Growth

"Placed end to end there are 3,600,000 km of humans on the face of the earth."

Professor Wayne Cutfield

Liggins Institute

Declaration

Pfizer sponsored speaker

BEG, BORROW OR STEAL (BBC2)
Jamie Theakston:
Where do you think Cambridge University is?
Contestant:
Geography isn't my strong point.
Jamie Theakston:
There's a clue in the title.
Contestant:
Leicester

THE WEAKEST LINK (BBC2) Anne Robinson: Oscar Wilde, Adolf Hitler and Jeffrey Archer have all written books about their experiences in what: - Prison, or the Conservative Party?
Contestant: The Conservative Party.

BEACON RADIO (WOLVERHAMPTON)

DJ Mark: For 10, what is the nationality of the Pope?

Ruth from Rowley Regis: I think I know that one. Is it Jewish?

UNIVERSITY CHALLENGE

Bamber Gascoyne: What was Gandhi's first name?

Contestant: Goosey?

LINCS FM PHONE-IN Presenter: Which is the largest Spanish-speaking country in the world? Contestant: Barcelona. Presenter: I was really after the name of a country. Contestant: I'm sorry, I don't know the names of any countries in Spain .

NATIONAL LOTTERY (BBC1) Question: What is the world's largest continent? Contestant: The Pacific.

ROCK FM (PRESTON) Presenter: Name a film starring Bob Hoskins that is also the name of a famous painting by Leonardo da Vinci. Contestant: Who Framed Roger Rabbit?

JAMES O'BRIEN SHOW (LBC) James O'Brien: How many kings of England have been called Henry? Contestant: Er, well, I know there was a Henry the Eighth ... ER. ER ... Three?

CHRIS SEARLE SHOW (BBC RADIO BRISTOL) Chris Searle: In which European country is Mount Etna? Caller: Japan.

Chris Searle: I did say which European country, so in case you didn't hear that, I can let you try again.

Caller: Er .. Mexico ?

PAUL WAPPAT (BBC RADIO NEWCASTLE)

Paul Wappat: How long did the Six-Day War between Egypt and Israel last?

Contestant (long pause): Fourteen days.

Case 1

A concerned mother presents her 5 year old son with short stature

Really only noticed he is short now

What are the common ages of presentation with short stature?

Case 1

What are the common ages of presentation with short stature?

