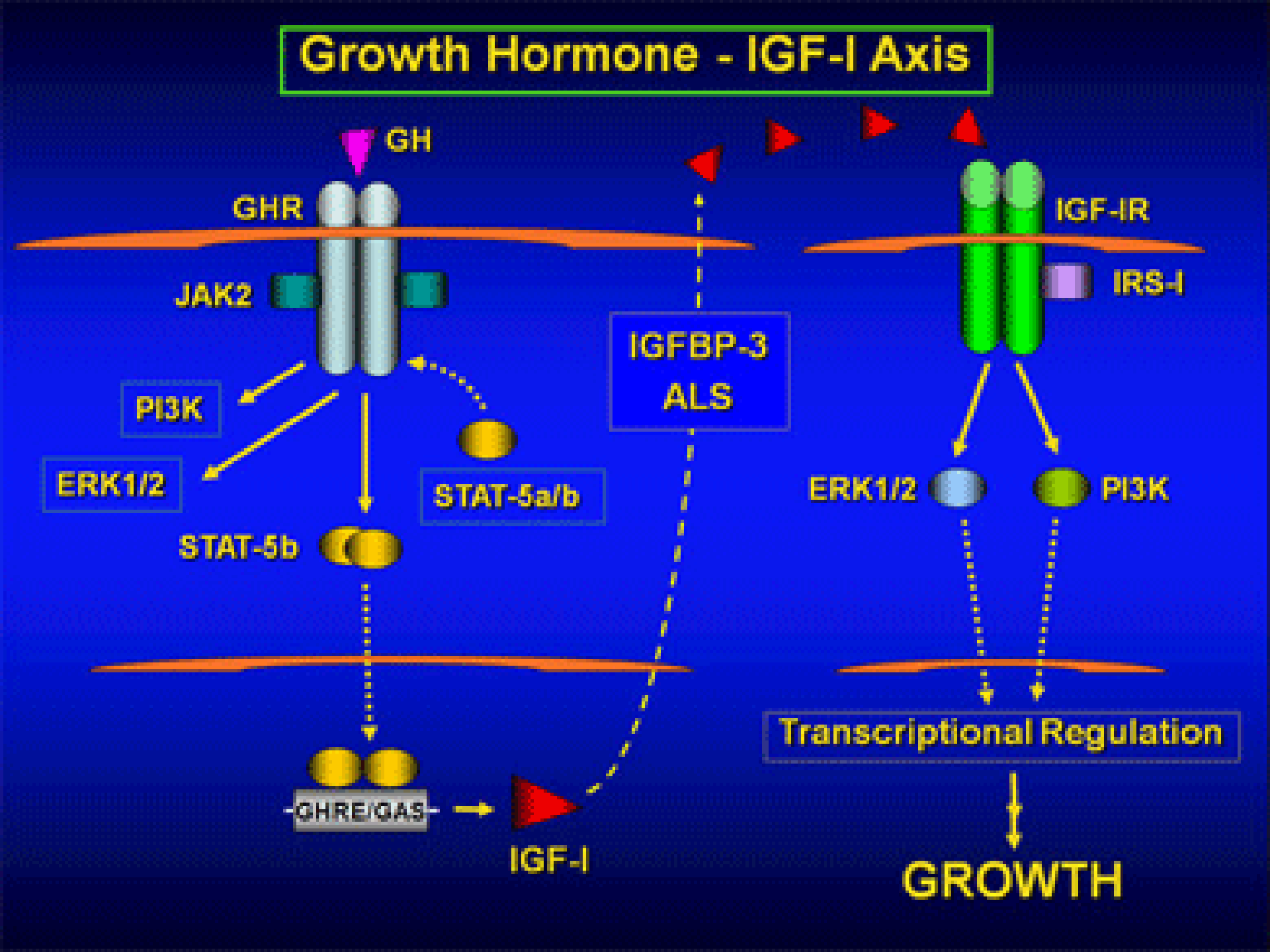
- Growth hormone deficiency and resistance
- Thyroxine deficiency
- Cortisol excess
- Precocious puberty
- Idiopathic short stature

