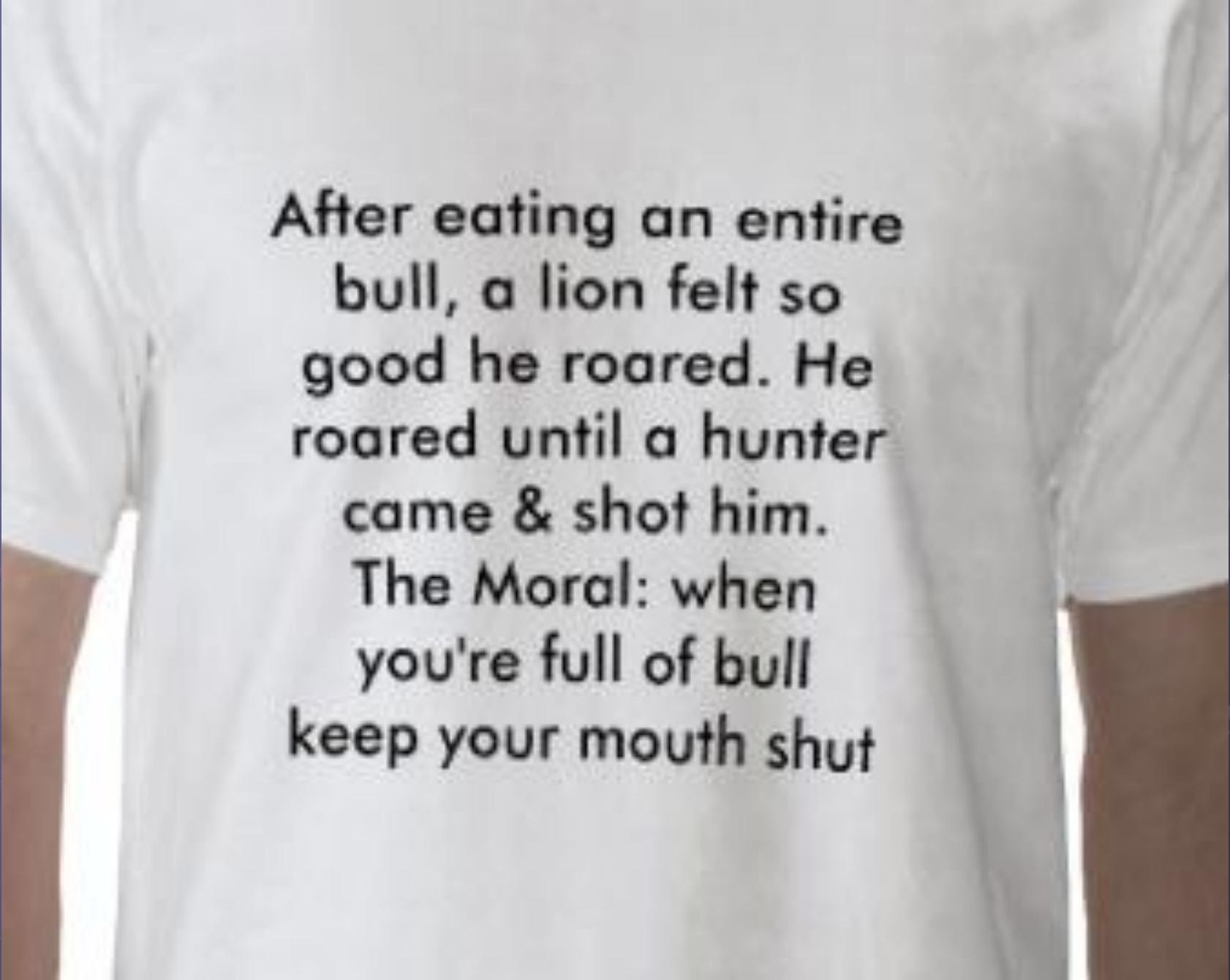




Disclosure

- Presentation sponsored by Pfizer
 - Growth hormone is funded in NZ for...
 - Growth hormone deficiency
 - Turner syndrome and PWS
 - Severe short stature (non GH deficient)
 - Chronic renal failure (children)
 - Adult GH deficiency
- Not everything I say is politically correct
- “Common” is a relative term
- Not all my pictures are from google

A person is wearing a white t-shirt. The back of the t-shirt features a printed story and a moral. The text is in a black, sans-serif font. The background of the image is a dark blue gradient with a pattern of small, light blue dots and lines.

After eating an entire
bull, a lion felt so
good he roared. He
roared until a hunter
came & shot him.
The Moral: when
you're full of bull
keep your mouth shut

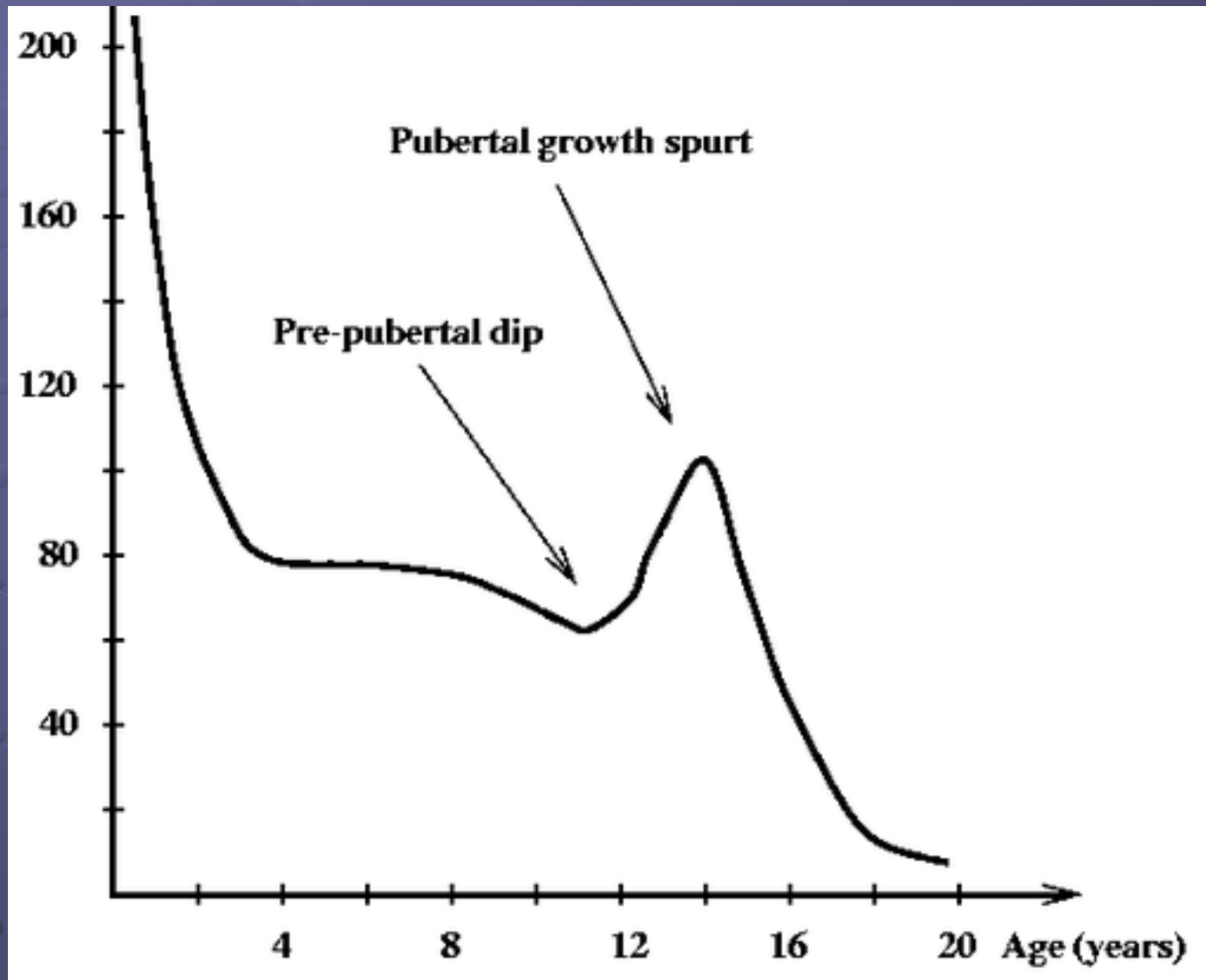
Outline of talk

- Growth Cases
- Puberty Cases
- Paediatric Endocrine Potpourri
- Please interrupt for questions along the way

Growth phases



Human growth phases



Assessment of growth

● General

- Height, weight & HC, ideally serial measures
- Parents heights
- Body proportions, general health
- Pubertal stage

● Investigations

- Chronic disease: Coeliac, FBC, ESR etc, MSU. RFT, LFT and iron studies.
- Bone age
- Hormonal: TFTS, IGF-1, Prolactin, karyotype

Mid parental height

Table 3

To calculate the potential height of a boy, the mother's height is given an additional 13cm and averaged with the father's height. This mid parental or "target height" can be plotted on a growth chart to estimate the centile the boy should grow along.

e.g. FATHER 180cm

MOTHER 157cm + 13cm = 170cm

AVERAGE 175cm = potential height = 50th height centile

(See Diagram 3)

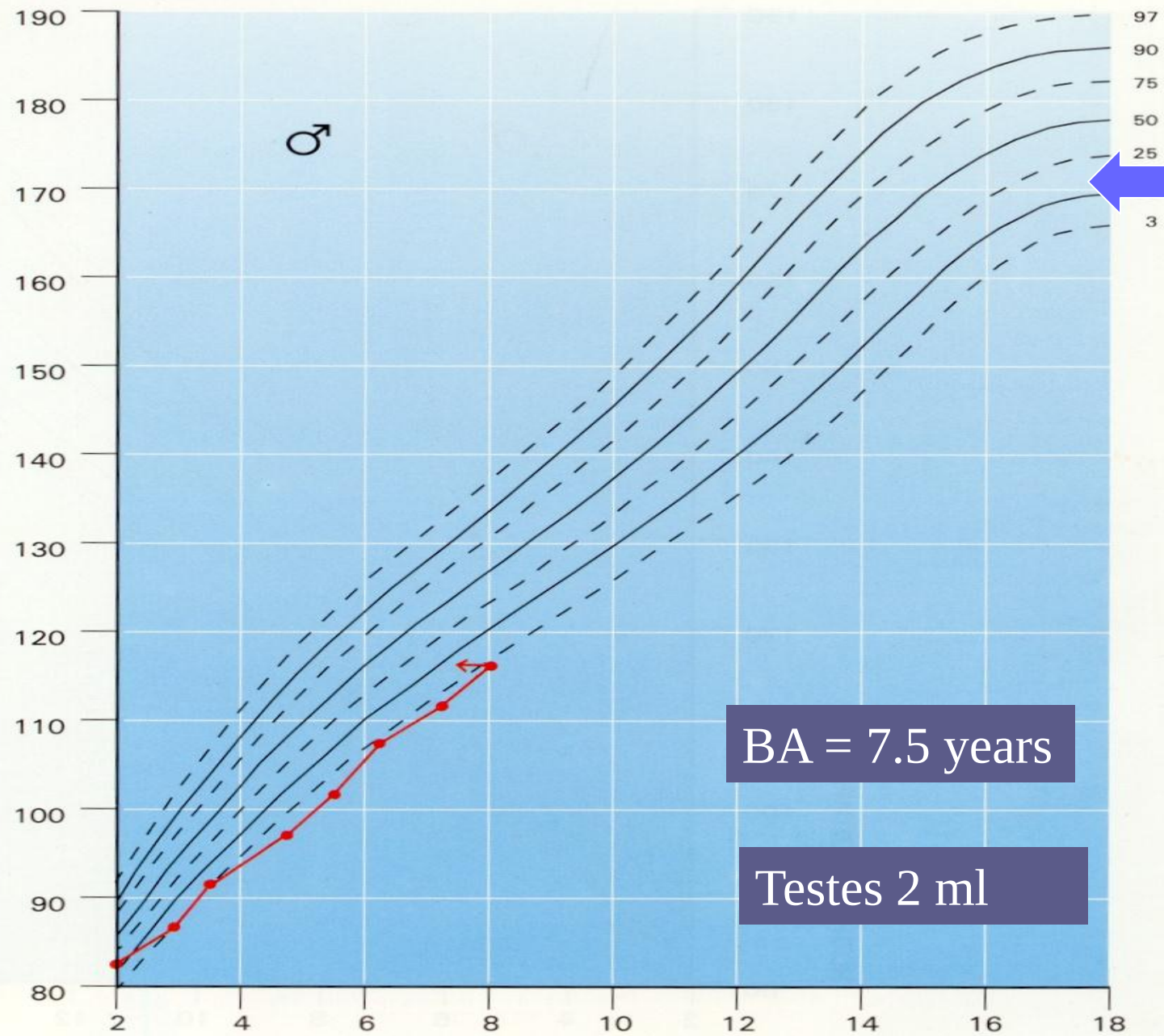
To estimate a girl's height, subtract 13cm from the father's height and follow the same steps as above.

Growth Case

Eight Year old boy

Always shorter than peers

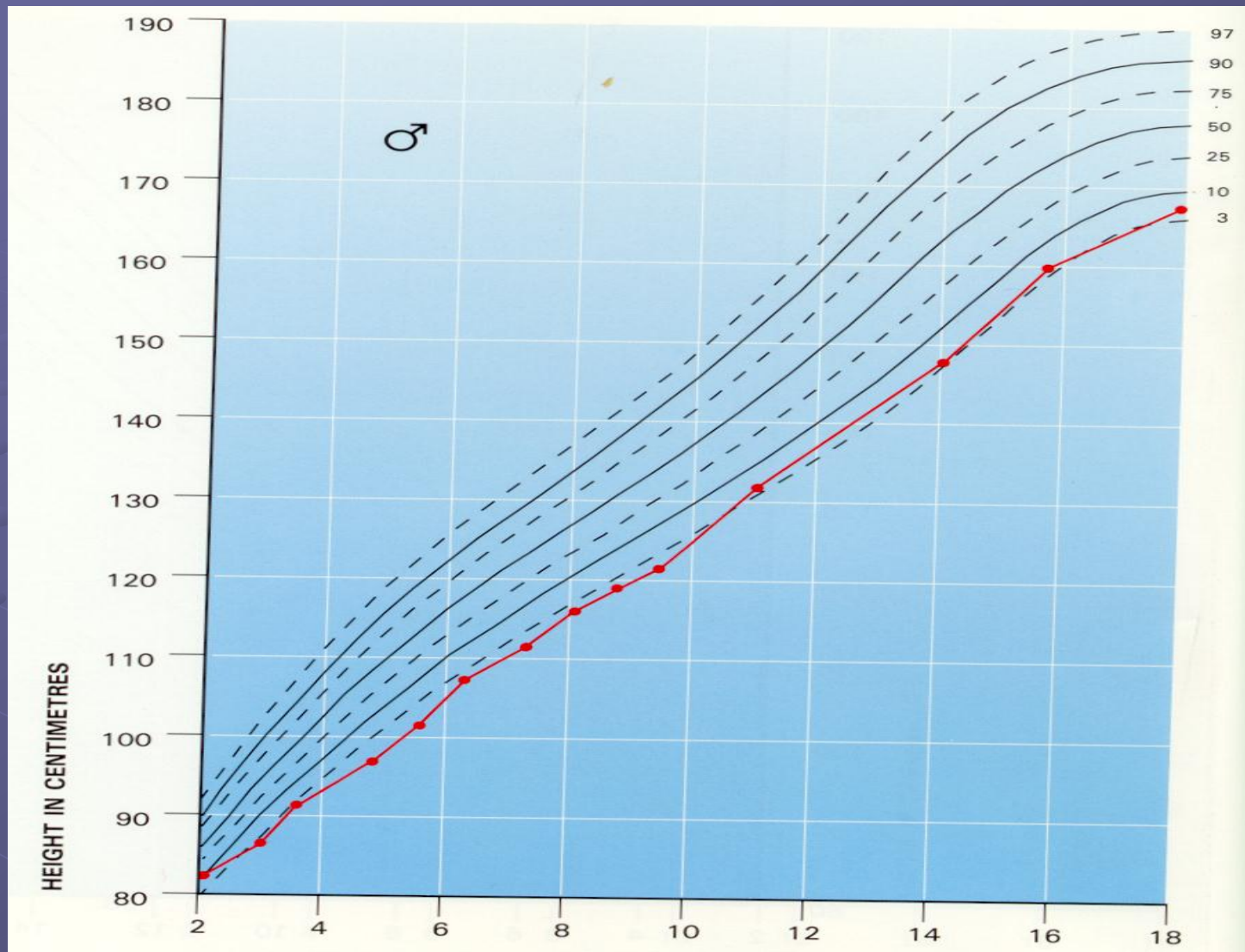
Can he be taller?