Starting school

Starting high school

Case 1

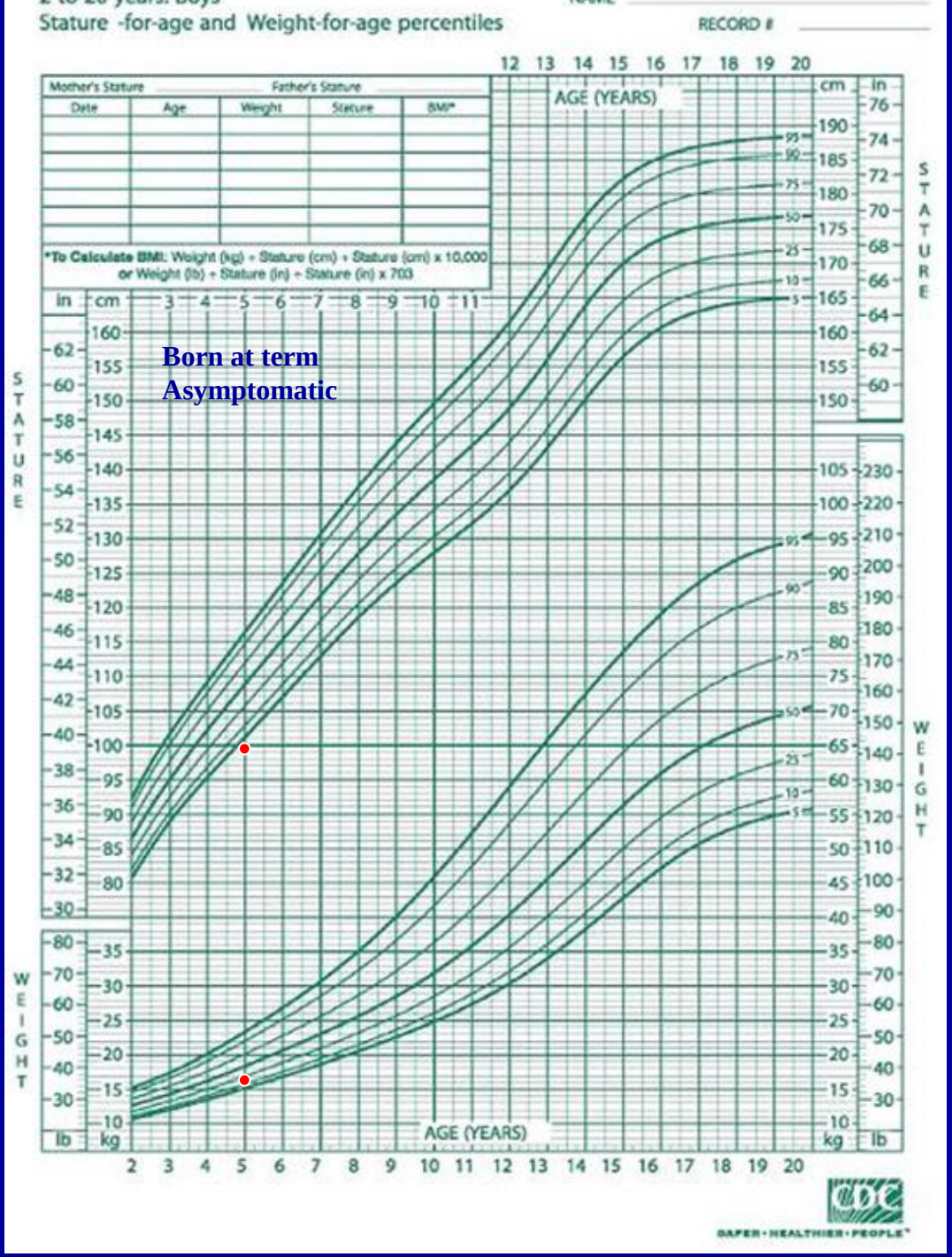
A concerned mother presents her 5 year old son with short stature

Really only noticed he is short now

Born at term, normal delivery

Completely healthy

Case 1


Stature -for-age and Weight-for-age percentiles
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
AGE (YEARS)
STATURE
WEIGHT
Born at term
Asymptomatic
95
90
75
50
25
10
5
cm
in
kg
lb
HEALTHIER PEOPLE

Case 1

A concerned mother presents her 5 year old son with short stature

Really only noticed he is short now

Born at term, normal delivery

Completely healthy

What more do you want to know and why?

Case 1

What do you want to know and why?

No interval history of note

No medications

No pregnancy illnesses/drugs

Birth weight 3,600 gm

Father 166 cm

Mother 151 cm

Parents school teachers

Only child

Mid-parental height

Mother and fathers heights

MPH = M(cm) + F (cm) ±13 cm /2

MPH range ±8 cm

(151+13+166)/2 =165 (157-173) cm

3rd percentile

Plot on growth chart

Case 1

What diagnostic investigations should you perform now?

Case 1

What diagnostic investigations should you perform now?

None!!

Short stature screening

1375 referrals to CHMC Cincinnati

325 had Ht <3rd PC, normal history/exam

Normal variant short stature 99%

- familial short stature 23%
- constitutional delay 41%
- idiopathic short stature 36%

Sisley J Pediatr 2013; May 21 [Epub]

Short stature screening

New pathology 1.3% (2 coeliac disease)

Screening cost to identify new pathology case: $US105,107.00

"Healthy short children do not warrant non-directed, comprehensive screening"

Sisley J Pediatr 2013; May 21 [Epub]

Case 1

What is the single most important piece of clinical information you should try and obtain?