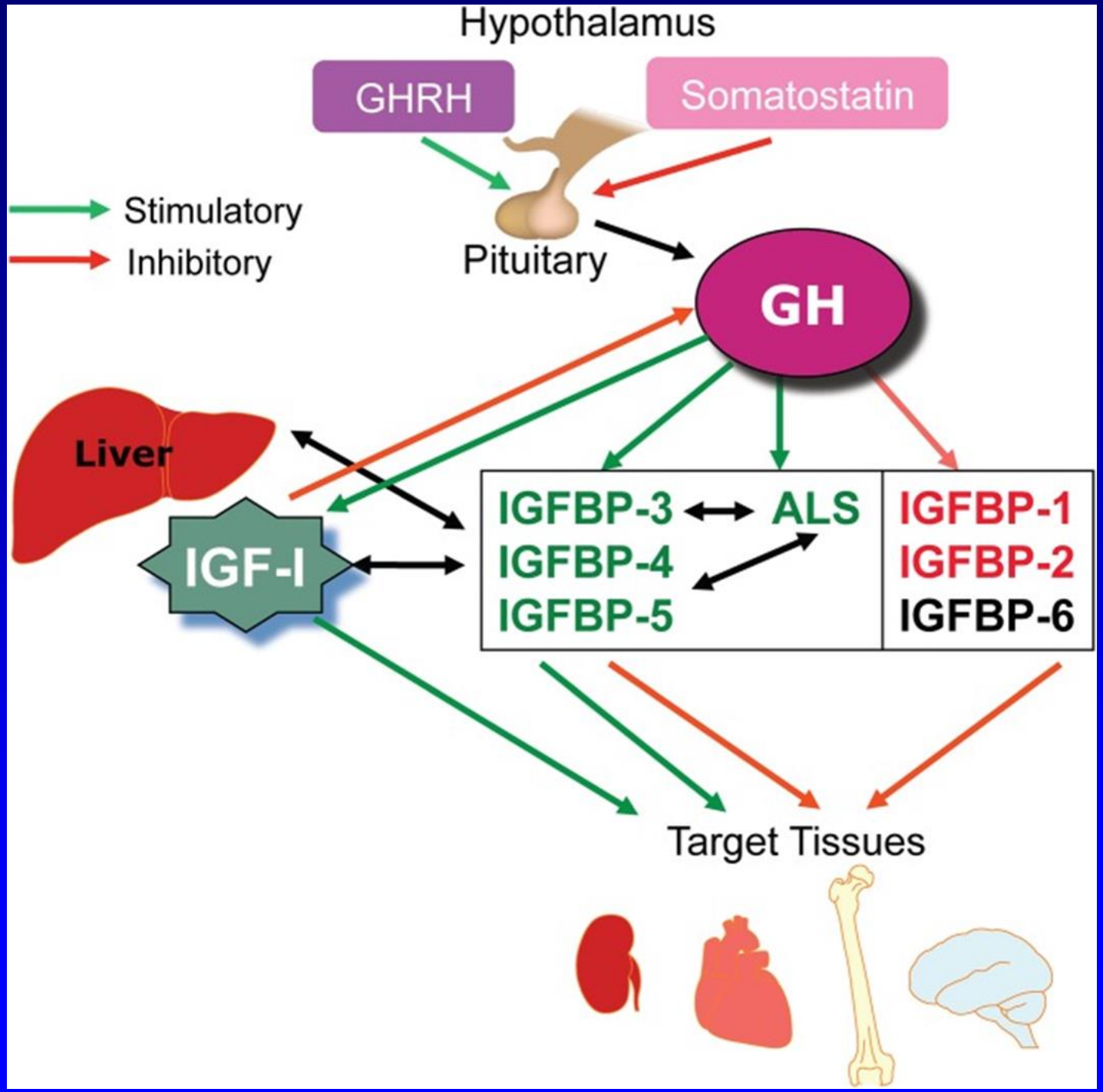
Growth hormone

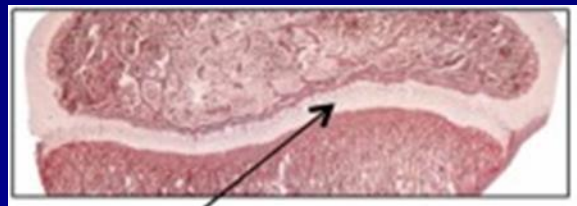
- anterior pituitary protein secreted by somatotrophs .
- antagonizes insulin action, promotes lipolysis in fat, and augments protein synthesis.
- Secretion is pulsatile
- Stimulated be sleep and exercise, inhibited by leptin and glucose