MPH

BA = 7.5 years

Testes 2 ml

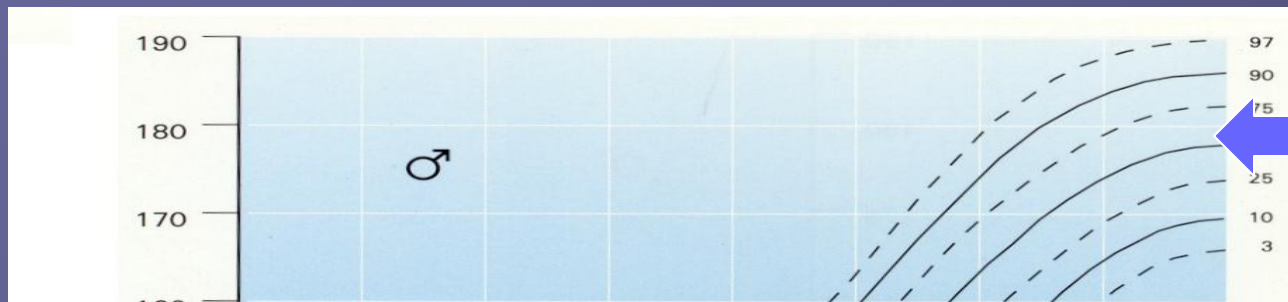


Familial short stature

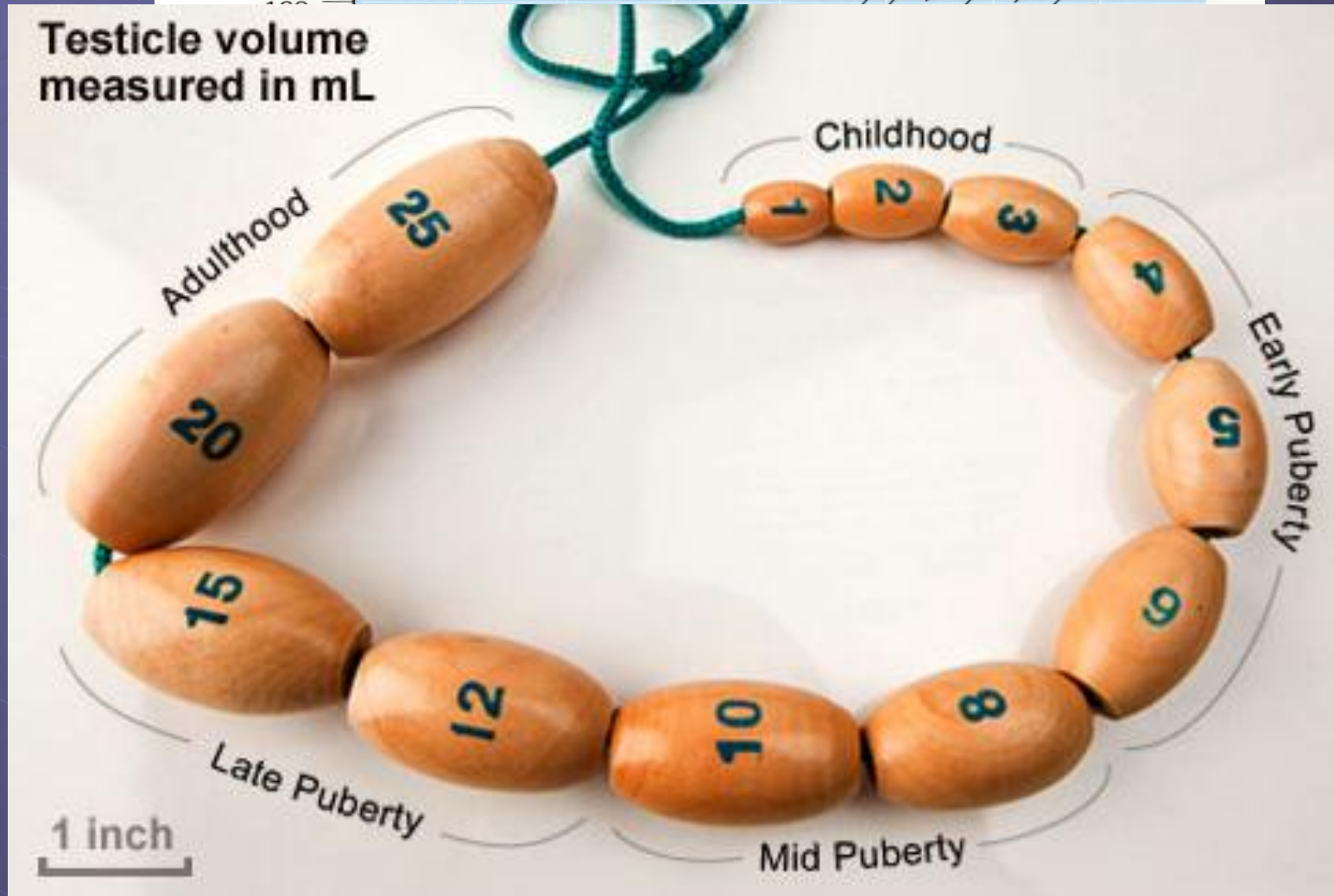
Growth Case

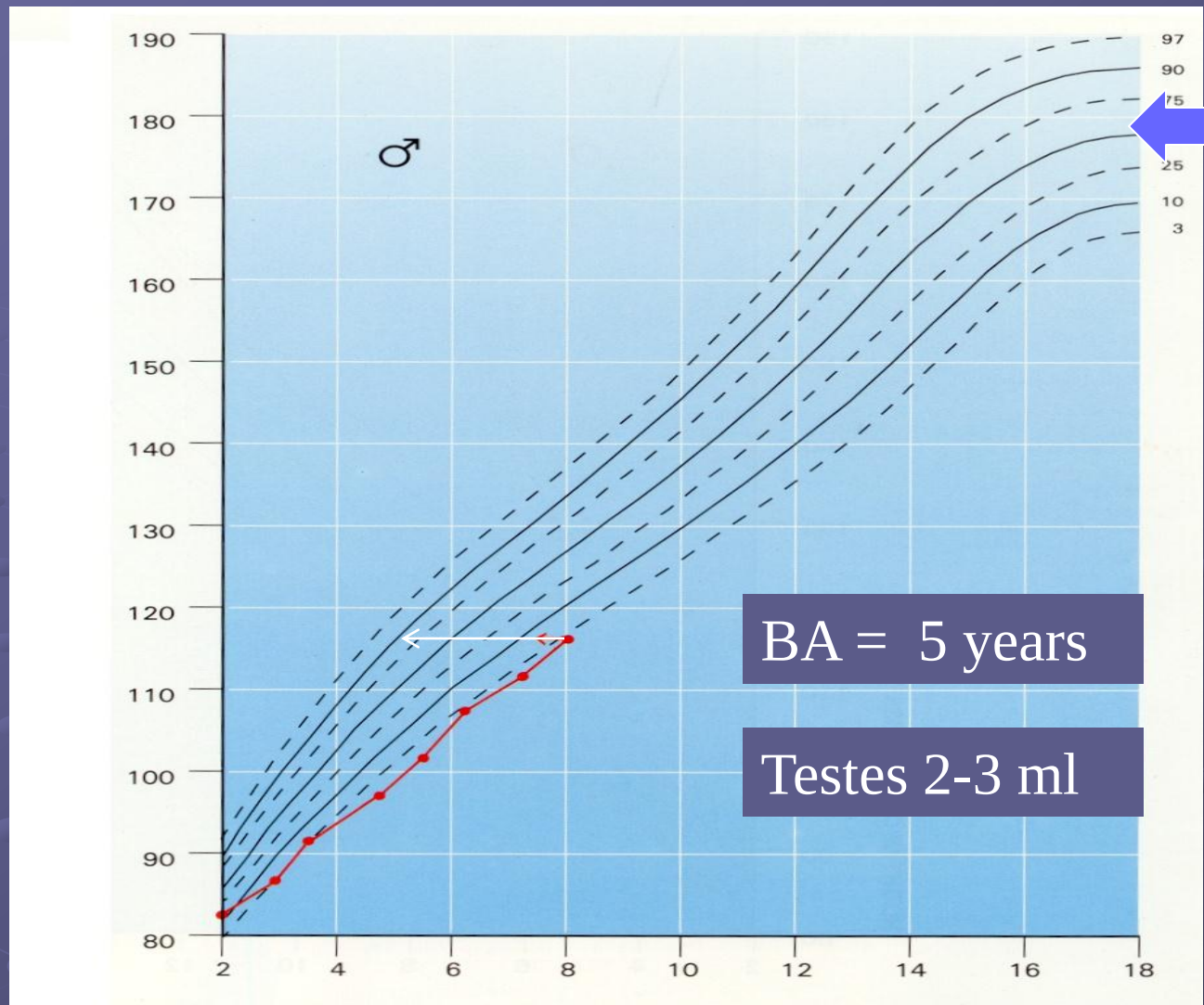
Parents normal height

Delayed bone age



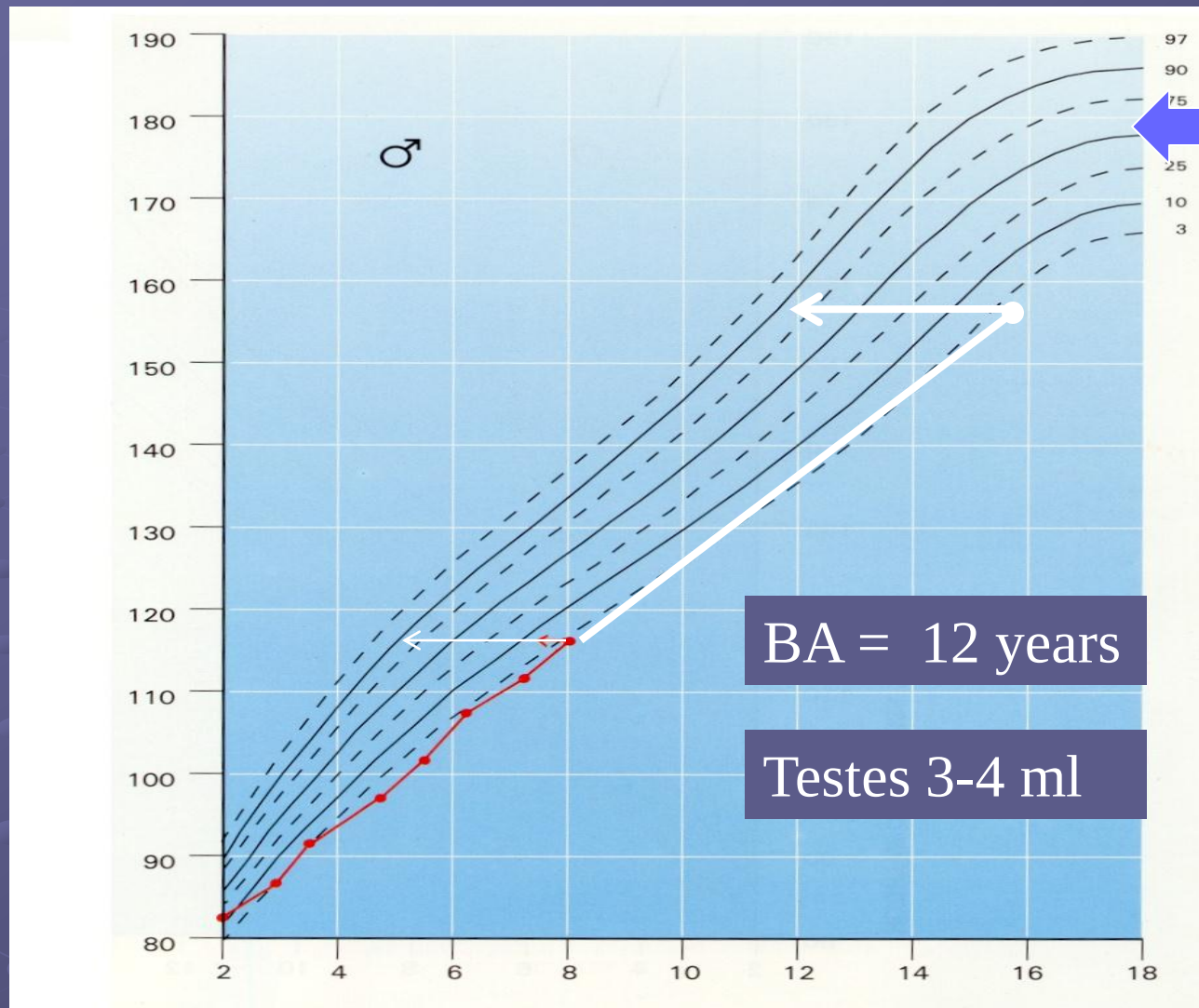
MPH





Dad is 178 cm, didn't stop growing till university

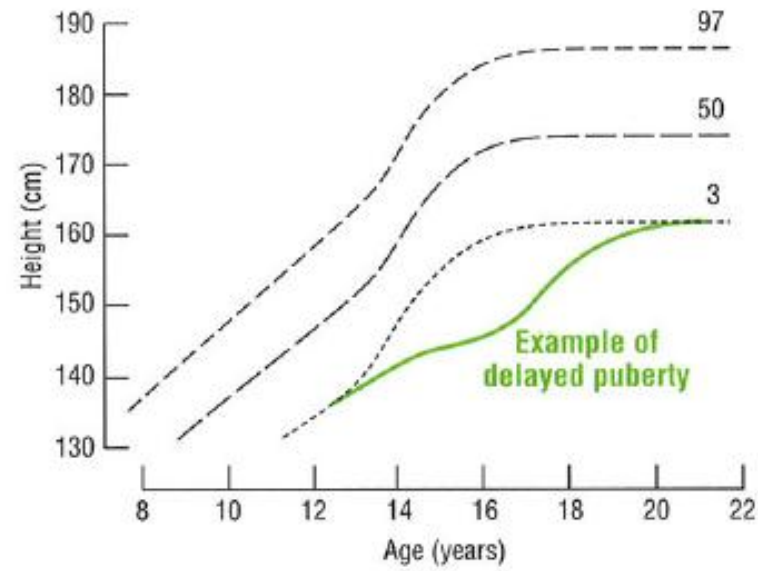
Diagnosis: Constitutional delay in growth and puberty



Still Prepubertal

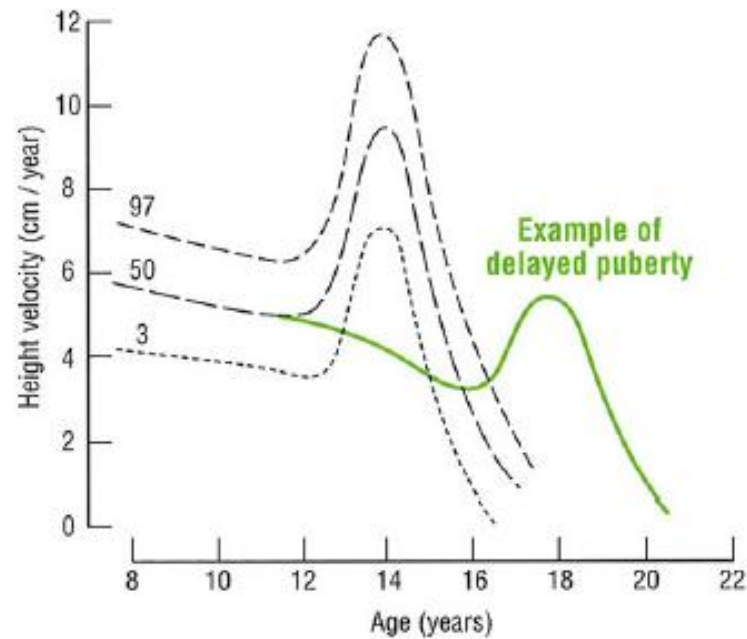
“not bothered”: but then again if there is anything to do.

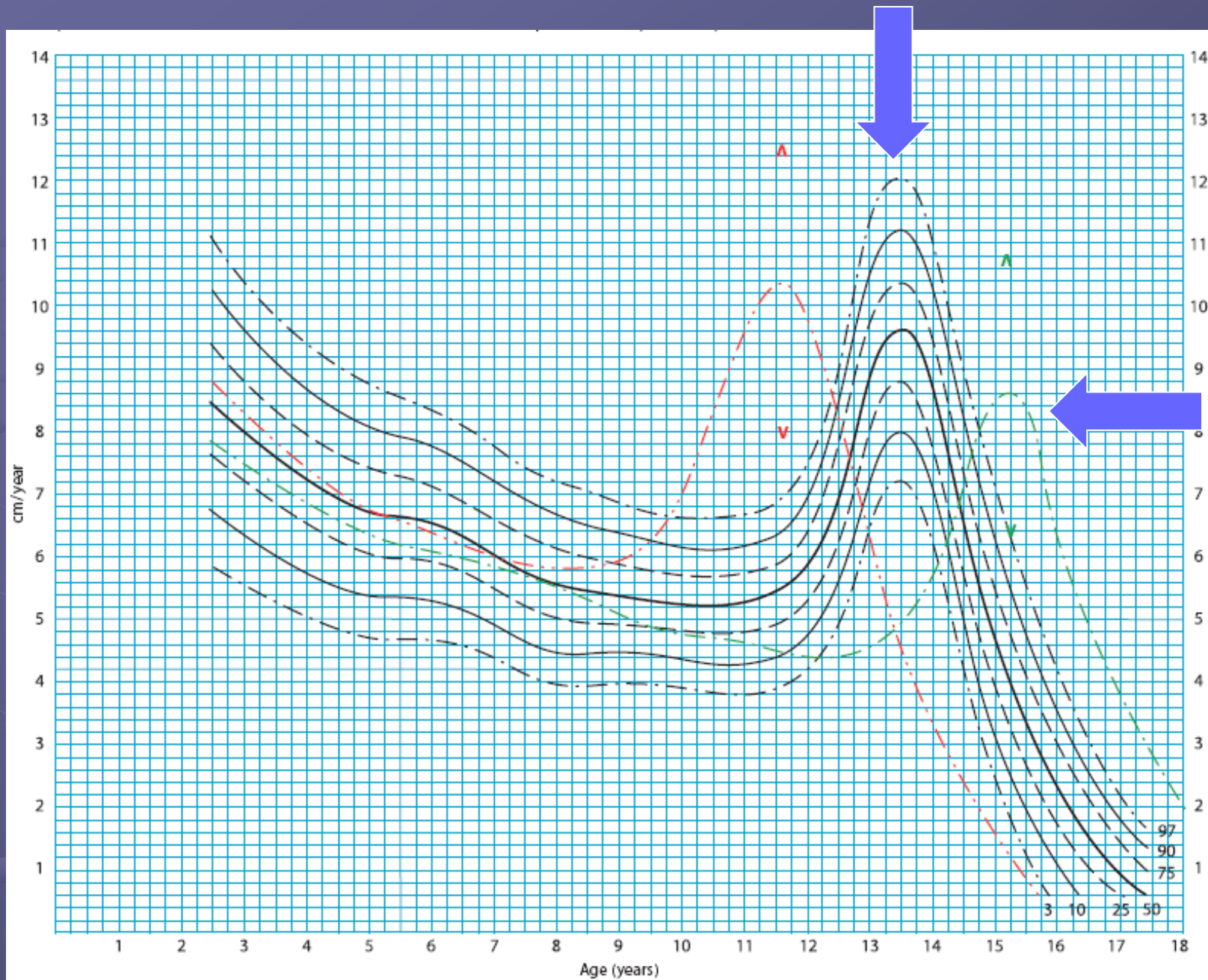
a) Growth



Mid Parental Height

b) Velocity



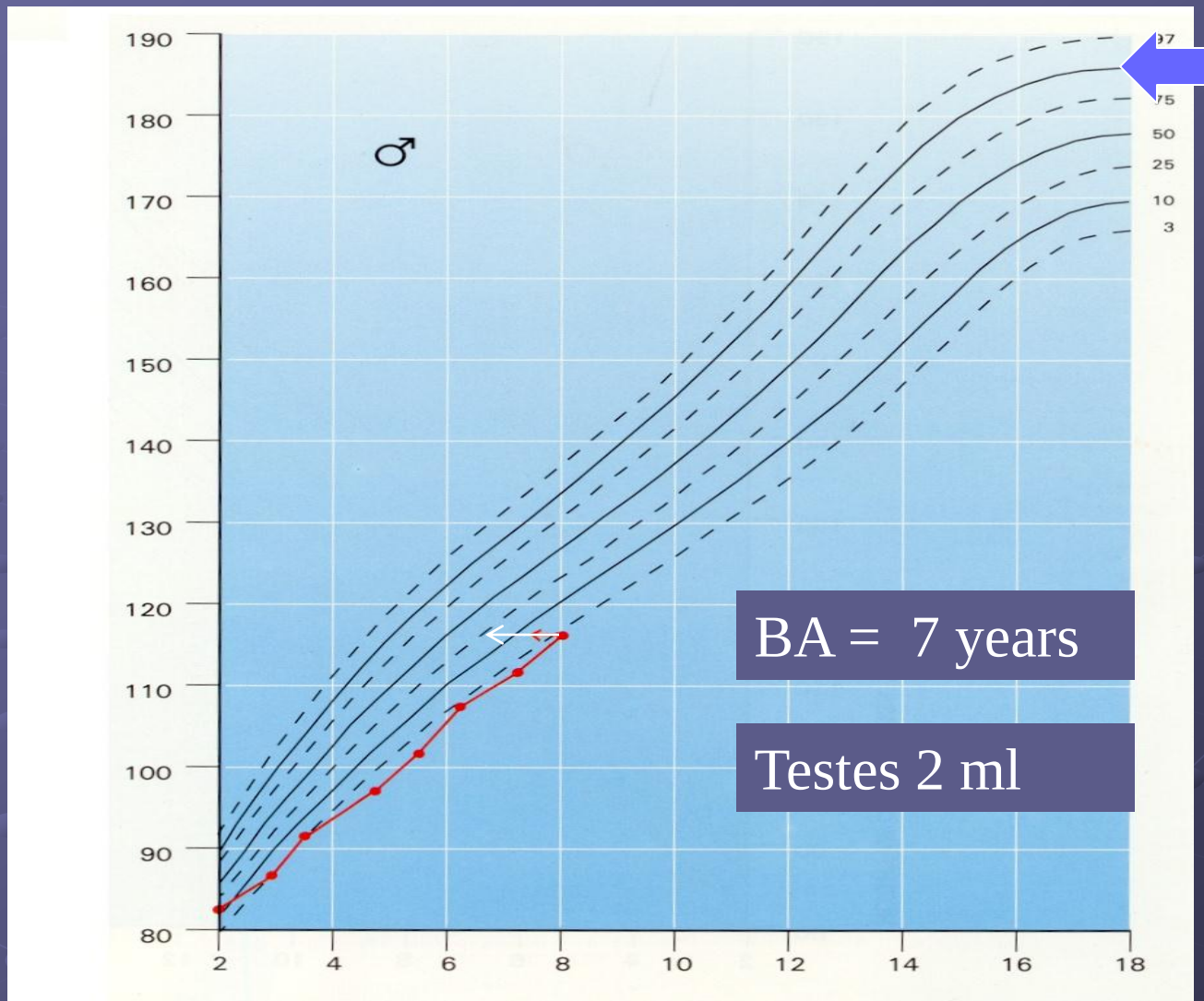


Data Source: Tanner, J. & Davies, P. S. W. 1985, *Journal of Pediatrics*, 107.