Height velocity (HV)

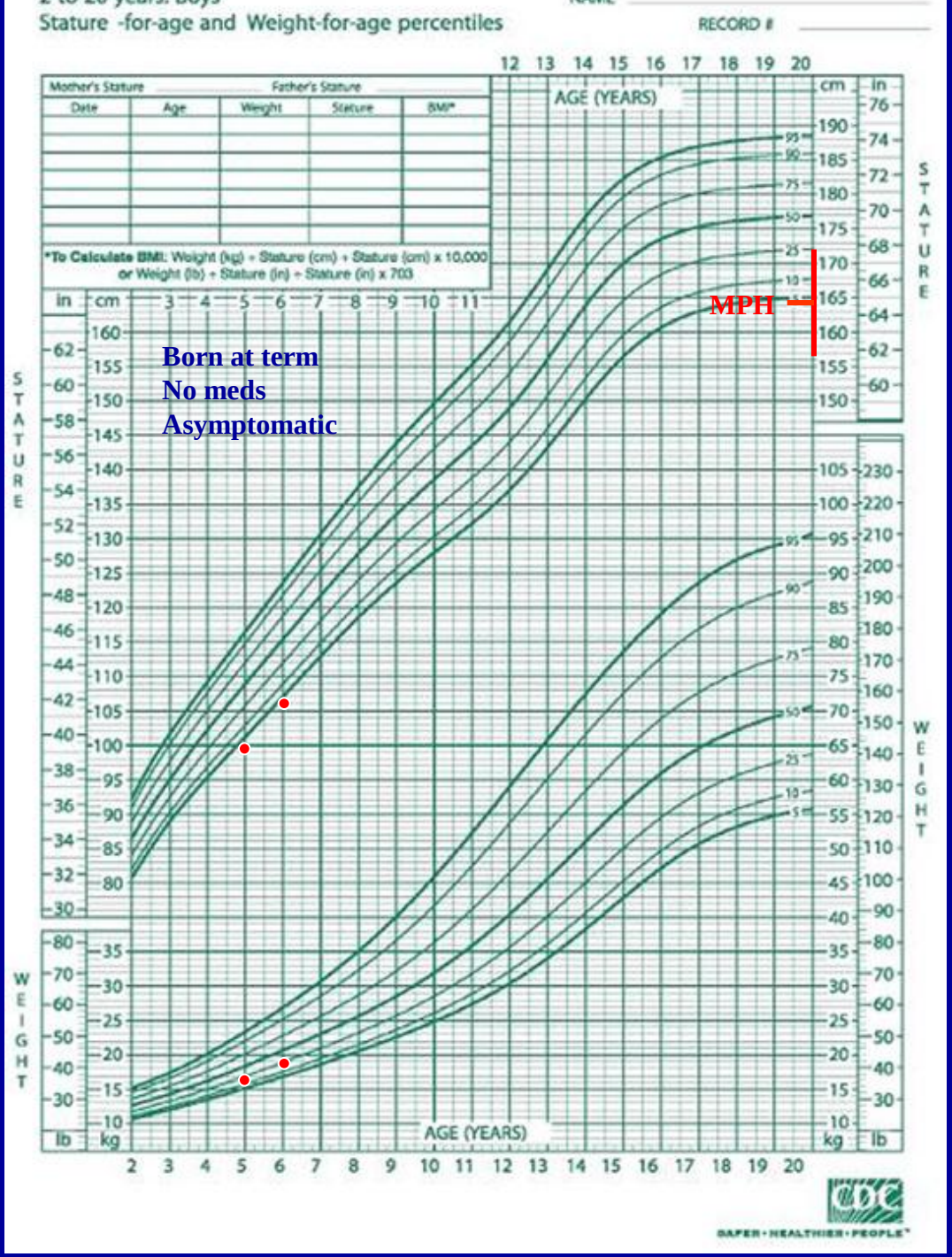
Measured over a minimum of 6 months

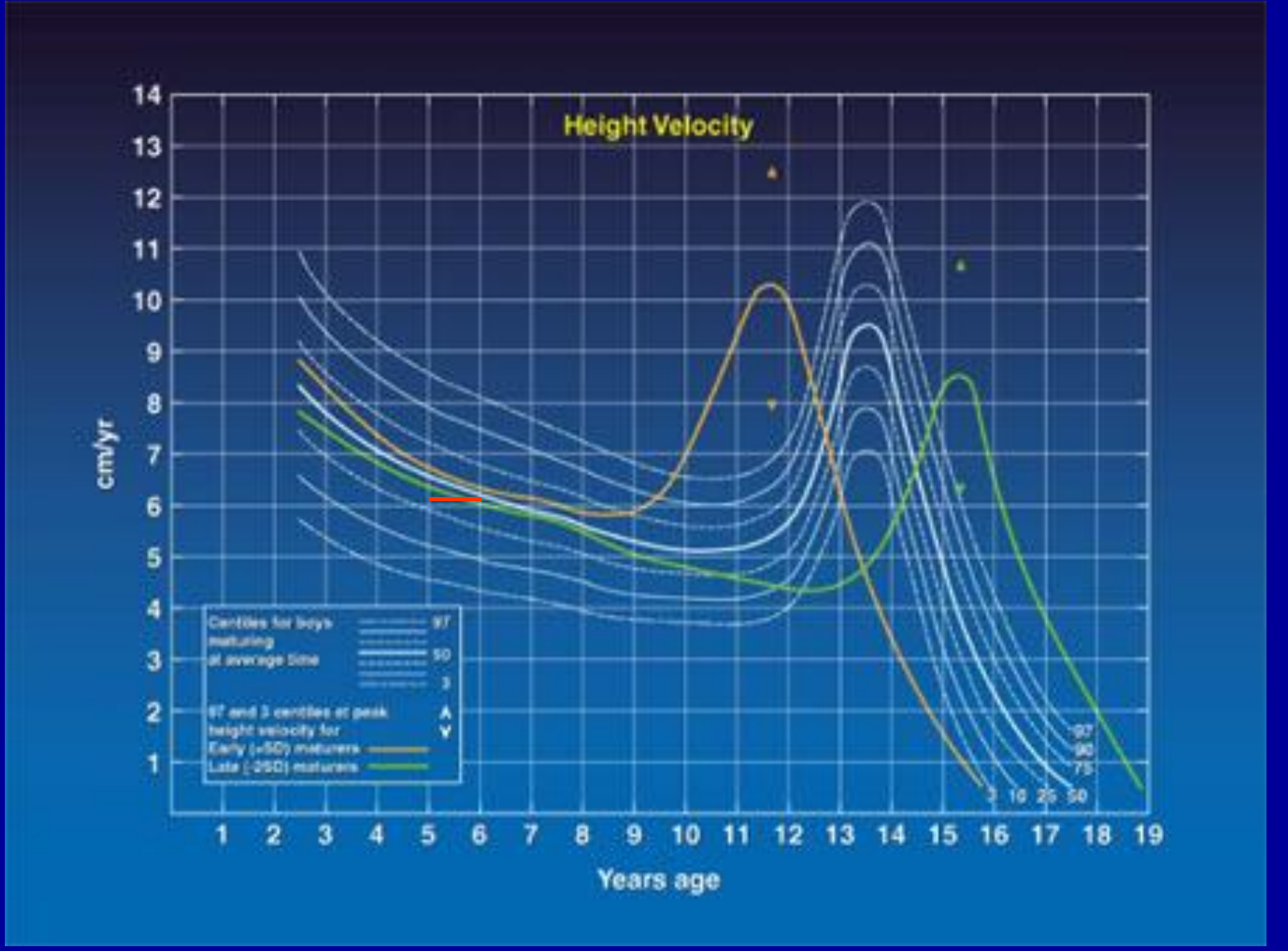
HV differentiates normal variant short stature from pathological short stature

HV cannot be calculated over shorter interval because of errors in measurement

Normal height velocity 25-75 PC

Case 1


Stature -for-age and Weight-for-age percentiles
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
AGE (YEARS)
STATURE
WEIGHT
MPH
Born at term
No meds
Asymptomatic
HEALTHIER PEOPLE


Height Velocity
cm/yr
14
13
12
11
10
9
8
7
6
5
4
3
2
1
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
Years age
Centiles for boys maturing at average time
97
50
3
97 and 3 centiles at peak height velocity for
A
V
Early (+SD) maturers
Late (-2SD) maturers
97
90
75
50
3 10 25 50

Case 1

What is the most useful investigation you can perform?

A bone age: estimated at 5 yrs matching chronological age

Case 1

What is the most likely diagnosis?