The Growth Hormone / IGF Axis




Growth Hormone - IGF-I Axis
GH
GHR
JAK2
PI3K
ERK1/2
STAT-5b
STAT-5a/b
GHRE/GAS
IGF-I
IGFBP-3
ALS
IGF-IR
IRS-I
ERK1/2
PI3K
Transcriptional Regulation
GROWTH


Hypothalamus
GHRH
Somatostatin
Stimulatory
Inhibitory
Pituitary
GH
Liver
IGF-I
IGFBP-3
ALS
IGFBP-4
IGFBP-5
IGFBP-1
IGFBP-2
IGFBP-6
Target Tissues



Growth plate

Epiphysis

Resting zone

Proliferative zone

Hypertrophic zone

Metaphysis

Hypothalamus

Pituitary

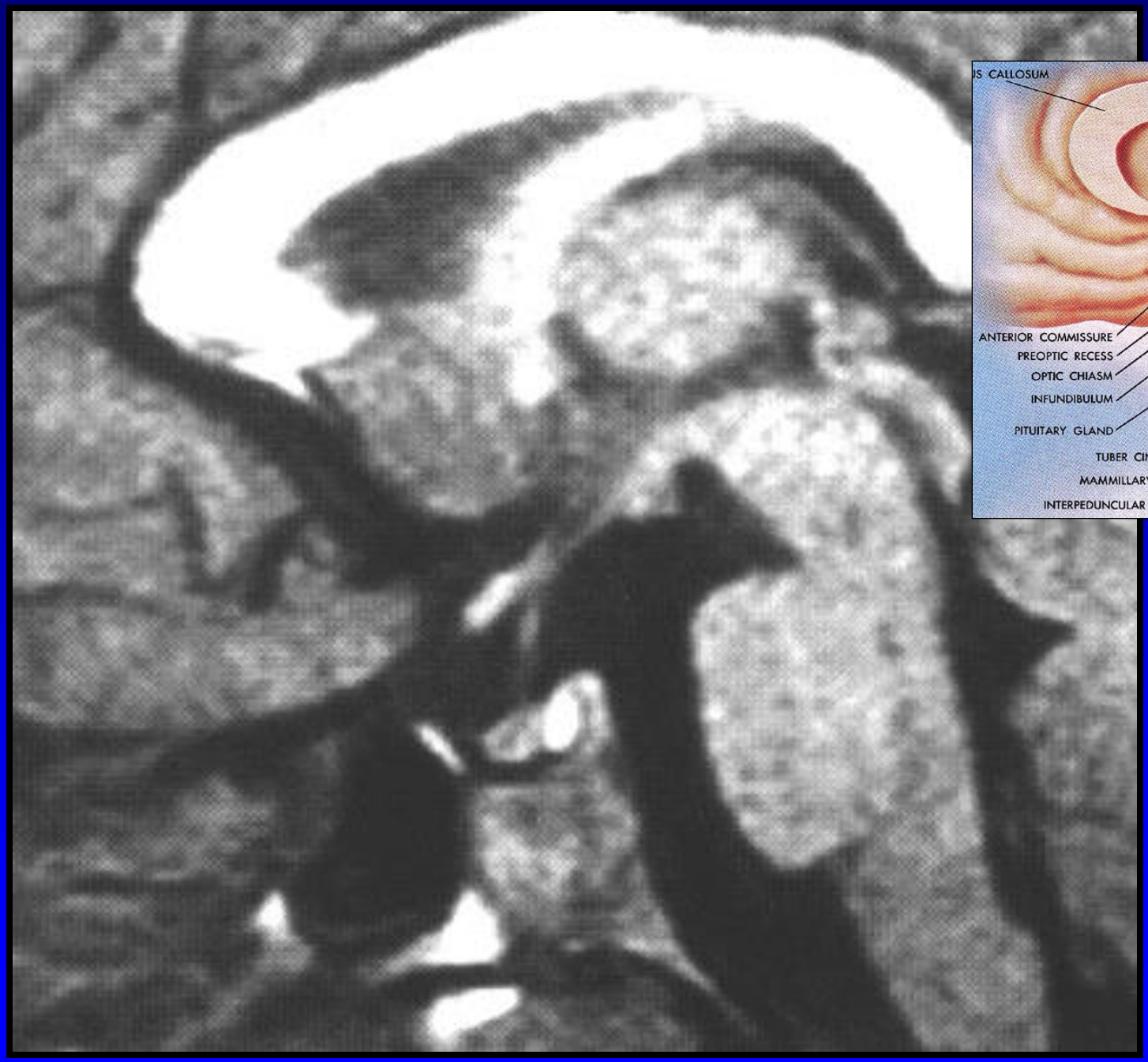
GH

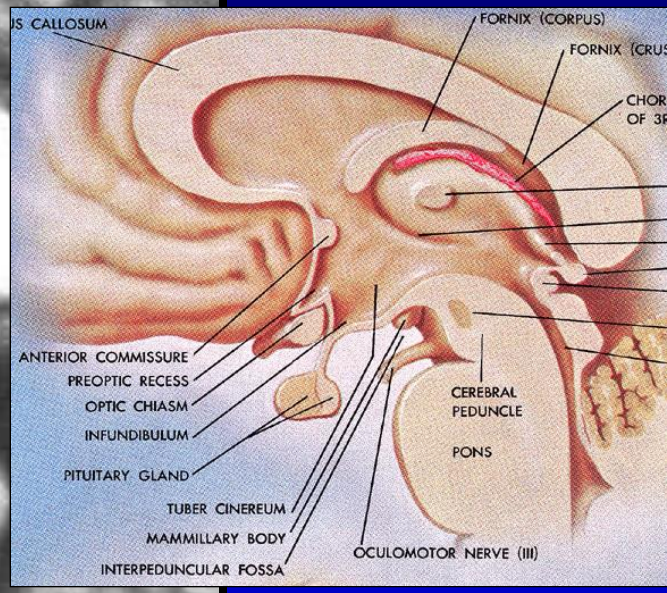
local IGF-I

Circulating IGF-I

negative feedback loop

The complex modifying interactions of IGFBPs are not shown





L.J. Abernethy

Classification of growth hormone deficiency

- cause (congenital or acquired)
- nature (true permanent deficiency or functional/temporary insufficiency)
- severity (complete, severe or partial)
- whether isolated or part of multiple anterior pituitary deficiency

Causes of hypopituitarism

CONGENITAL

- Idiopathic
- Genetic defect

  (i) isolated GH deficiency (AR, AD, X-linked)

  (ii) multiple AP deficiency (eg PROP-1)

  (iii) Prader-Willi synd
- Midline defects (e.g. septo-optic dysplasia)

ACQUIRED

- Tumours (e.g. craniopharyngioma, optic glioma)
- Surgery
- Cranial radiotherapy (e.g. for medulloblastoma)
- Granulomatous disease (e.g. Langerhans cell histiocytosis)

Idiopathic short stature

- Definitions vary according to different centres