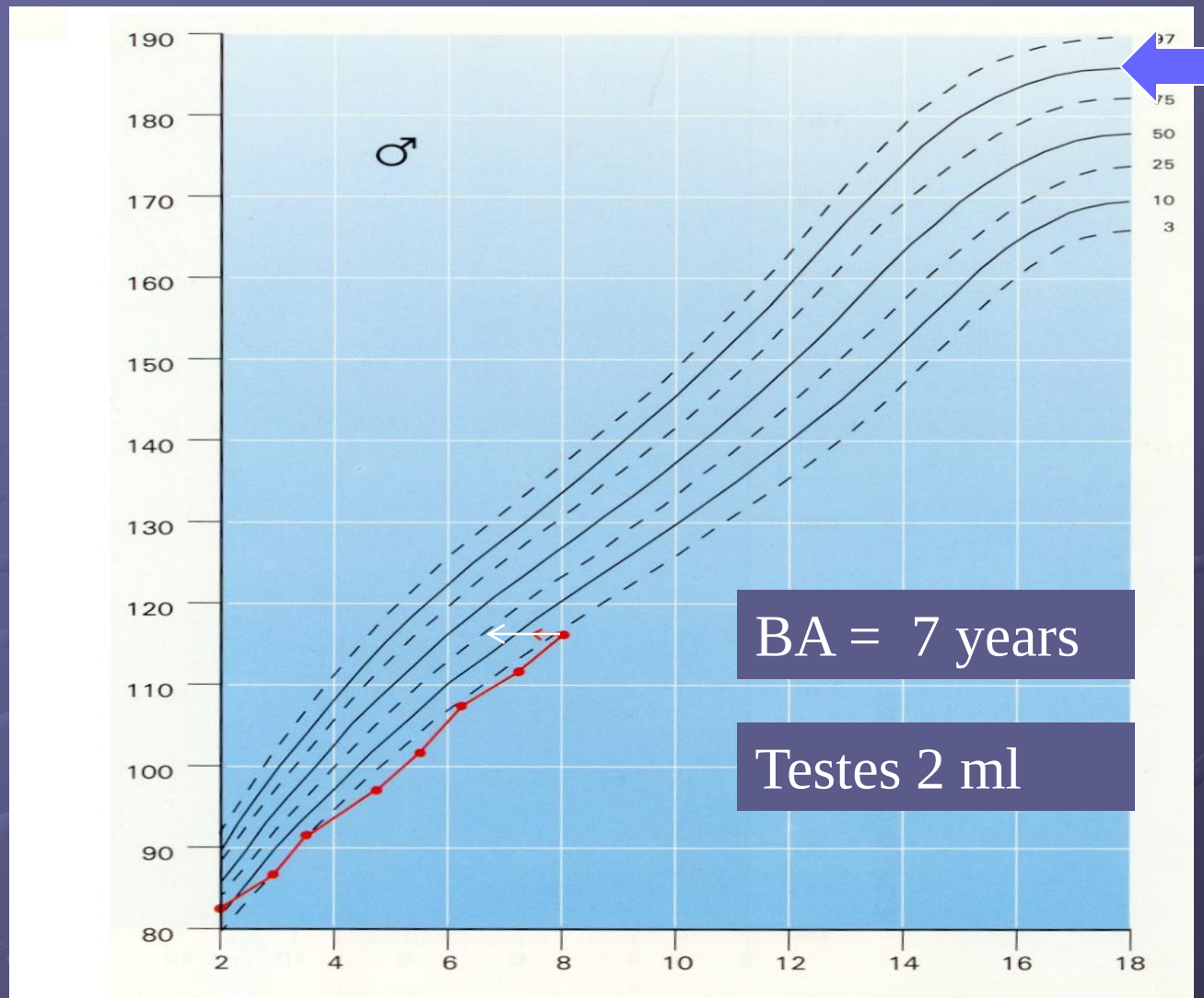
Growth Case

Parents Tall

No history of constitutional delay



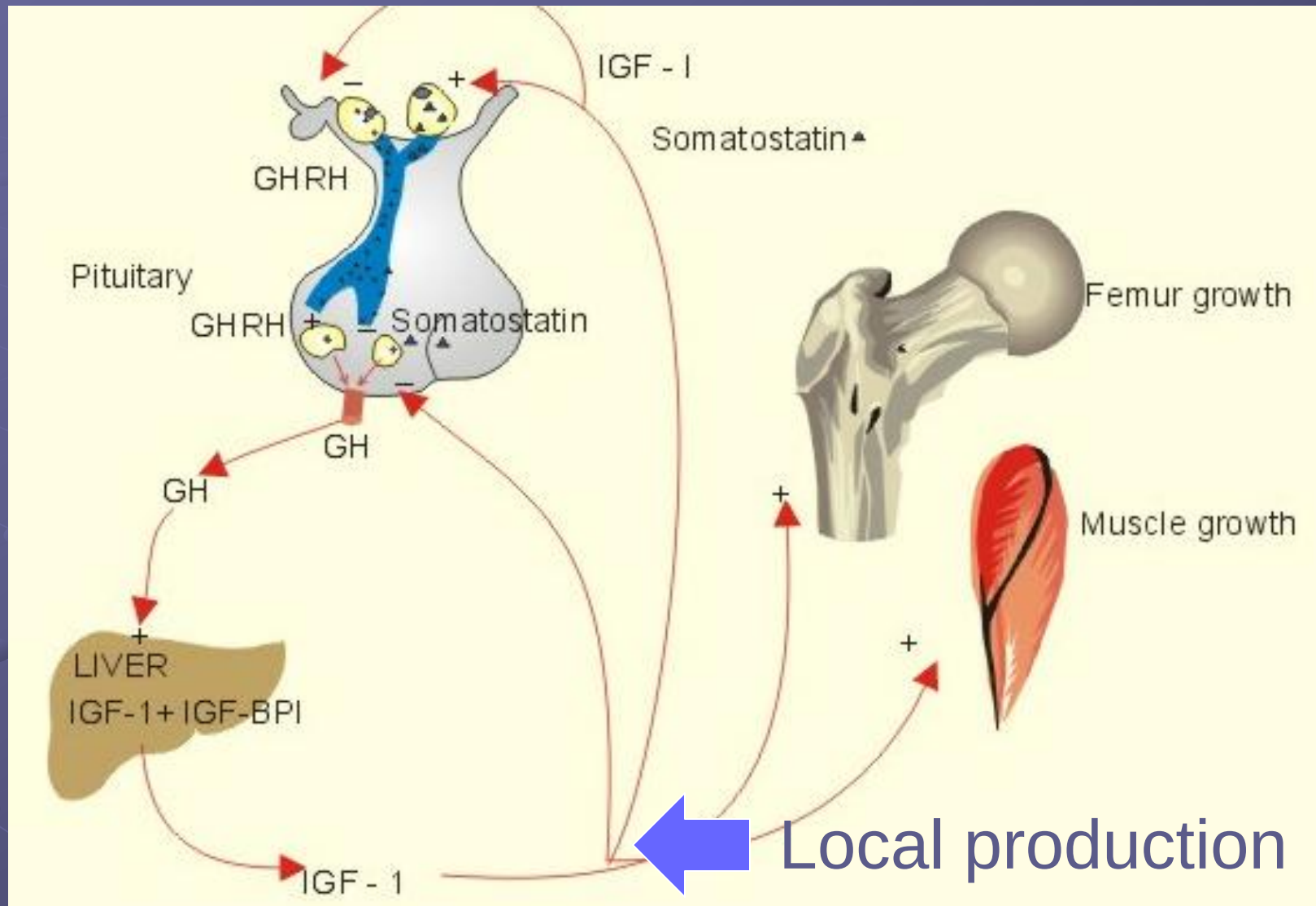
MPH

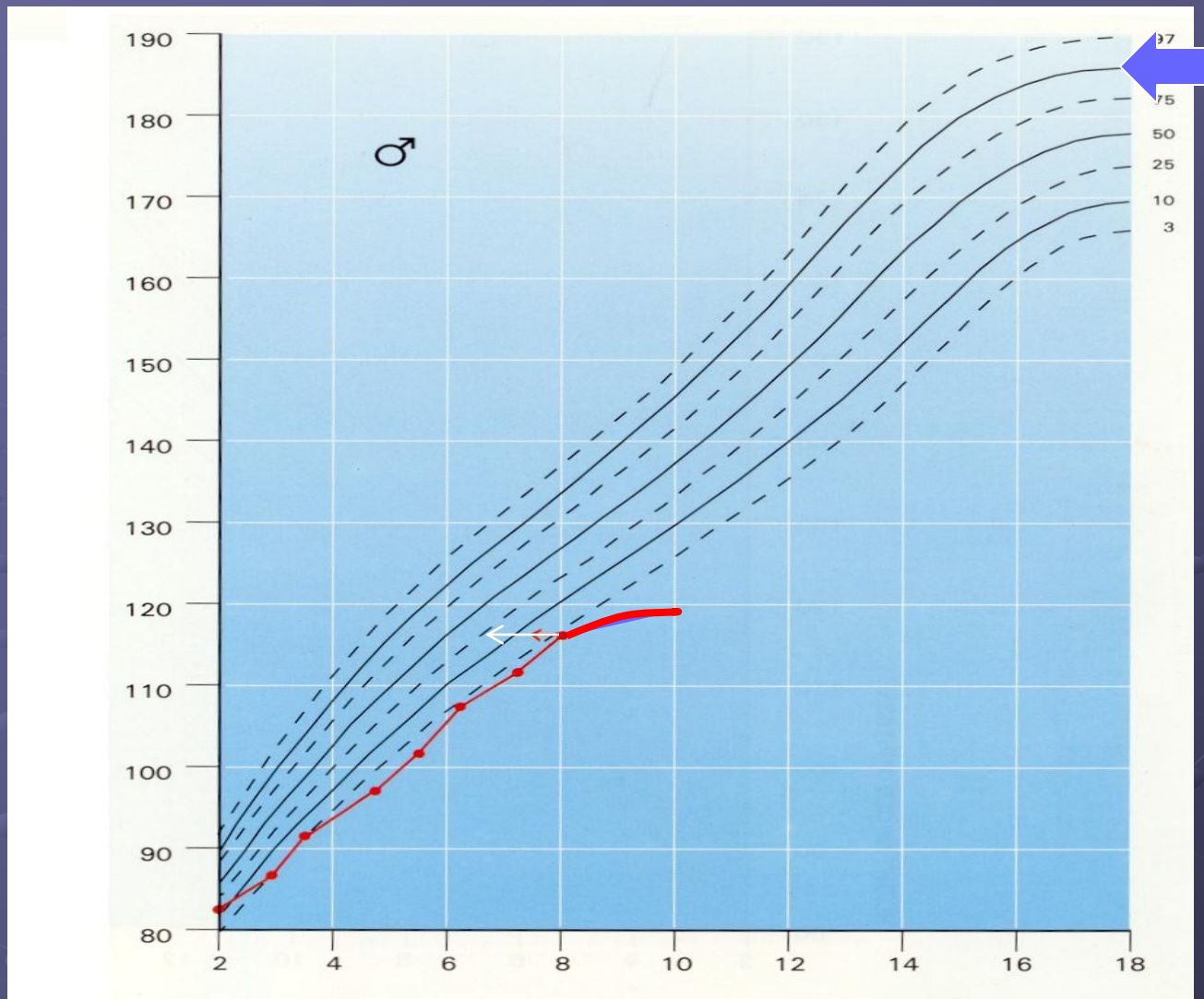


MPH

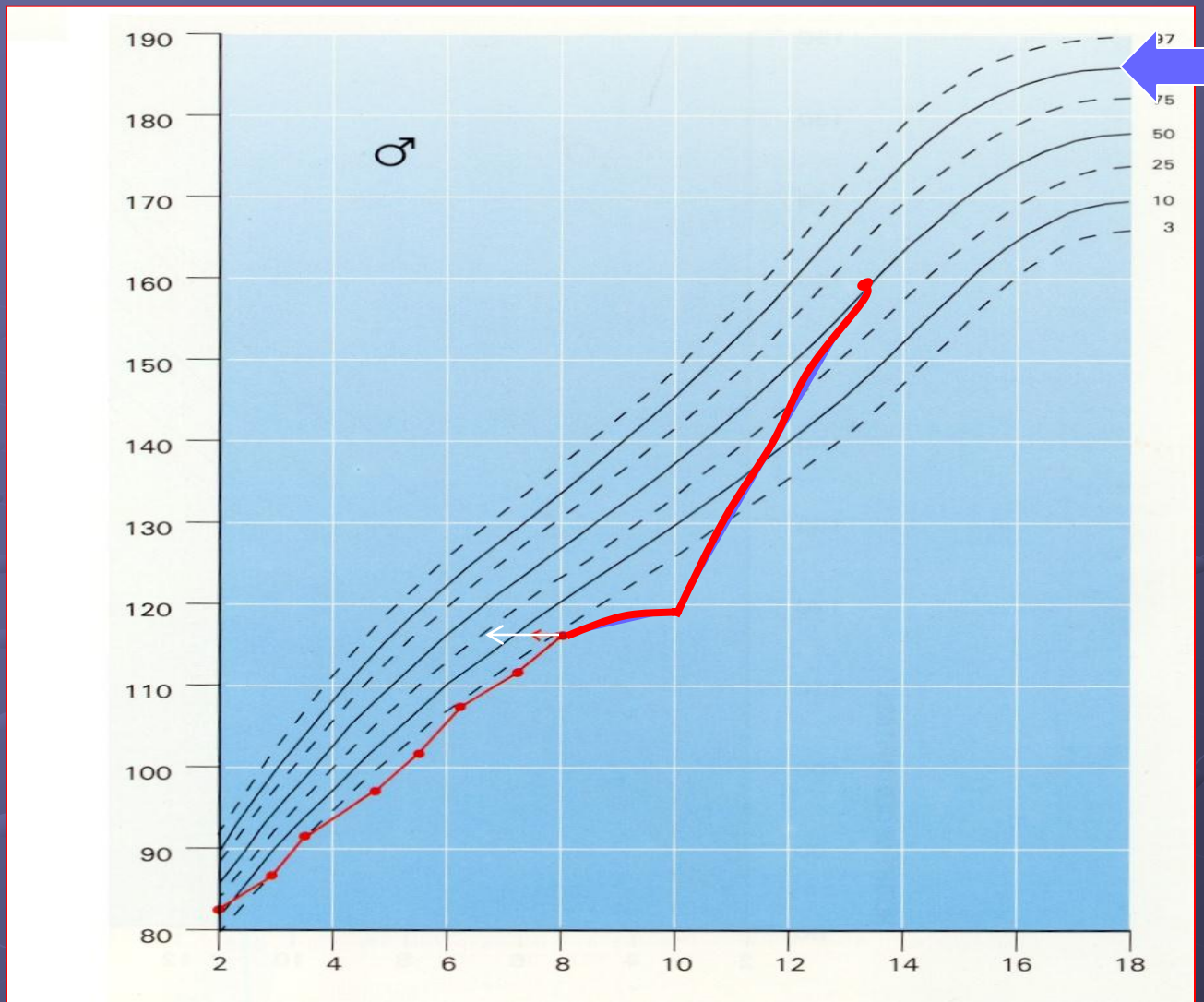
No history of constitutional delay in family
Low IGF-1.....but skinny

IGF-1





Now growth failure!
Growth hormone deficient on formal testing
MRI Interrupted pituitary stalk