Case 1

What is the most likely diagnosis?

Familial short stature

Case 2

A concerned mother presents her 13 year old son with short stature

Noticed at starting secondary school how short he was compared to peers – “they all look like men!”

Case 2

Mild asthma treated with flixotide 200 mcg bid

No pregnancy illnesses/drugs

Birth weight 3,250 gm at term

Father 175 cm

Mother 165 cm

MPH 176.5 cm (50^{th} percentile)

Father accountant, mother lawyer

Youngest of three children

What other aspects of history do you want to know?

Case 2

Mother menarche 14 yrs

Father still growing when started university

18 yr old brother stopped growing at secondary school

16 year old sister menarche at 14 yrs

Case 2

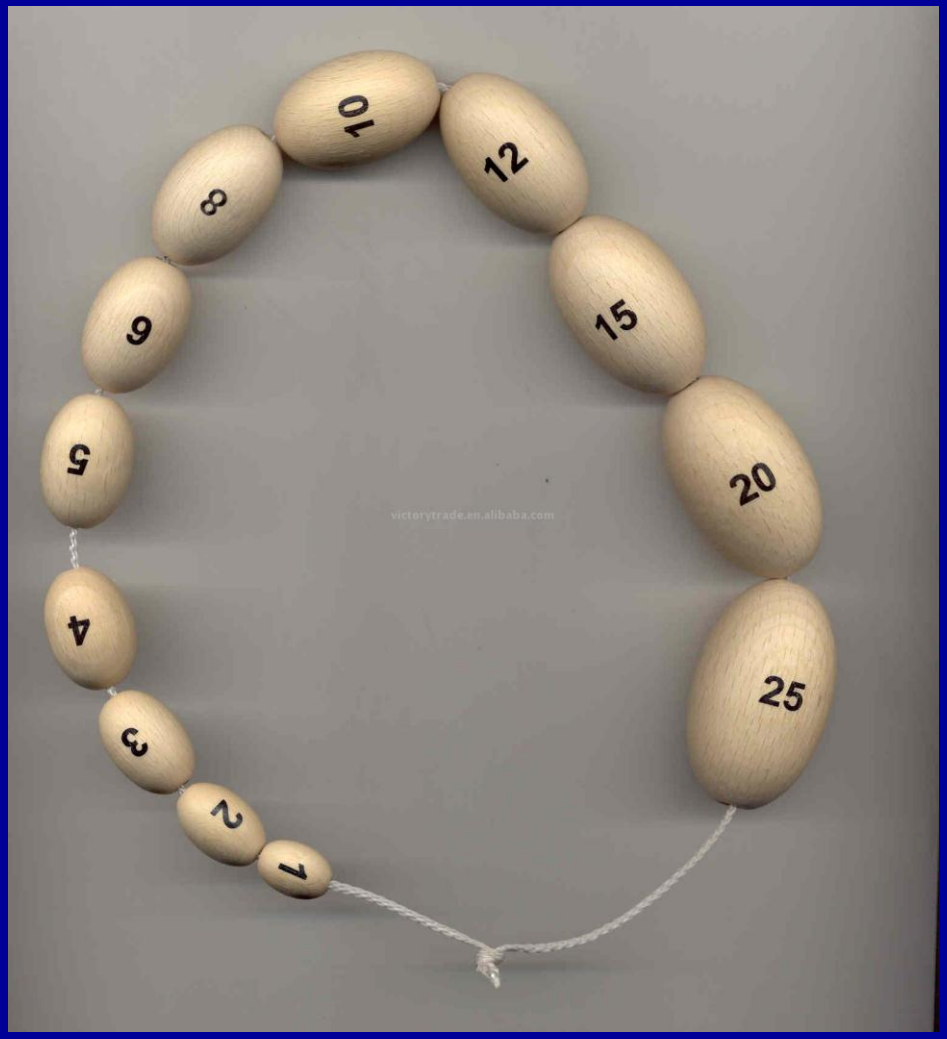
Examination normal

Testes 3 ml

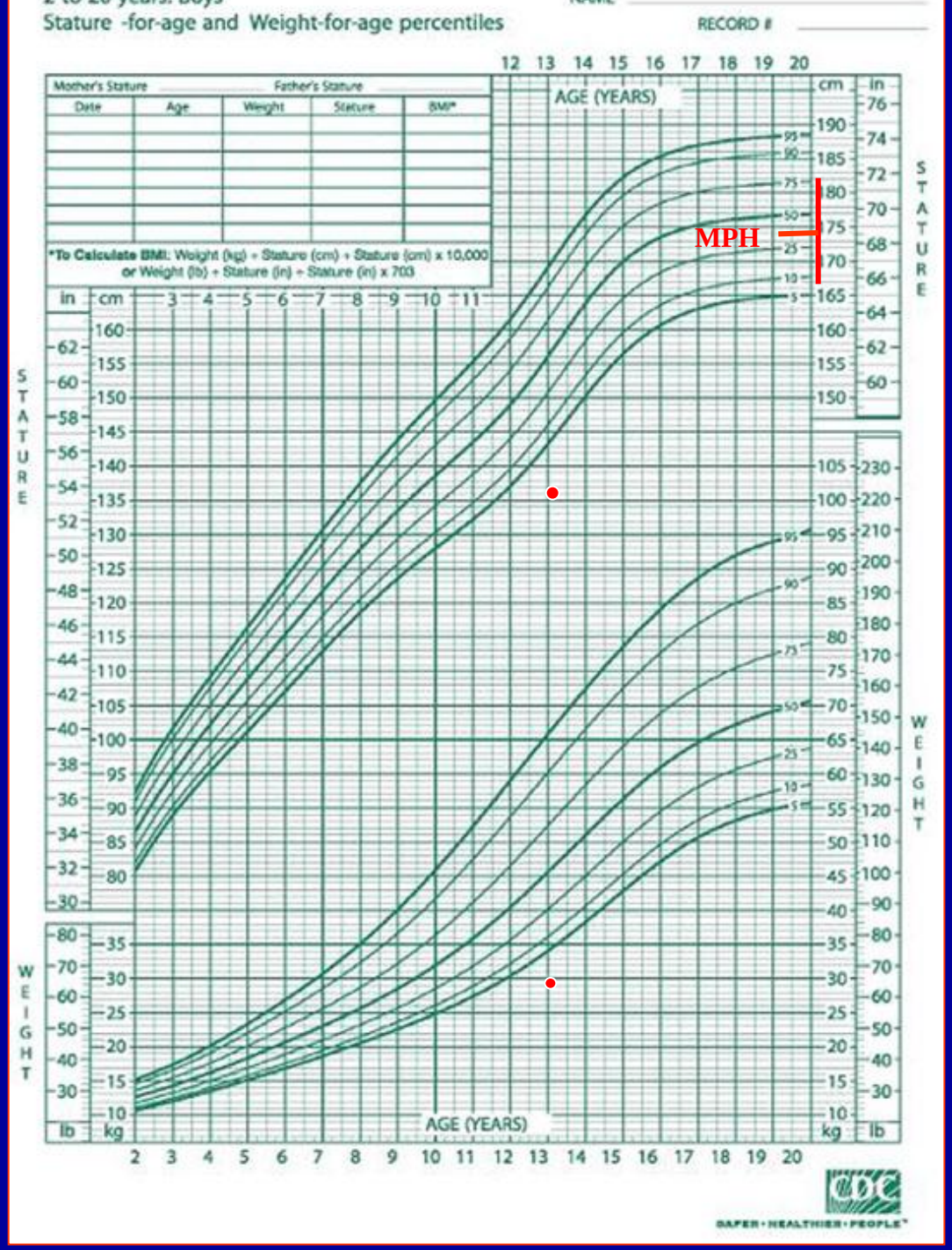
Tanner stage 1 pubic hair

Orchidometer

The paediatric endocrinologist's "rosary beads"