- One definition is significant short stature (< -2.5 SD) ?? not attributable to normal familial short stature or constitutional delay or to other causes of short stature
- Heterogenous condition which may include partial GH resistance, mild skeletal dysplasias etc.

Evaluation of the child with short stature - history

- History of growth pattern and previous measurements
- Parental heights,puberty
- Birthweight,postnatal hx
- General health
- Psychosocial situation

Evaluation of the child with short stature - auxology

- Accurate measurement of child and parents
- Sibling measurement in selected cases
- Plot height and weight (nice dots!)
- Sitting height and leg length if disproportion suspected
- Plot mid parental height and target range
- Bone age by single observer

Evaluation of the child with short stature - examination

- General appearance and nutrition
- Body proportions
- Dysmorphic features
- Systemic examination including heart
- BP
- Pubertal status
- Fundi

Investigation of short stature

- Low threshold for karyotype in girls with short stature.
- Short stature screening
- Further short stature investigation

Short stature screening

- FBC and film, ESR, TTG a'bodies,LFT,Blood gas
- Karyotype
- TFT, IGF-1,IGFBP3, prolactin, cortisol
- Creatinine, Lytes, calcium and phosphate
- Urinalysis and culture

Further investigation of short stature

- Endocrine stimulation testing
  - ITT/arginine/clonidine/glucagon
- Pituitary imaging
- Genetic evaluation – clinical, laboratory
- Skeletal survey

Treatment

- Treat the cause.