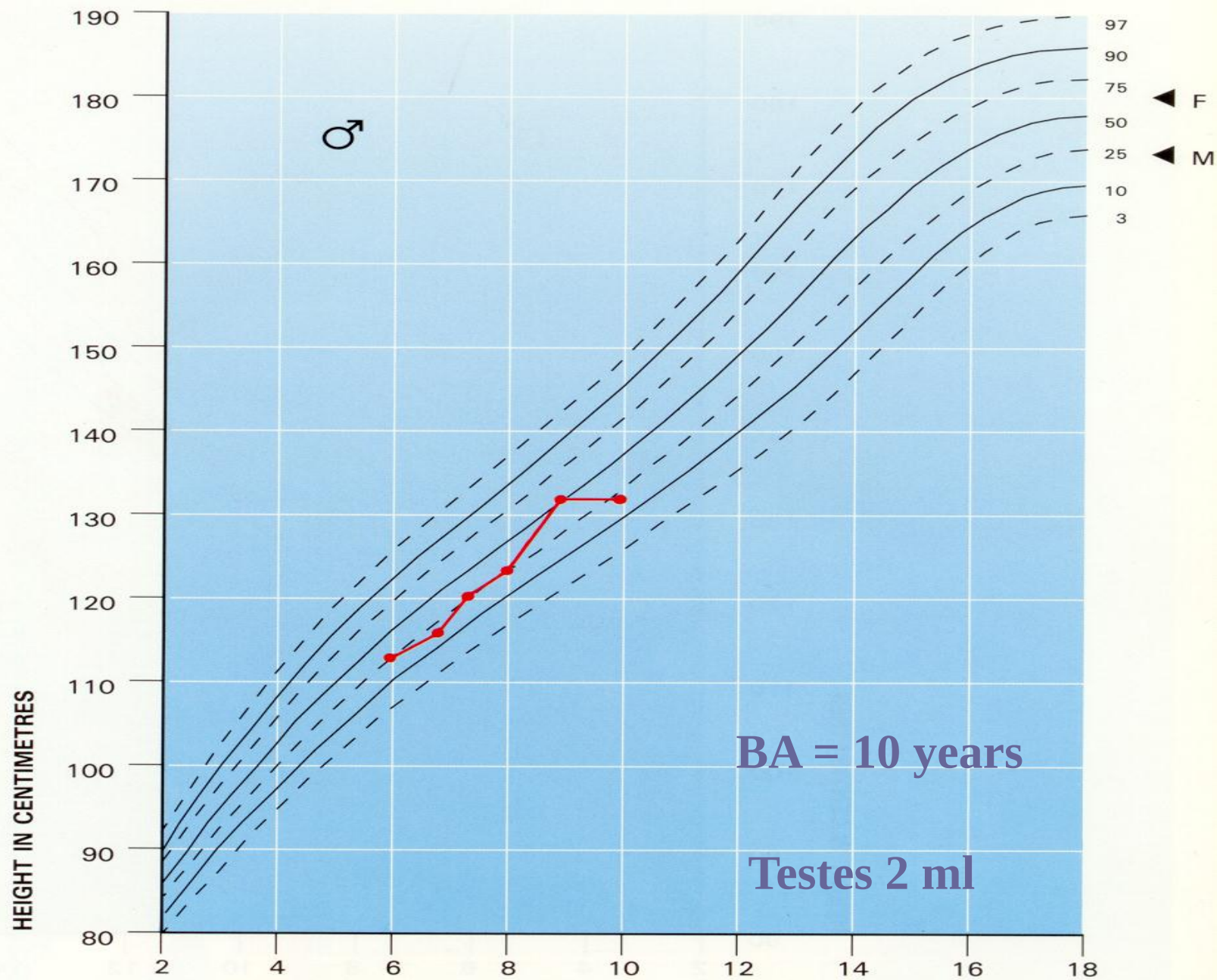


Response to Growth hormone
Return to target or mid parental height

Growth Case

Ten year old boy

Stopped Growing since the last visit
one year ago

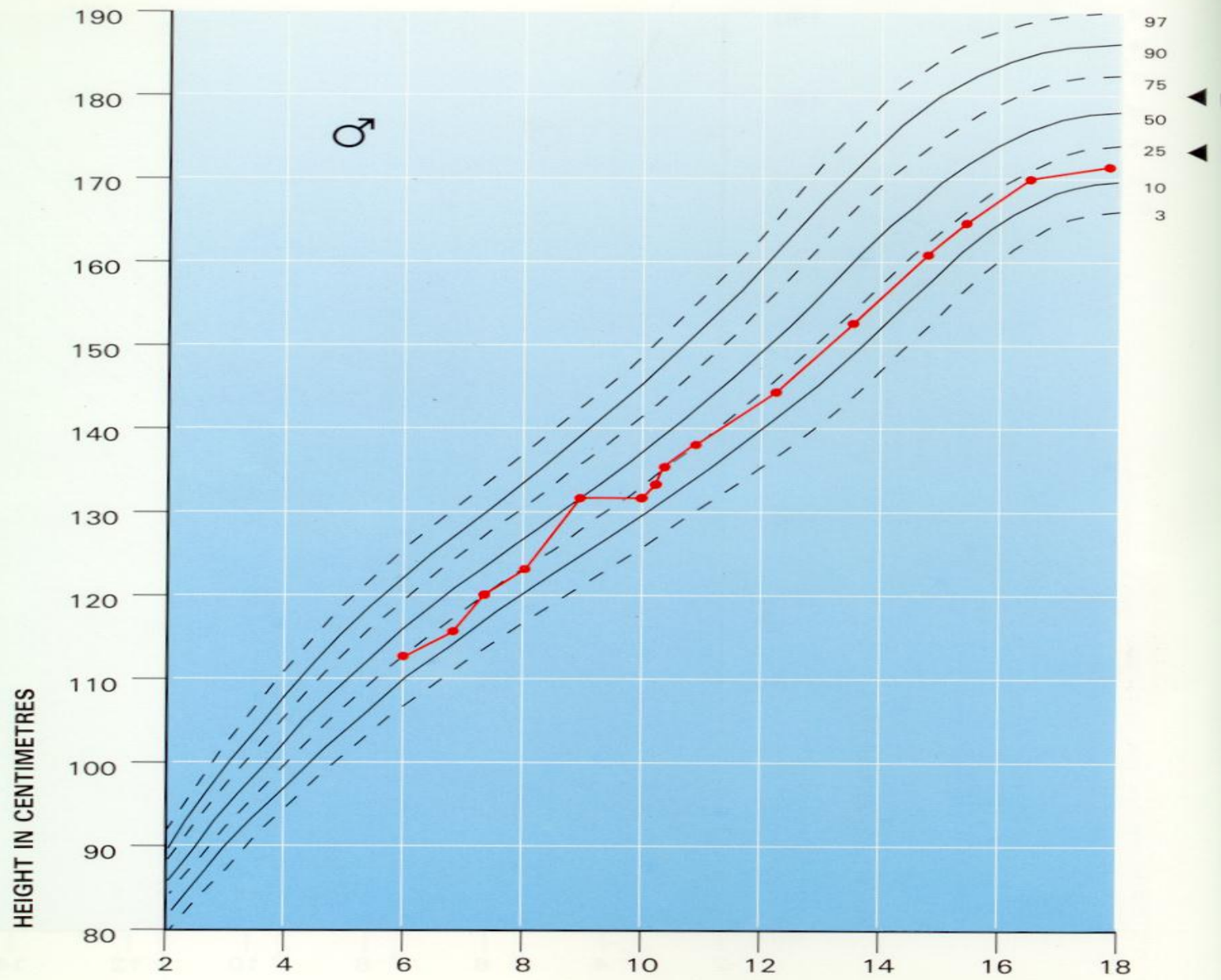


Not Grown

? Investigate

N Exam

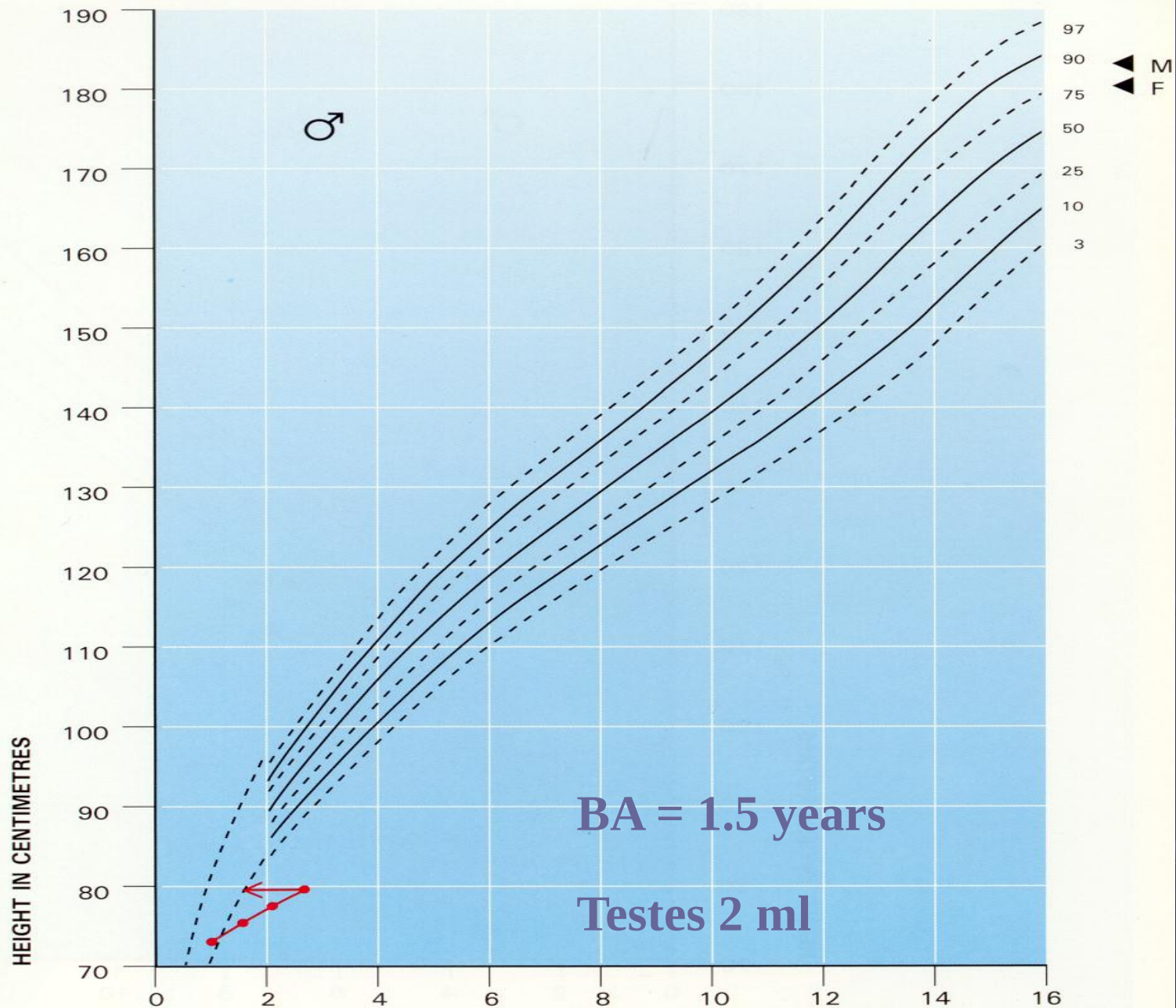
Measurement error



Growth Case

Three Year Old Boy

Not Growing too well



Relevant History and Examination

Birth weight 3.3 Kg

Family History None

Developmental history

? Often tired

Normal vision

Central Adiposity

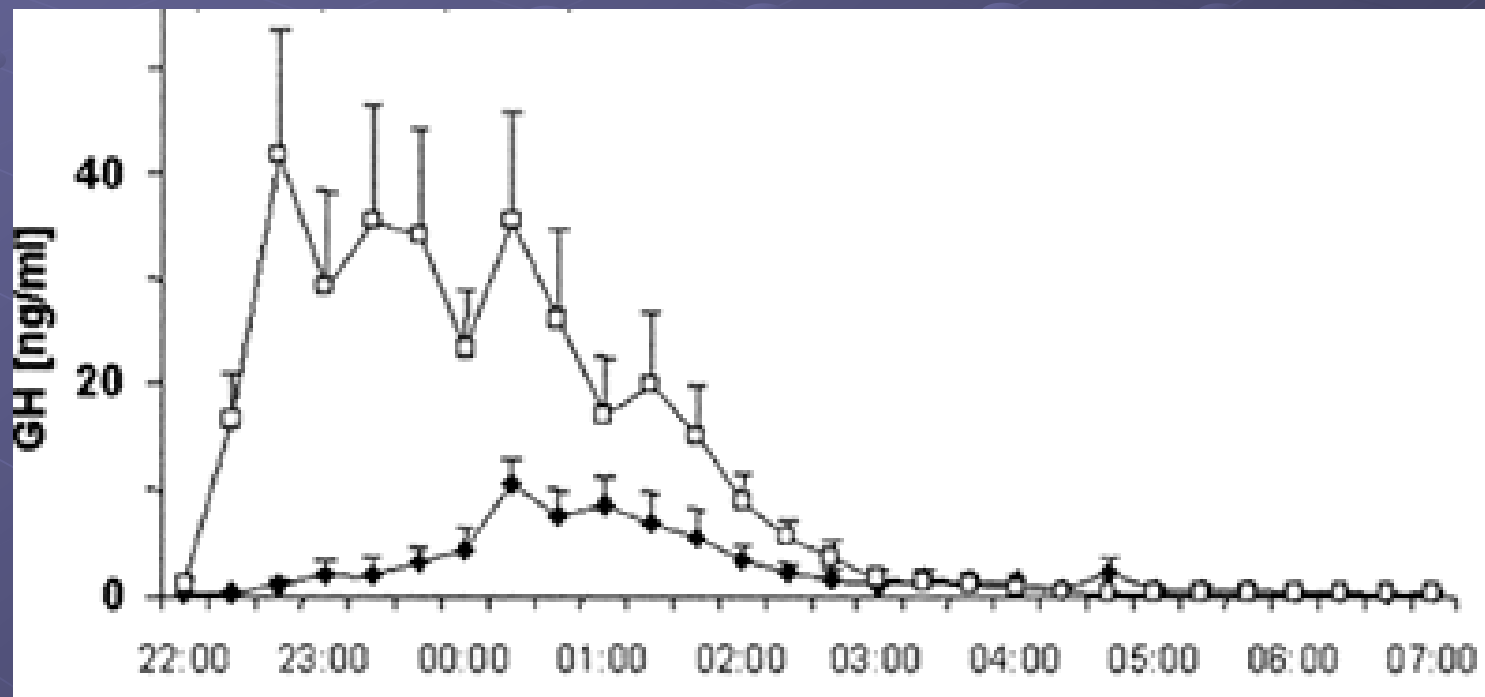
Tests required

● FBC	N
● ESR and CRP	N
● RFT	N
● Coeliac markers	N
● TSH, T4	N
● SKELETAL SURVEY	N (delayed BA)
● HCO3	N
● IGF-1	low
■ ?? GH deficient	

GH stimulation

Arginine and Clonidine

Growth Hormone peak >5 is
normal (mcg/l)



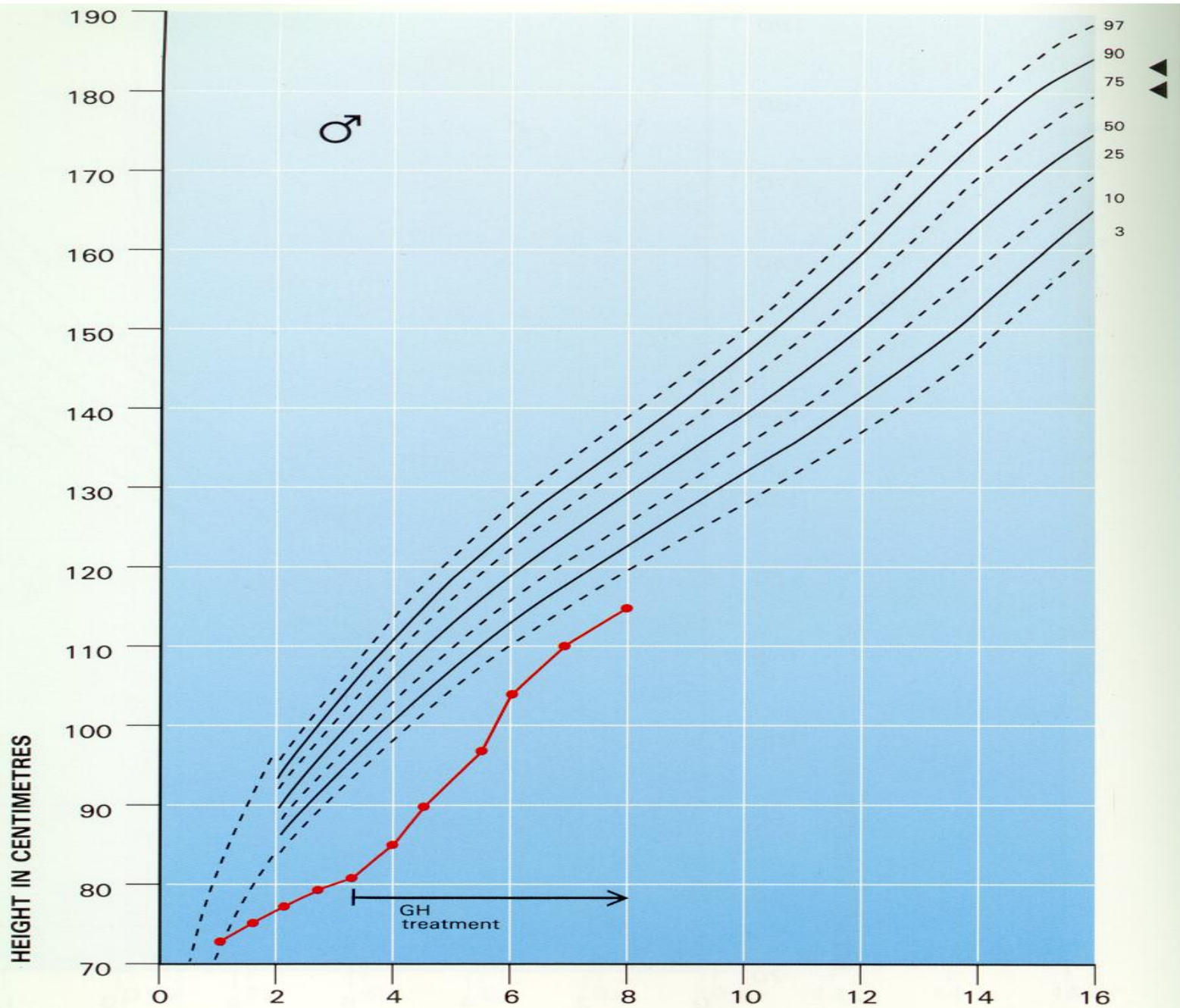
GH stimulation

(Arginine and Clonidine)

	Arginine	Clonidine
T0	1.0	1.4
T 30	1.2	1.5
T 60	1.5	1.6
T 90	1.8	2.1

Peak GH to stimulus is less than 3
Growth Hormone deficient
Normal cortisol function

Small ant pituitary on MRI



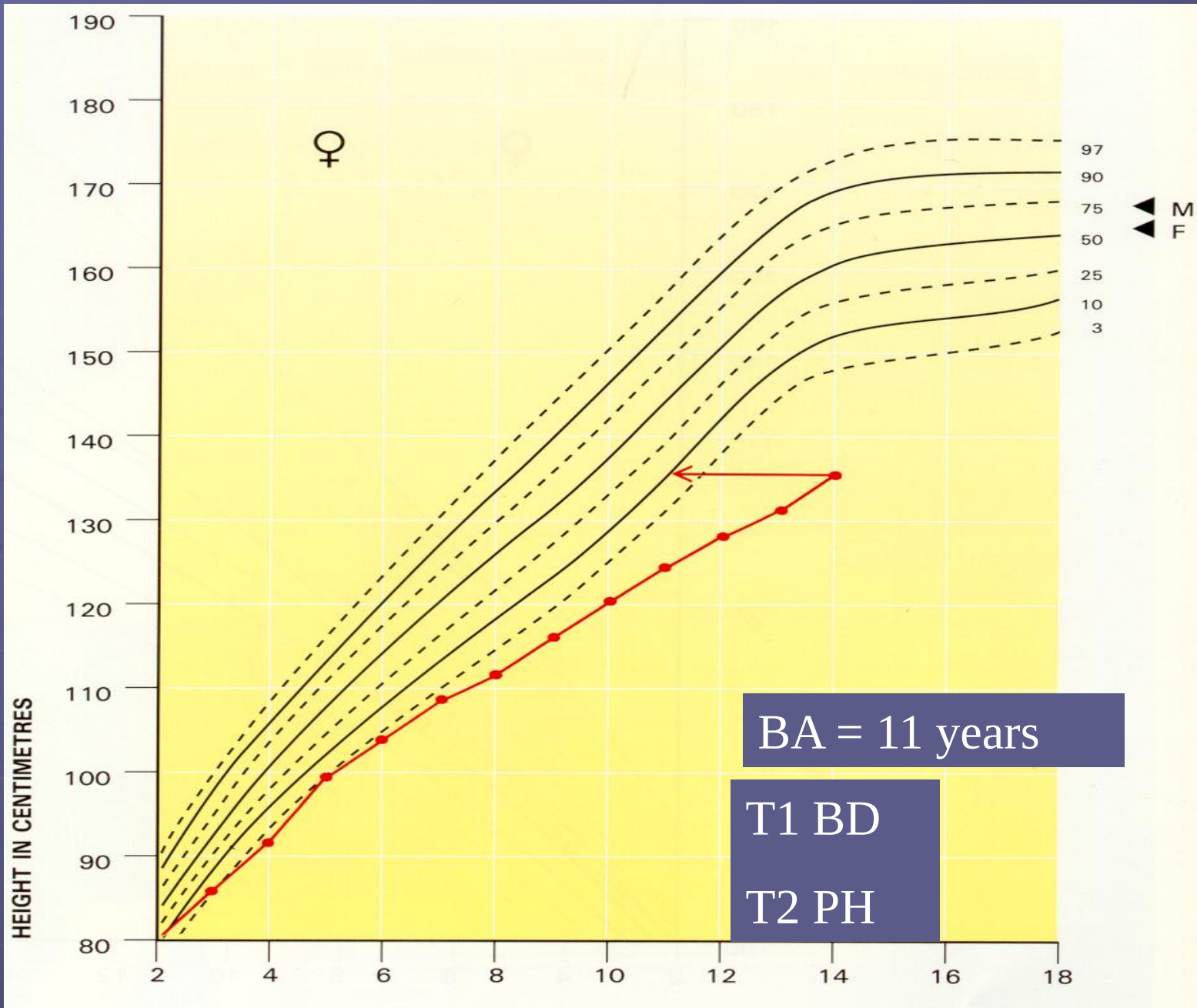
Growth Case - 4

Fourteen Year Old Girl

Shorter than Peers

Not in Puberty

Puffy feet as a baby



Investgations

- Karyotype 45 XO
- Normal TFT
- Elevated LH and FSH: primary gonadal failure
- Turner syndrome



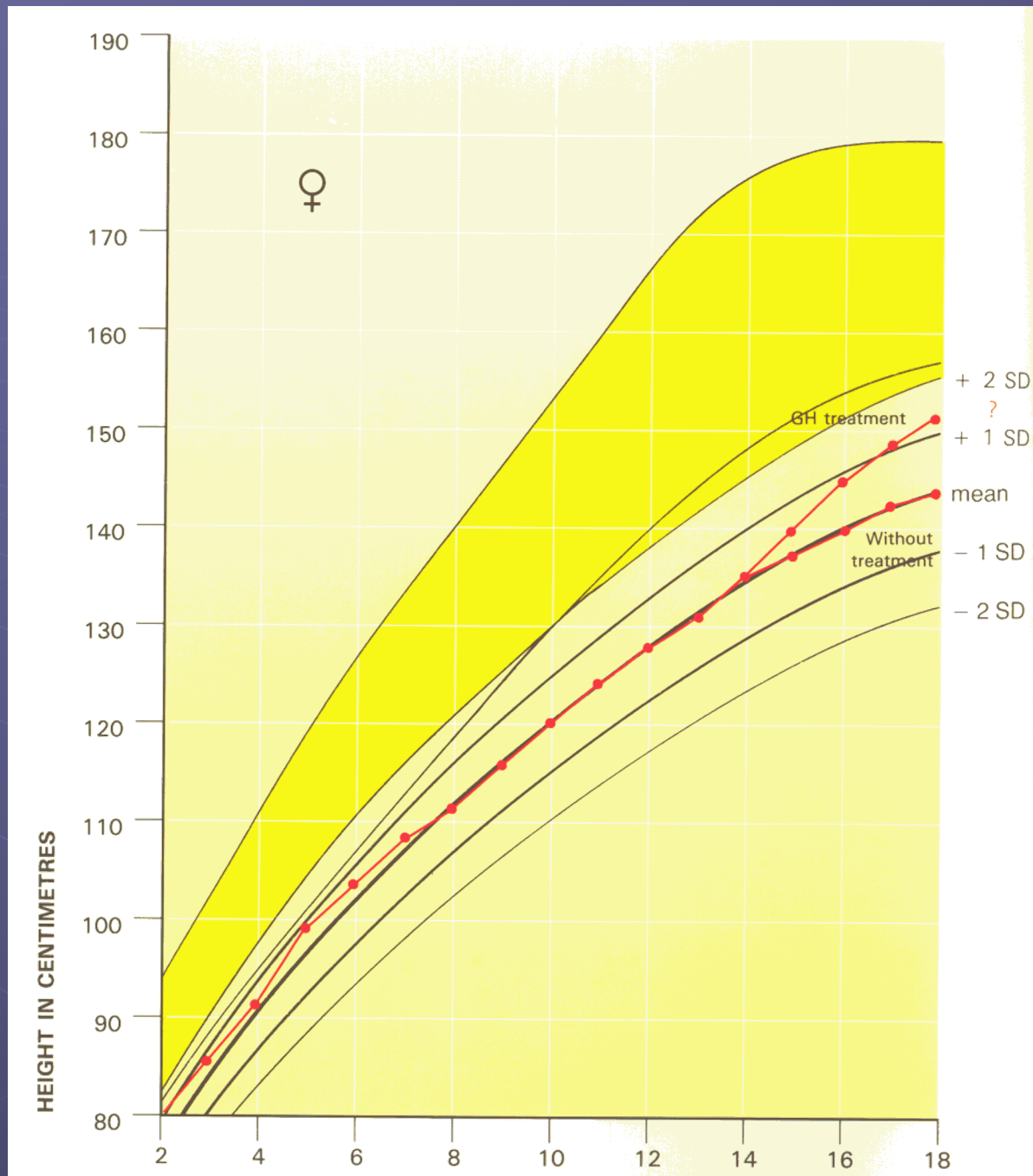


Investgations

● Karyotype 45 XO

● ? Other karyotypes

- 55% 45 XO
- 17% 46 X I (Xq)
- 13% 45 X/ 46 XX



Turner syndrome

? What other treatment or tests does she need and why

Renal and Cardiac imaging

Pubertal induction treatment

- Prevent Osteoporosis
- Secondary sexual characteristics
- Promote growth

Turner syndrome

? Why are turner girls short

- A) Growth Hormone deficiency
- B) Heart Defects
- C) Skeletal dysplasia
- D) Gonadal failure

Turner syndrome

? Why are turner girls short

- A) Growth Hormone deficiency
- B) Heart Defects
- C) **Skeletal dysplasia**
- D) Gonadal failure

Case 5

Thirteen year old girl

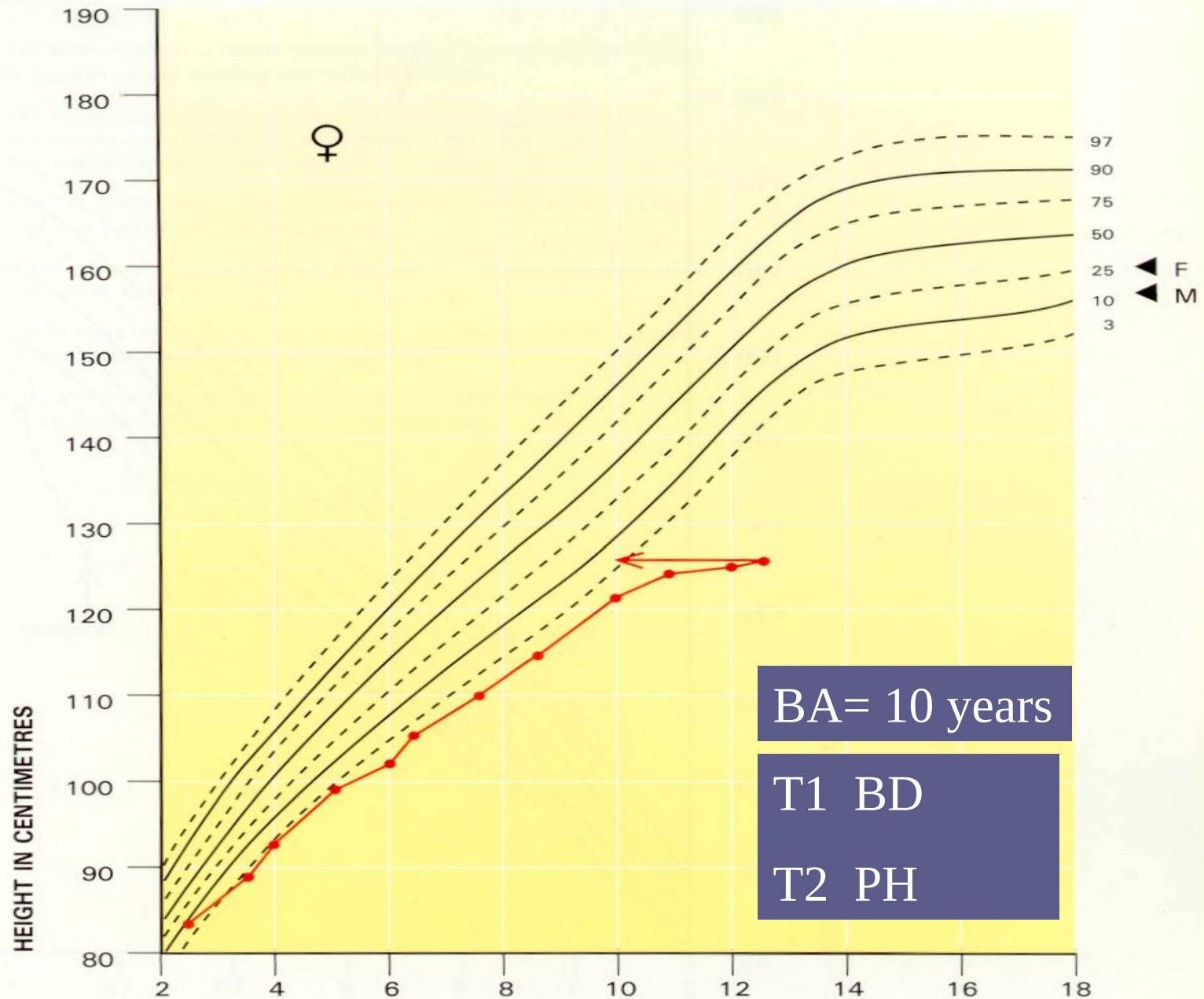
Always been short

Recently moved school

No pubertal development

Weight Loss

Chronic Abdominal Pain



Investigations

TFT

N

IGF-1

Low

LH/FSH

Low

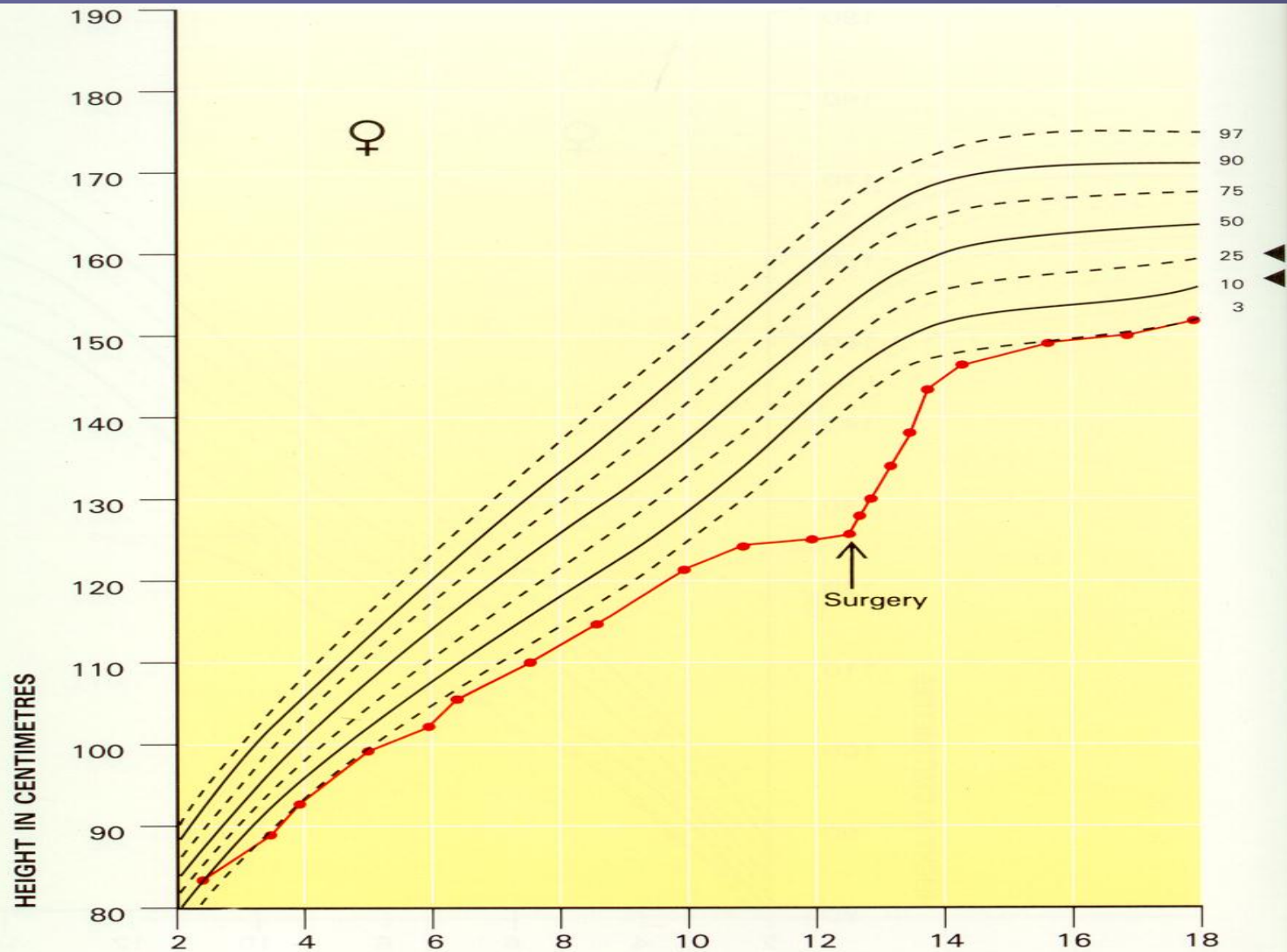
FBC Hb 97

ESR 60

Platelets 600

Further investigations

- Stool calprotectin High
- Abnormal Barium meal
- Distal Ileal Inflammation



Familial short stature
Inflammatory bowel disease

Puberty cases



Definitions- Normal Puberty

● Normal Puberty (All in tempo)

- Central activation of the H-P-Gonadal axis
- Progressive sequential changes
- Appropriate rate (over 3-4 years)

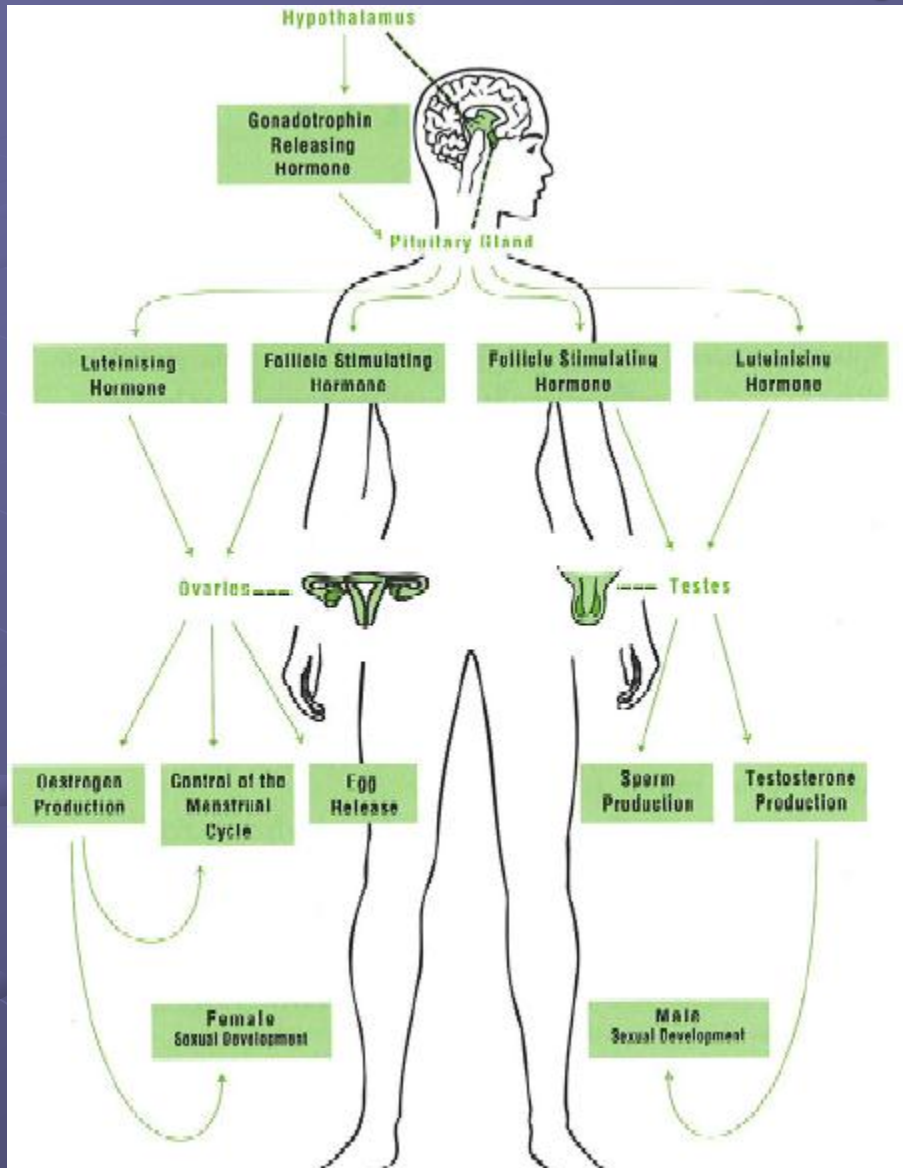
● Girls (First Sign)