Conditions where growth hormone therapy is recommended

- Growth hormone deficiency
- Turner syndrome/Noonan Syndrome/SHOX
- Prader-Willi syndrome.
- SGA with no catch up by 4 years
- Chronic renal insufficiency.
- ISS ??

Treatment of GH deficiency

Recombinant human growth hormone (RHGH)

- Daily bedtime subcutaneous injections of aqueous solutions of biosynthetic (recombinant) GH
- Weekly preparation liscenced for pGHD
- Follow up q 3 months

norditropin® nordilet® 5mg/1.5 ml

mg	Dose	IU
0.07	1	0.21
0.13	2	0.39
0.20	3	0.60
0.27	4	0.81
0.33	5	0.99
0.40	6	1.20
0.47	7	1.41
0.53	8	1.59
0.60	9	1.80
0.67	10	2.01
0.73	11	2.19
0.80	12	2.40
0.87	13	2.61
0.93	14	2.79
1.00	15	3.00
1.07	16	3.21
1.13	17	3.39
1.20	18	3.60
1.27	19	3.81
1.33	20	3.99
1.40	21	4.20
1.47	22	4.41
1.53	23	4.59
1.60	24	4.80
1.67	25	5.01
1.73	26	5.19
1.80	27	5.40
1.87	28	5.61
1.93	29	5.79

norditropin® nordilet® 10mg/1.5 ml

mg	Dose	IU
0.13	1	0.39
0.27	2	0.81
0.40	3	1.20
0.53	4	1.59
0.67	5	2.01
0.80	6	2.40
0.90	7	2.79
1.07	8	3.21
1.20	9	3.60
1.33	10	3.99
1.47	11	4.41
1.60	12	4.80
1.73	13	5.19
1.87	14	5.61
2.00	15	6.00
2.13	16	6.31
2.27	17	6.81
2.40	18	7.20
2.53	19	7.59
2.67	20	8.01
2.80	21	8.40
2.93	22	8.79
3.07	23	9.21
3.20	24	9.60
3.33	25	9.99
3.47	26	10.41
3.60	27	10.80
3.73	28	11.19
3.87	29	11.61

norditropin® nordilet® 15mg/1.5 ml

mg	Dose	IU
0.20	1	0.60
0.40	2	1.20
0.60	3	1.80
0.80	4	2.40
1.00	5	3.00
1.20	6	3.60
1.40	7	4.20
1.60	8	4.80
180	9	5.40
2.00	10	6.00
2.20	11	6.60
2.40	12	7.20
2.60	13	7.80
2.80	14	8.40
3.00	15	9.00
3.20	16	9.60
3.40	17	10.20
3.60	18	10.80
3.80	19	11.40
4.00	20	12.00
4.20	21	12.60
4.40	22	13.20
4.60	23	13.80
4.80	24	14.40
5.00	25	15.00
5.20	26	15.60
5.40	27	16.20
5.60	28	16.80
5.80	29	17.40

Clicks into mg

Dose in mg

Differs according to the indication of growth hormone treatment

Side Effects of GH Treatment

- Metabolic effects (hyperglycemia)
- Antibodies to growth hormone
- Progression of pre-existing scoliosis
- Slipped capital femoral epiphysis
- Pseudotumor cerebri
- Transient gynecomastia
- Increased growth and pigmentation of nevi
- Carpal tunnel syndrome
- Edema / Arthralgia
- Hypothyroidism
- Second neoplasms

Meningioma

- Pancreatitis

Mini Review

HORMONE RESEARCH

Horm Res 2009;72:206–217
DOI: 10.1159/000236082

Received: April 7, 2009
Accepted: June 15, 2009
Published online: September 29, 2009

Diagnostic Approach in Children with Short Stature

Wilma Oostdijk[a] Floor K. Grote[a] Sabine M.P.F. de Muinck Keizer-Schrama[b]
Jan M. Wit[a]

[a]Department of Pediatrics, Leiden University Medical Center, Leiden, and [b]Department of Pediatrics, Erasmus MC – Sophia Children's Hospital, Rotterdam, The Netherlands

ELSEVIER

The Journal of Pediatrics

Volume 164, Issue 5, Supplement, May 2014, Pages S1-S14.e6

Supplement

Etiologies and Early Diagnosis of Short Stature and Growth Failure in Children and Adolescents

Alan D. Rogol MD, PhD [1], Gregory F. Hayden MD [2]