- Breast development before
- Growth Spurt

● Boys (First Sign)

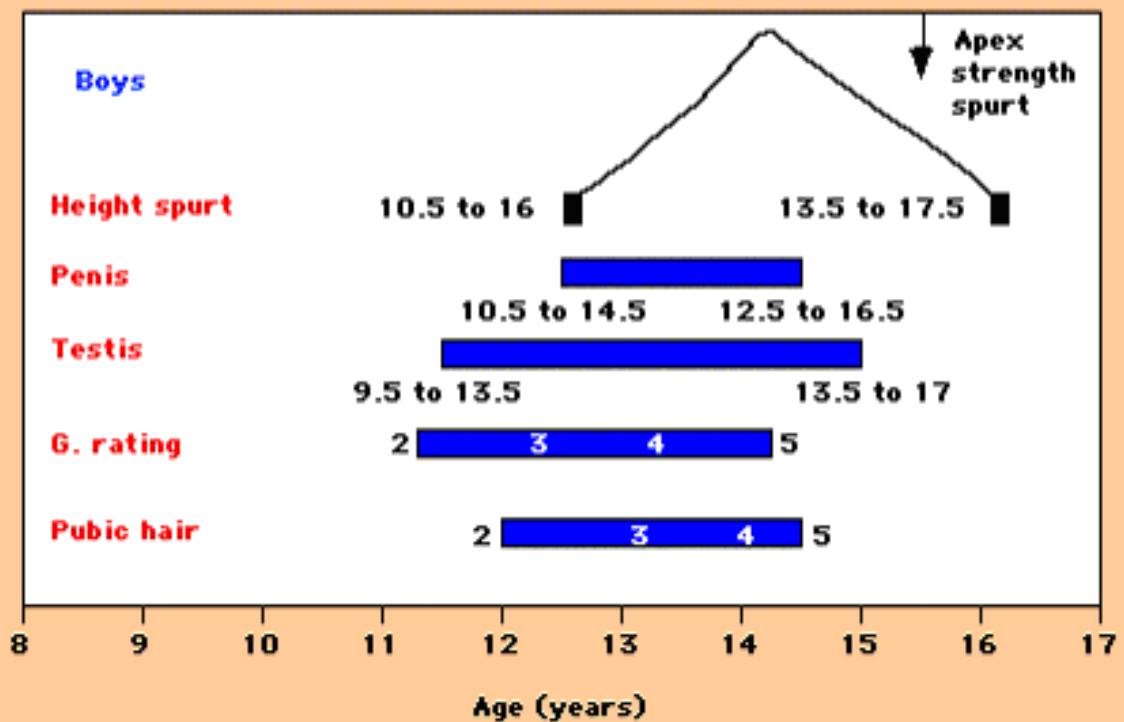
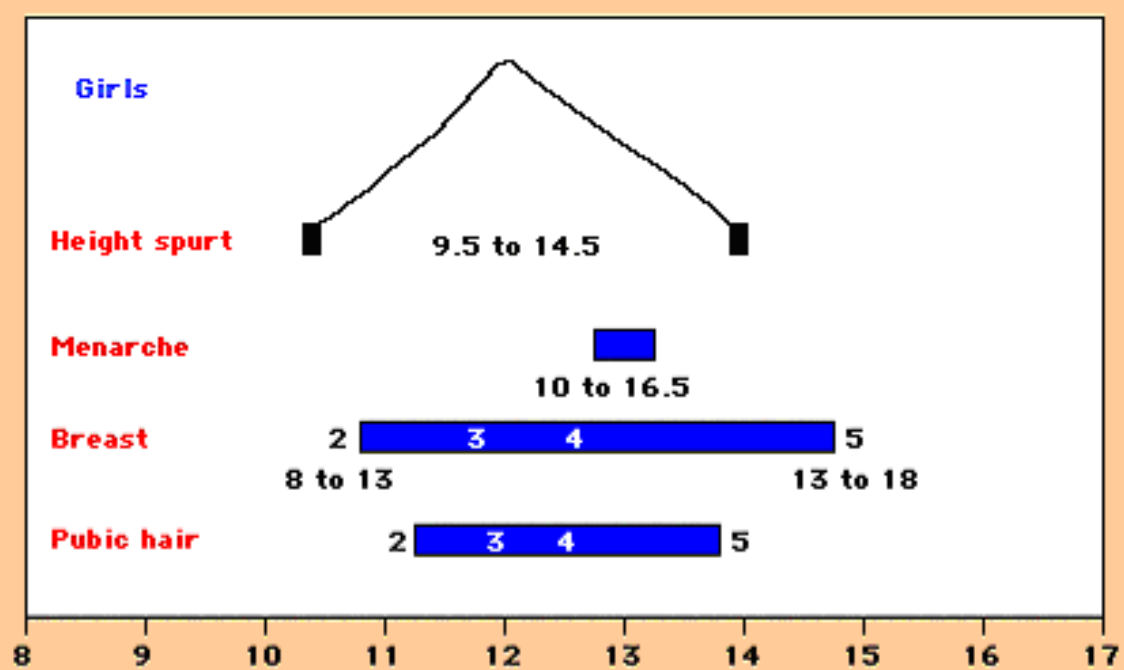
- Increased testicular enlargement
- >4ml (orchidometer)
- Growth spurt later

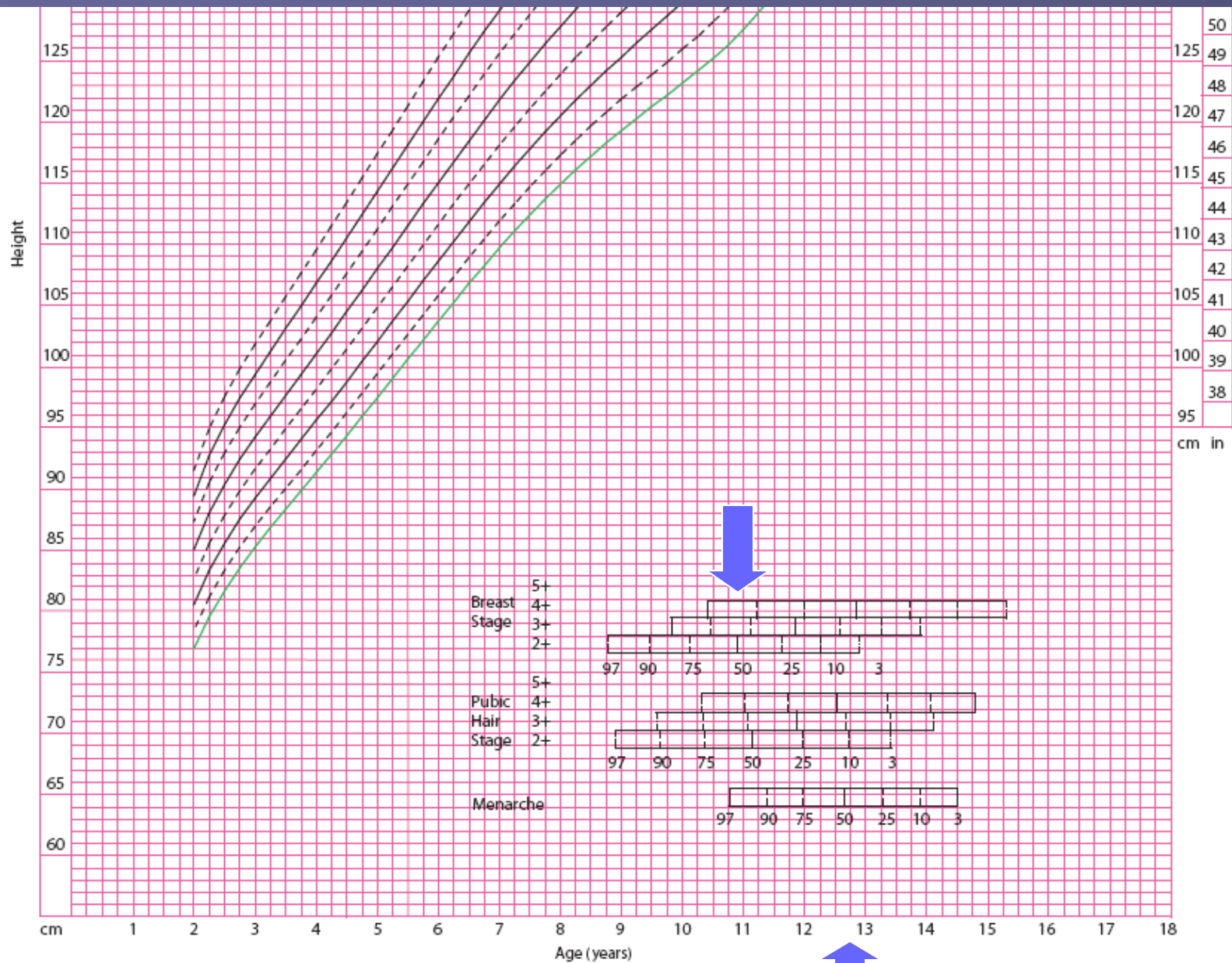
Normal puberty



● www.apeg.org.au

● See Booklets in PDF format





Data Source: www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm

Delayed Puberty

Definition

No signs of puberty within 2 SD of the mean age of onset.

● Males >14 years

● Females >13 years

What is the differential diagnosis?

- **Normal variant**

Constitutional delay in growth and development (CDGD)

By far the most common

- **Primary Gonadal Failure**

Hypergonadotropic Hypogonadism

Raised LH and FSH

- **Secondary/Central Gonadal Failure**

Hypogonadotropic Hypogonadism

Low FSH and LH

Hypergonadotropic Hypogonadism

Raised LH/FSH

Males

Klinefelters (47XXY or variants)

Vanishing testis syndrome

Trauma/Infection

Noonan Syndrome

Females

Turner Syndrome or X deletions

Radiation

Chemotherapy

Noonan Syndrome

Autoimmune ovarian failure

Hypogonadotropic Hypogonadism

Low basal LH/FSH

CDGD (>85%)

- **Chronic illness**
- **Anorexia nervosa/ malnutrition**
- **Excessive physical training**
- **Pituitary/Hypothalamic disease**
 - **Isolated (Kallmann)**
 - **Multiple pituitary abnormality**
 - **(tumours, congenital hypopituitarism)**
 - **Syndromes**

What hx is relevant?

Birth/ postnatal trauma

Chronic illness/ medications (esp: steroids)

Malignancy

Growth pattern

Dental eruption

Weight/ physical activity

Family history of CDGD

Heights of sibs and parents

Delayed Puberty Treatment Goals

Promote virilisation

Promote growth

Precipitate puberty

Not compromise final height

Puberty Case

- 16 year old boy
- Puberty seems to be stuttering
- Mild learning concerns
- Height 90%, weight 25% “lanky
- PH3, TV 6 ml
- SPL 6 cm
- Testosterone 3, LH 20, FSH 15

Klinefelter's syndrome



1:500-1000

most common sex chromosome aneuploidy in males

Puberty Case

- 15 year old girl with ammenorrhoea
- No puberty changes at all
- Height and weight 25%
- Chronic epileptic

Puberty case

- General exam Normal
- No puberty, Normal Fundi
- Invest
 - Bloods: Essentially N, incl TFT and prolactin
 - LH 1.0/FSH 2.0 Estradiol <30
 - Bone age is 10 (at 15 years)
 - ? Will I go into puberty

? Will I go into puberty

- Buserelin stimulation test
 - Potent form of GnRH
- LH Rise of >5 in 4 hours is Normal
- This case: LH 1.0 increased to 15
- Normal pituitary axis: Late bloomer

Early Puberty



Puberty Case

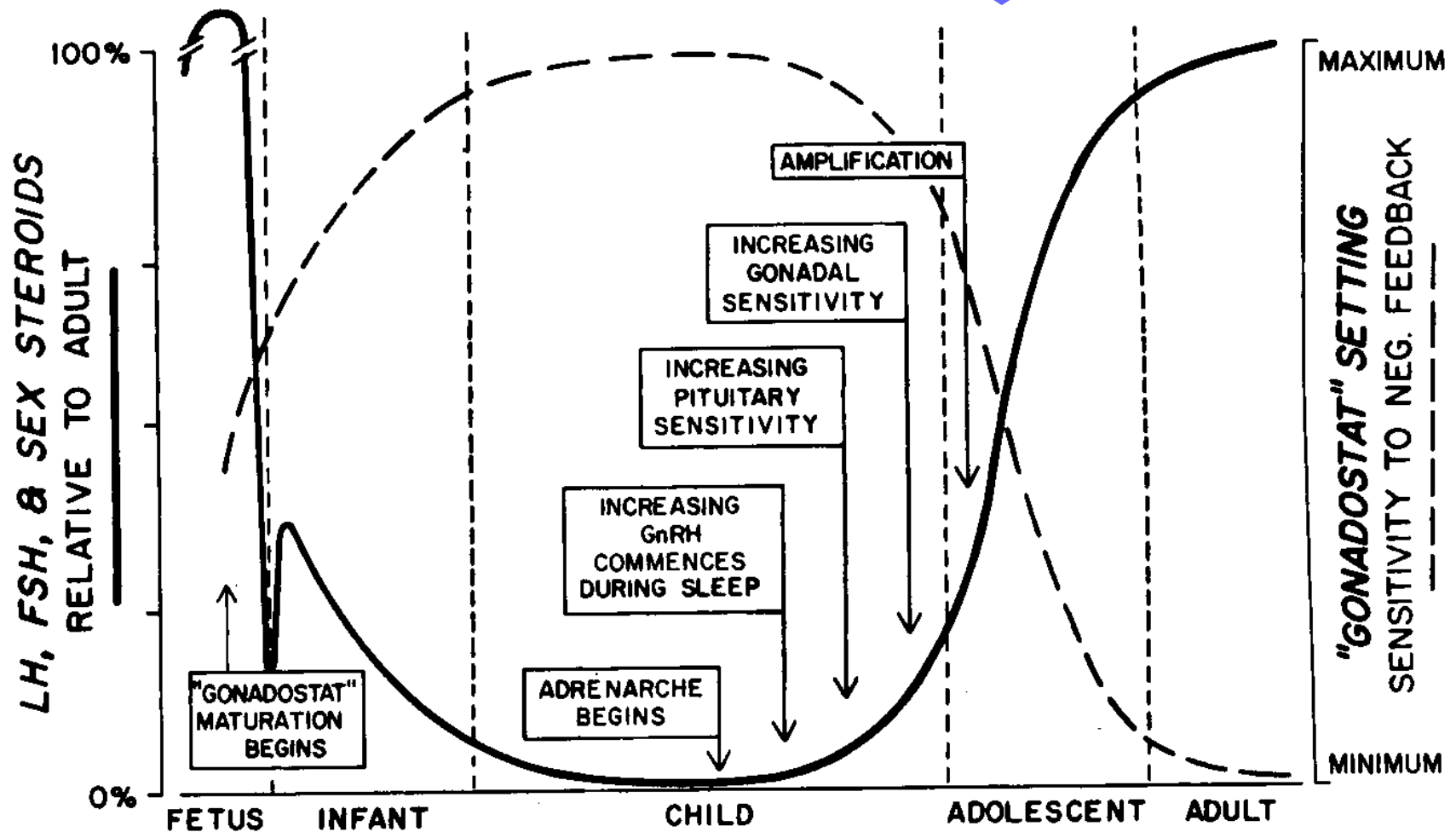
- Healthy term infant boy
- Noted to have pubic hair at 6 months
- No acceleration in height
- No Meds

6 month old: pubic hair

- Normal exam
 - 6 true pubic hair
 - Testes 2-3 ml
 - Normal phallus not enlarged
 - Abdomen normal
- No increased androgens, testosterone
- Low 17 OHP
- Tumour markers N (B hcg and AFP)

6 month old: pubic hair

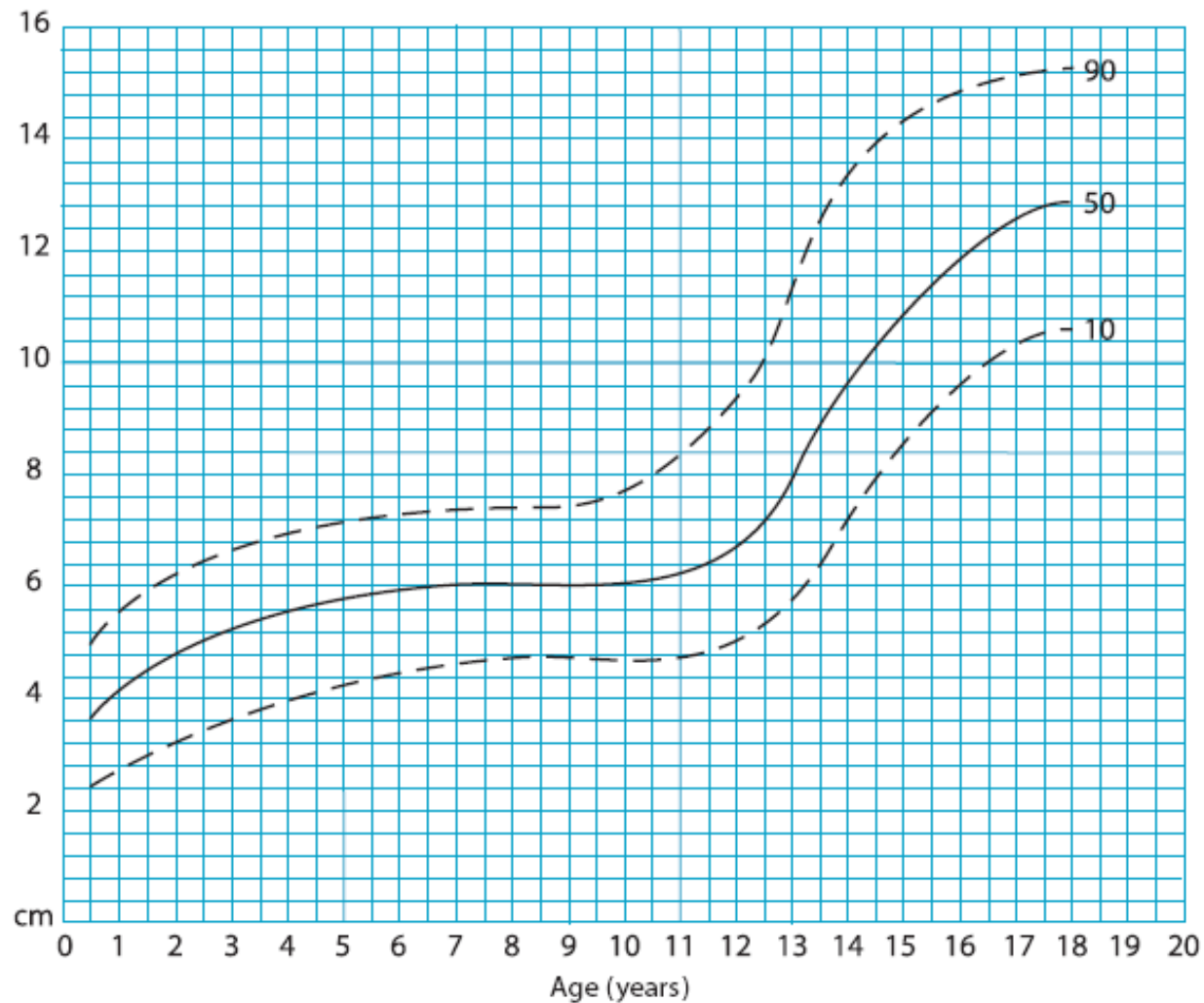
- Watched and no progress
- Pubic hair “removed” and not come again
- “mini-puberty” or exaggerated puberty
- “Benign pubic hair of infancy”
- Diagnosis of exclusion



The three puberties of life

Stretched Penile Length

Measured from the pubo-penile skin junction to the tip of the glans (Shonfeld & Be

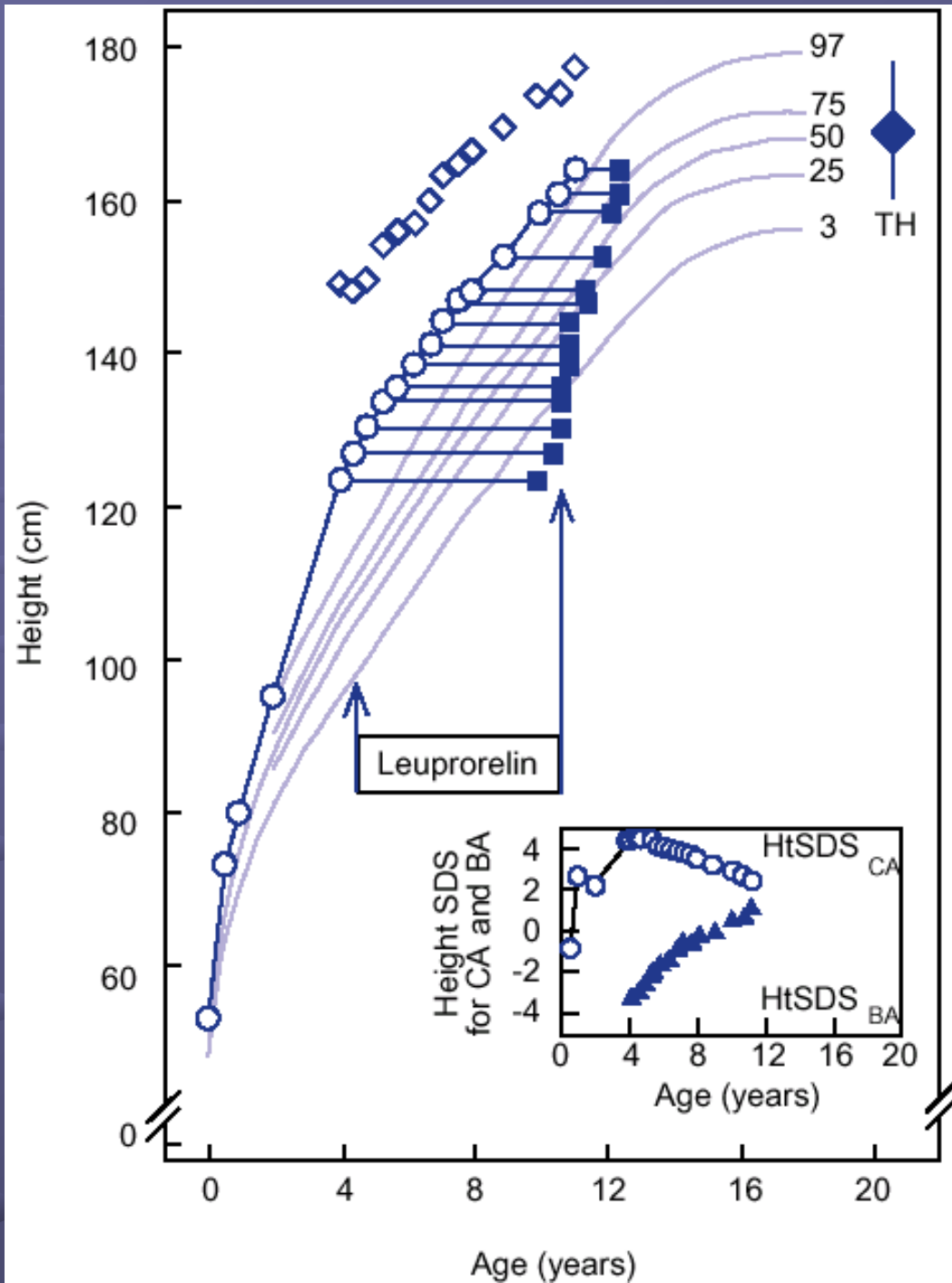


? Too early

- 5 year old girl with breast budding
- Normal child otherwise
- No medical hx (no Family Hx early puberty)
- Tanner 3 breast tissue
- Bone age 10-11
- Tall for age
- Emotional

? Too early

- GnRH stimulation test: LH 2.0 increased to 12 (pubertal and central rise)
 - Normal Thyroid function
- MRI head N
- Central precocious puberty:
- Start GnRH agonist



Example of idiopathic
Precocious puberty

Advanced Bone age

Effect of treatment with
Lucrin

Precocious Puberty -Definition

● Pathological process

- Too early
- Too fast
- Pathological hormonal milieu

● Arbitrary

- Females <8 years (menarche <9 years)
 - This will be 2% of healthy girls
- Males <9 years

● Clinical confirmation

- Clinical signs (and USS in females)
- Hormonal evaluation
- Bone age advancement
- Rate of acceleration

Investigation (First line)

- Bone Age (X-ray L hand and wrist)
- USS pelvis
 - Uterine size, endometrial thickness
 - sometimes useful info on ovaries
- Thyroid functions
- Done but not always that useful tests
 - FSH and LH
 - Testosterone
 - Oestradiol

Causes of Central PP

- Idiopathic in the majority of girls
- More common to find abnormality on males than females
- Structural Abnormality
 - Hypothalamic Hamartoma
 - Meningomyelocele
 - Hydrocephalus
 - NF-1
- CNS insult
 - Neonatal Encephalopathy
 - Cranial Irradiation
 - Trauma/Surgery

Puberty Case

- 6 year old girl with ? Early puberty
- Noted pubic hair and body odour 6 months ago
- No meds
- Otherwise well
- Born preterm at 32 weeks, low birth weight
- Mother: History fo PCOS

6 year old ? puberty

- Height and weight on 25%
 - Minor black heads
 - No breast budding
 - 3 true pubic hair, nil else of note
-
- Bone age not advanced
 - Test, Dheas N
 - 17 OHP 1.8
 - Androstenedione 3.0 “N”

Premature adrenarche

- Minor adrenal hormone activation
- No systemic features
- Exclude CAH and overproduction of androgens
- Keep Slim!
- Association with PCOS, SGA and Preterm

The Arche's

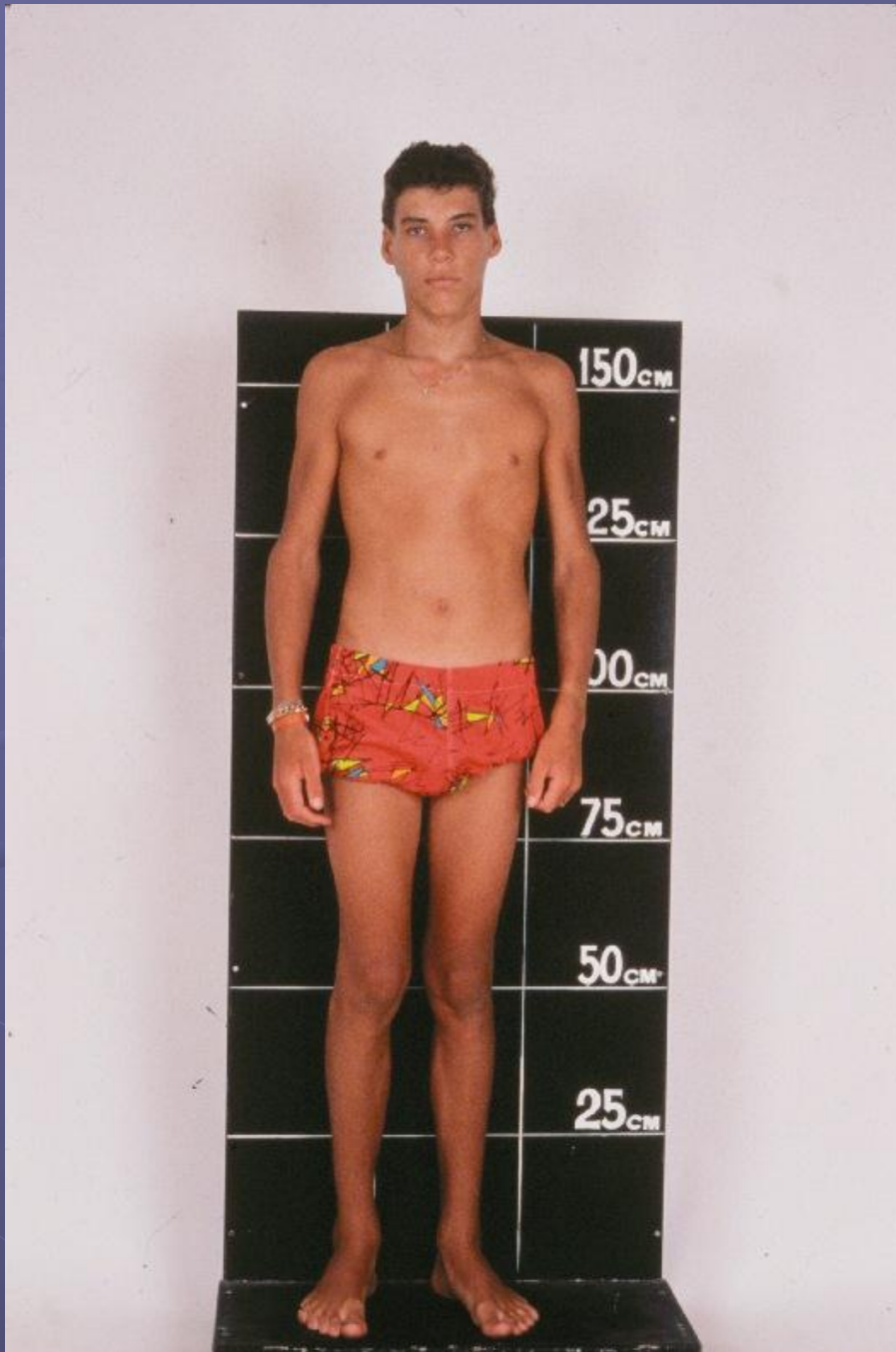
- Gonadarche
- Pubarche
- Thelarche
- Menarche
- Spermatarche
- Adrenarche

Potpourri





Prader Wili Syndrome



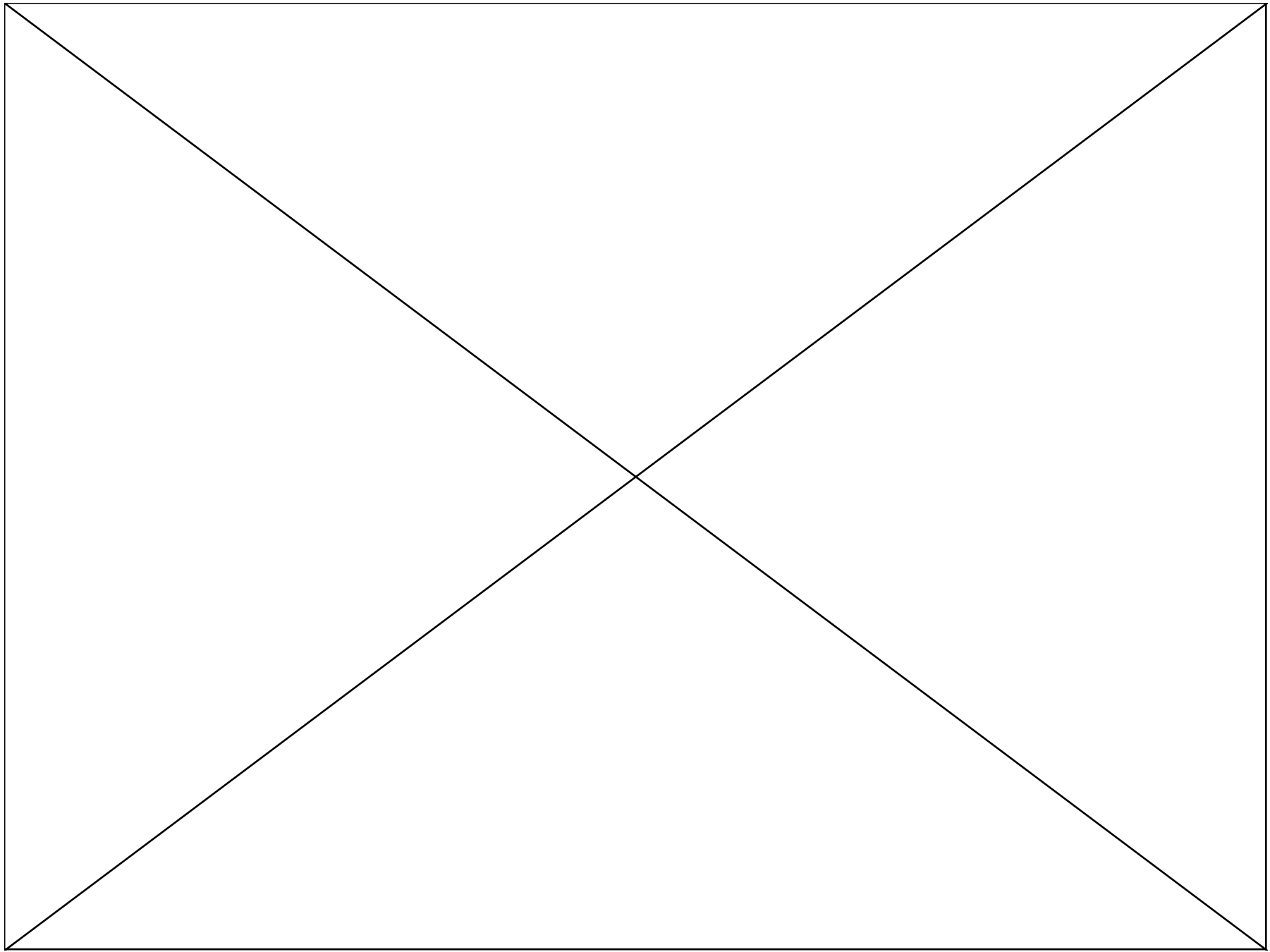
10 year old boy

Pituitary gigantism

This boy is the shortest in his class

- What is the diagnosis?
 - A) Turner syndrome
 - B) Williams Syndrome
 - C) Downs Syndrome
 - D) Noonans Syndrome





This boy is the shortest in his class

- What is the diagnosis?
 - A) Turner syndrome
 - B) Williams Syndrome
 - C) Downs Syndrome
 - D) **Noonans Syndrome**

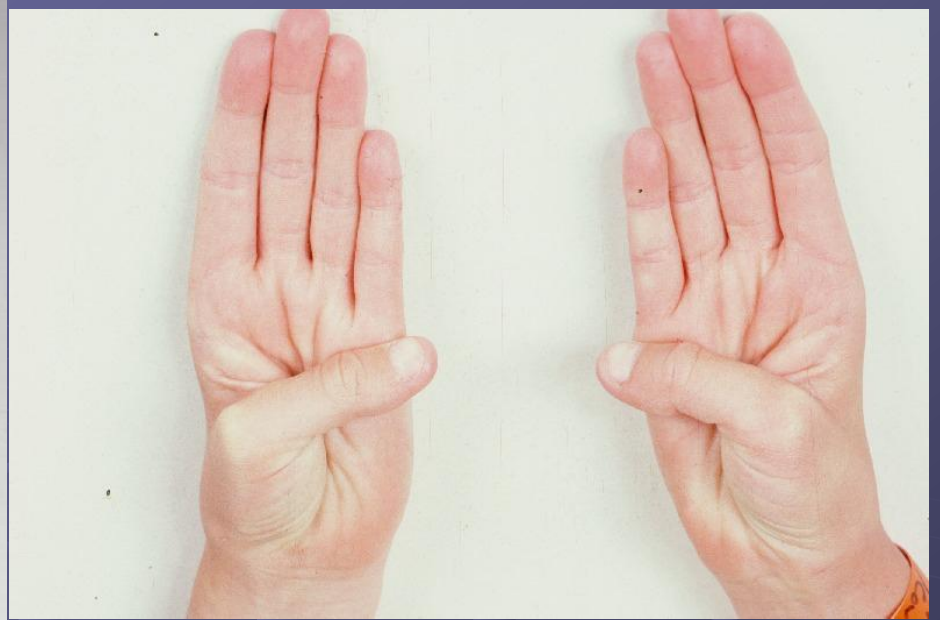




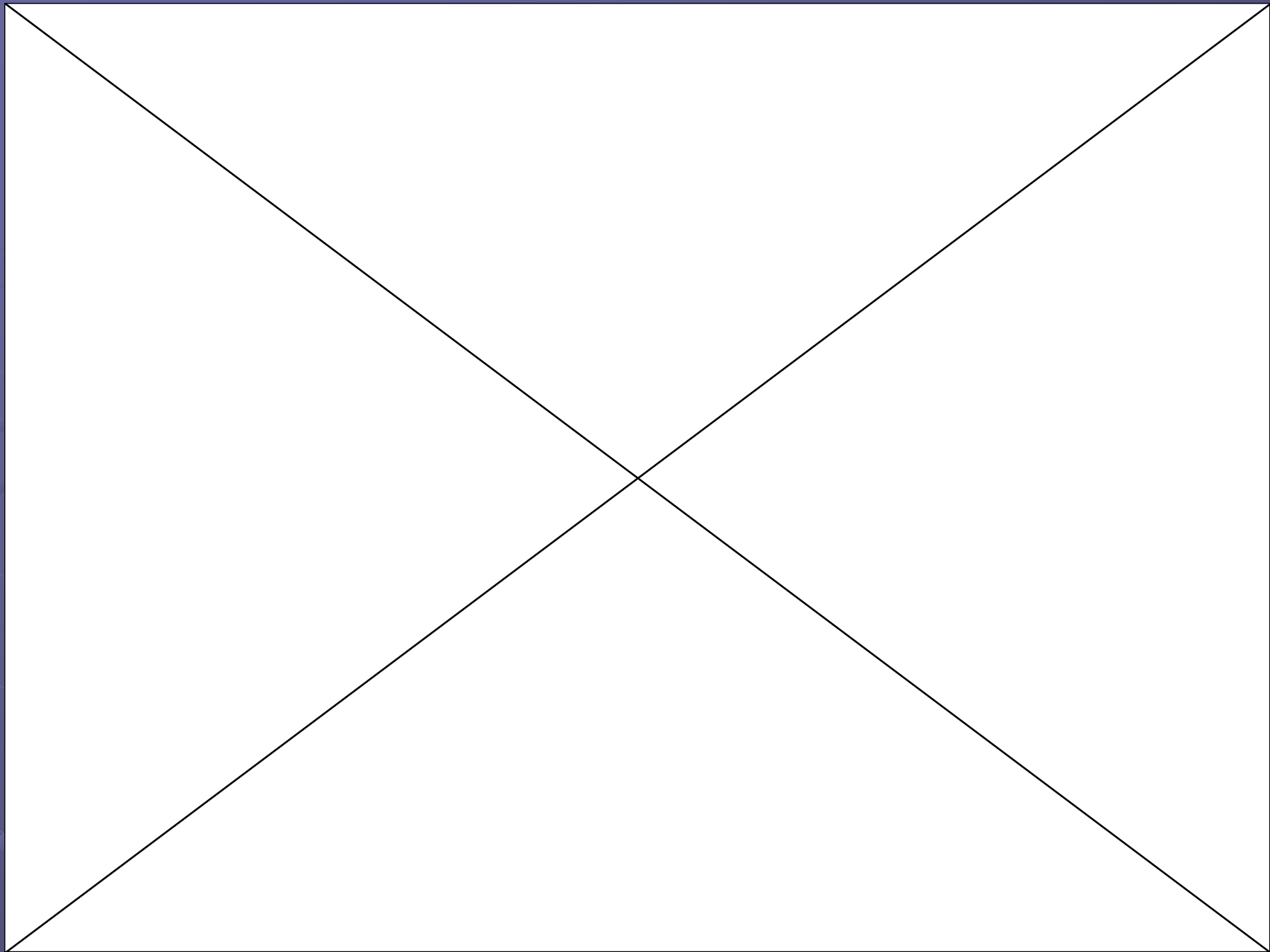
Name the lesion(s)

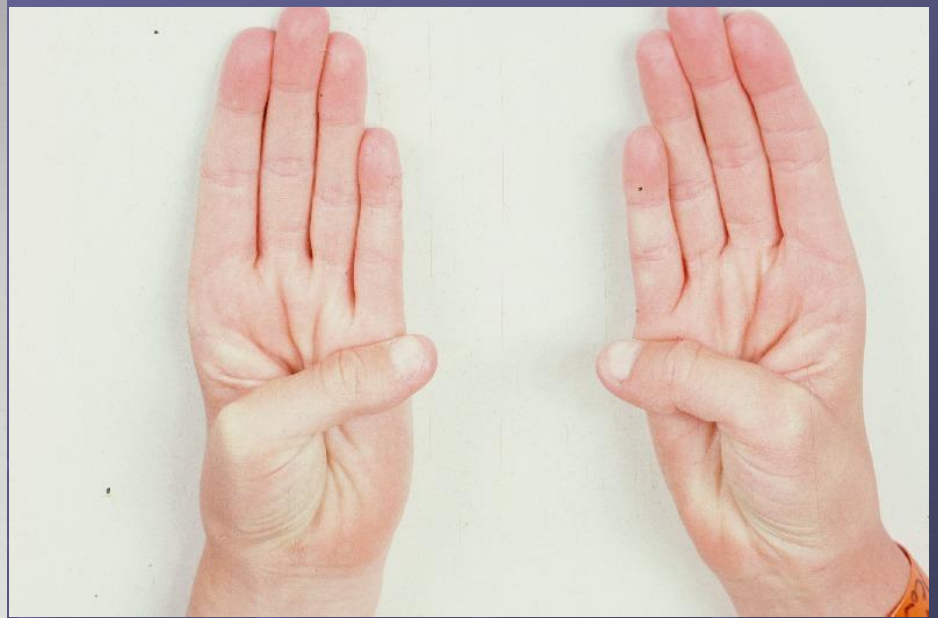
What is the underlying condition?

**Scoliosis and Café au Lait patch
NF-1**



- What is this condition?
- A) Hyperthyroidism
- B) Gigantism
- C) Marfans
- D) Sticklers





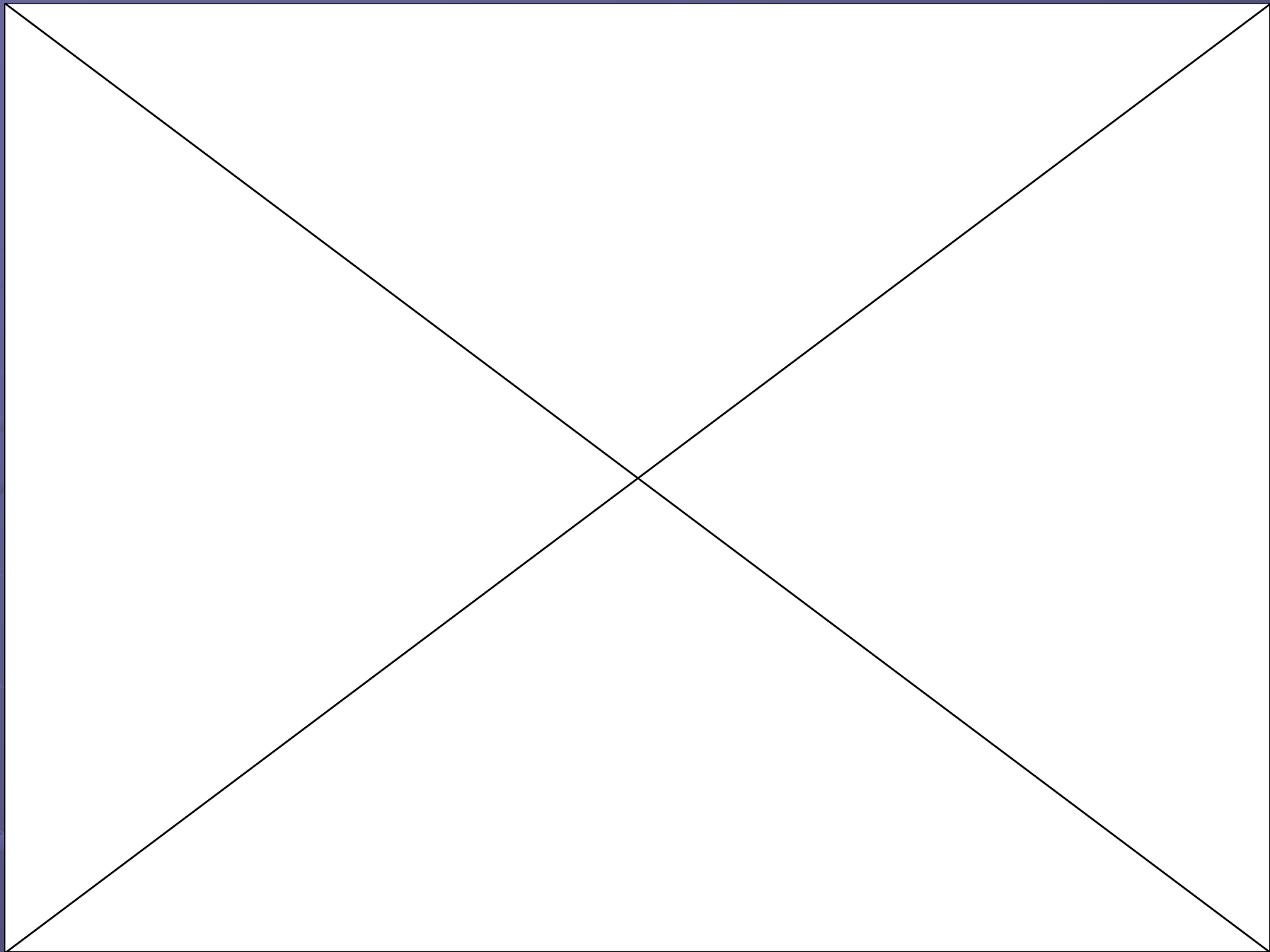
- What is this condition?
- A) Hyperthyroidism
- B) Gigantism
- C) Marfans
- D) Sticklers

This well built 8 year old boy has a bone age of 14 years and has been on 2 liquid medications since he was an infant.

● What is the autosomal recessive condition?

- A) Congenital hypothyroidism
- B) GH excess
- C) Congenital adrenal hyperplasia
- D) Haemachromotosis





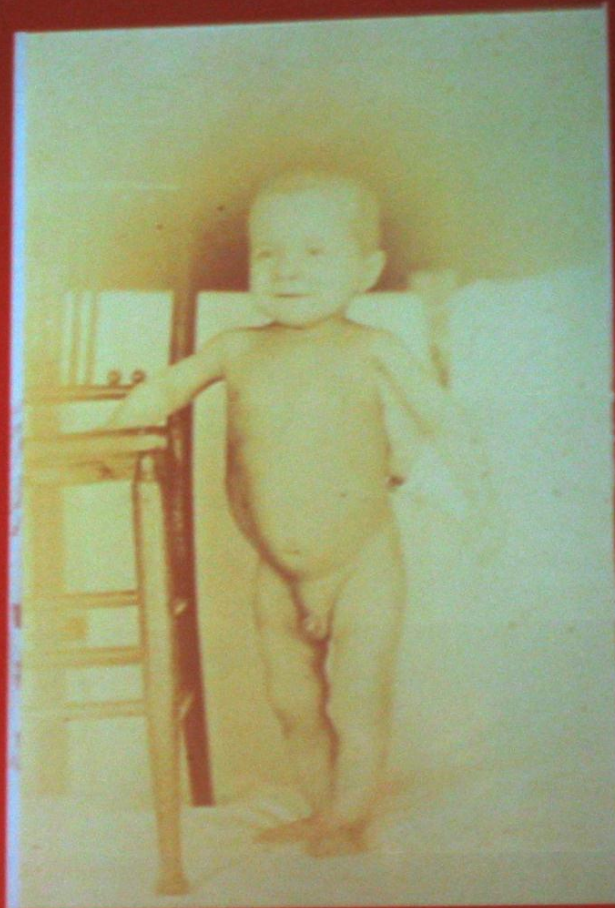
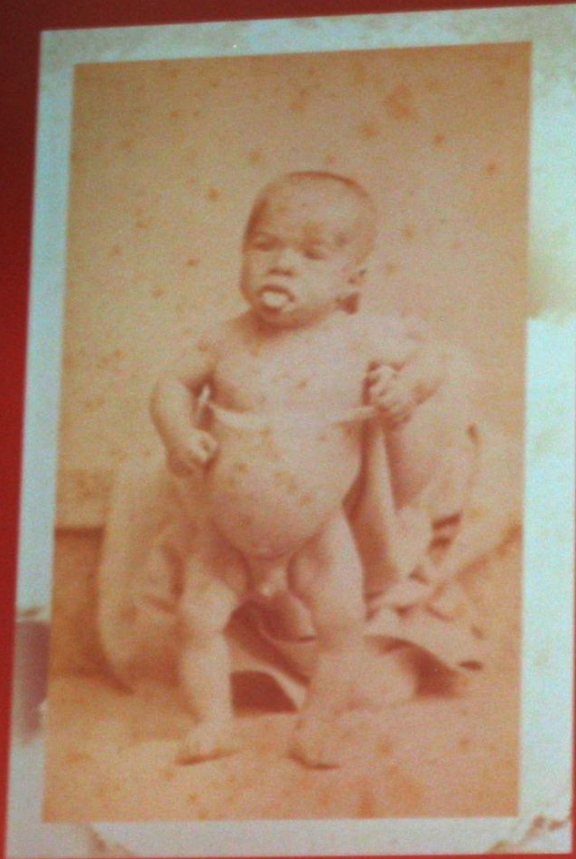
This well built 8 year old boy has a bone age of 14 years and has been on 2 liquid medications since he was an infant.

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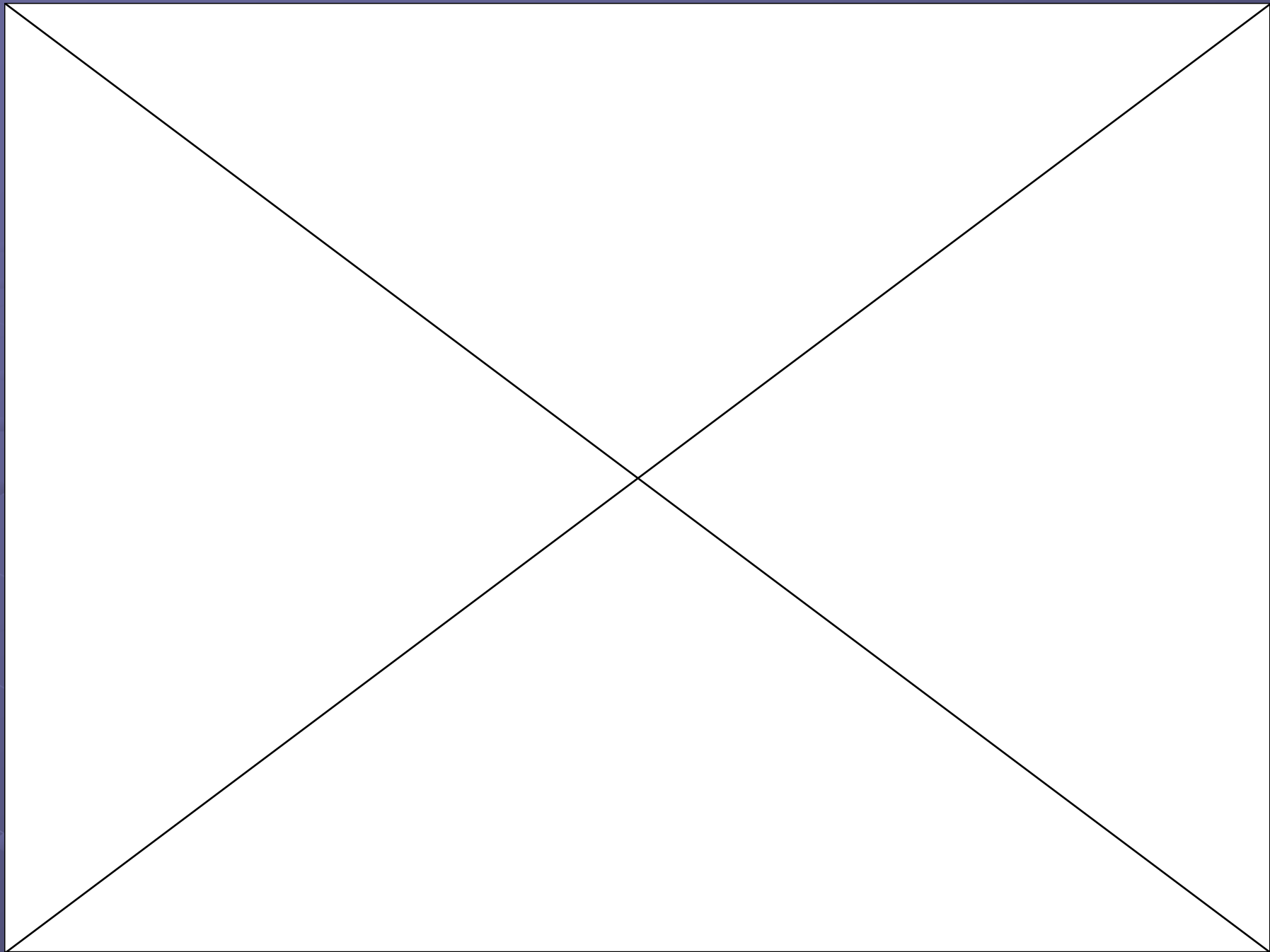






What condition has been treated?

- A) Growth Hormone Deficiency
- B) Congenital adrenal hyperplasia
- c) Ricketts
- d) Congenital hypothyroidism





What condition has been treated?

- A) Growth Hormone Deficiency
- B) Congenital adrenal hyperplasia
- c) Ricketts
- d) Congenital hypothyroidism**

Osler's Thyroid extract







Goiter



Cretinism



Vitiligo

Take home message

- Serial growth measurement are key
- Poor growth is a key indicator of underlying disease
- Androgens
 - Adrenal: Androstenedione, DHEAS
 - Testes/Ovary: Testosterone
- Short stature in girls
 - Exclude turner syndrome: karyotype
- Boy boobs are far worse then the man-flu
 - Check a karyotype

Resources: www.apeg.org.au see Hormones and me booklets



Australasian Paediatric Endocrine Group

March 06, 2012

Photographic acknowledgement: Phil Bergman



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➤ Subcommittees

➤ Position Statement & Management Guidelines

➤ Membership

➤ Conferences and Events

▼ Hormones & Me Booklet Series

➤ Transition Resources

➤ Clinical Resources & Links

➤ Fellows & Training

➤ News

➤ Research

Hormones & Me Booklet Series

This series of booklets is designed to be a patient resource for use by health professionals caring for children with endocrine disorders.

To download a copy of the booklet, please click on your choice below.

If you would like to order hard copies to give to your patients, please download the order form [HERE](#). Complete the form and fax back as per the details.

The Booklet Series is available here as PDF files. They are large in file size, and will take some time to download (download times shown are estimated for a standard dial-up connection and will vary). The best method for downloading a large PDF file is to RIGHT-CLICK on the link, and select "Save Target As..." (or similar) from the pop-up menu, then open the file when it has finished.*

*To view and print PDF files you may need to download and install the free Adobe Acrobat Reader.

Booklet	Download Size / Time (dial up speed)
Congenital Adrenal Hyperplasia (CAH)	4MB / 10 min
Congenital Hypothyroidism	2.36MB / 9.5 min
Craniopharyngioma	12.88MB / 51.8 min
Delayed Puberty	6.77MB / 27.2 min
Diabetes Insipidus	3MB / 8 min
Growth Hormone Deficiency in Adults	7.28MB / 29.2 min
Growth Problems in Children	7MB / 28 min
Hyperandrogenism in Children & Adolescents (HAA)	2.15MB / 8.6 min