Case 2


Stature -for-age and Weight-for-age percentiles
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
AGE (YEARS)
STATURE
WEIGHT
MPH
cm
in
lb
kg
95
90
75
50
25
10
5
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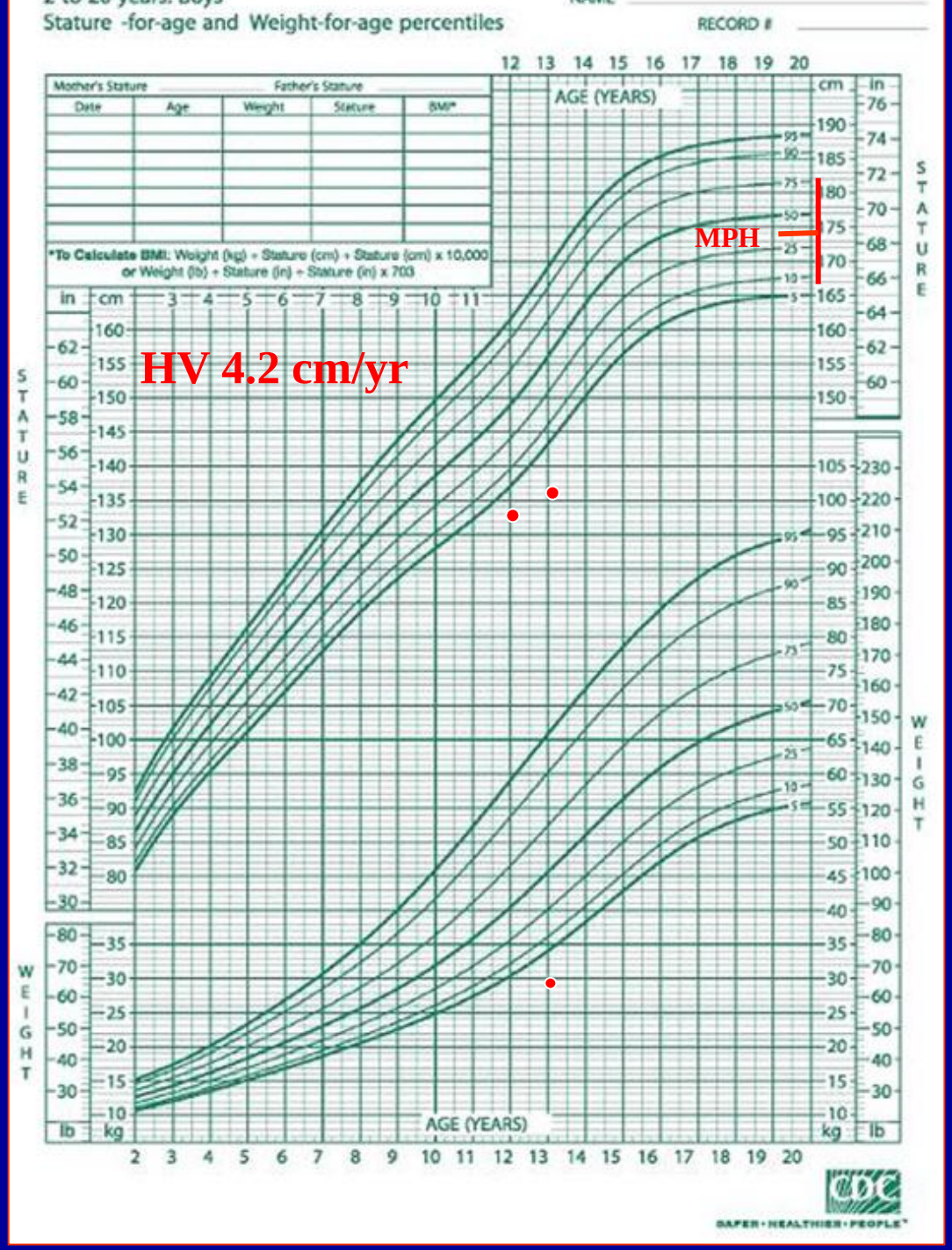
Case 2


Stature -for-age and Weight-for-age percentiles
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
AGE (YEARS)
STATURE
WEIGHT
HV 4.2 cm/yr
MPH
95
90
75
50
25
10
5
in
cm
lb
kg
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
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Case 2

Mild asthma treated with flixotide 200 mcg bid

No pregnancy illnesses/drugs

Birth weight 3,250 gm

Father 175 cm

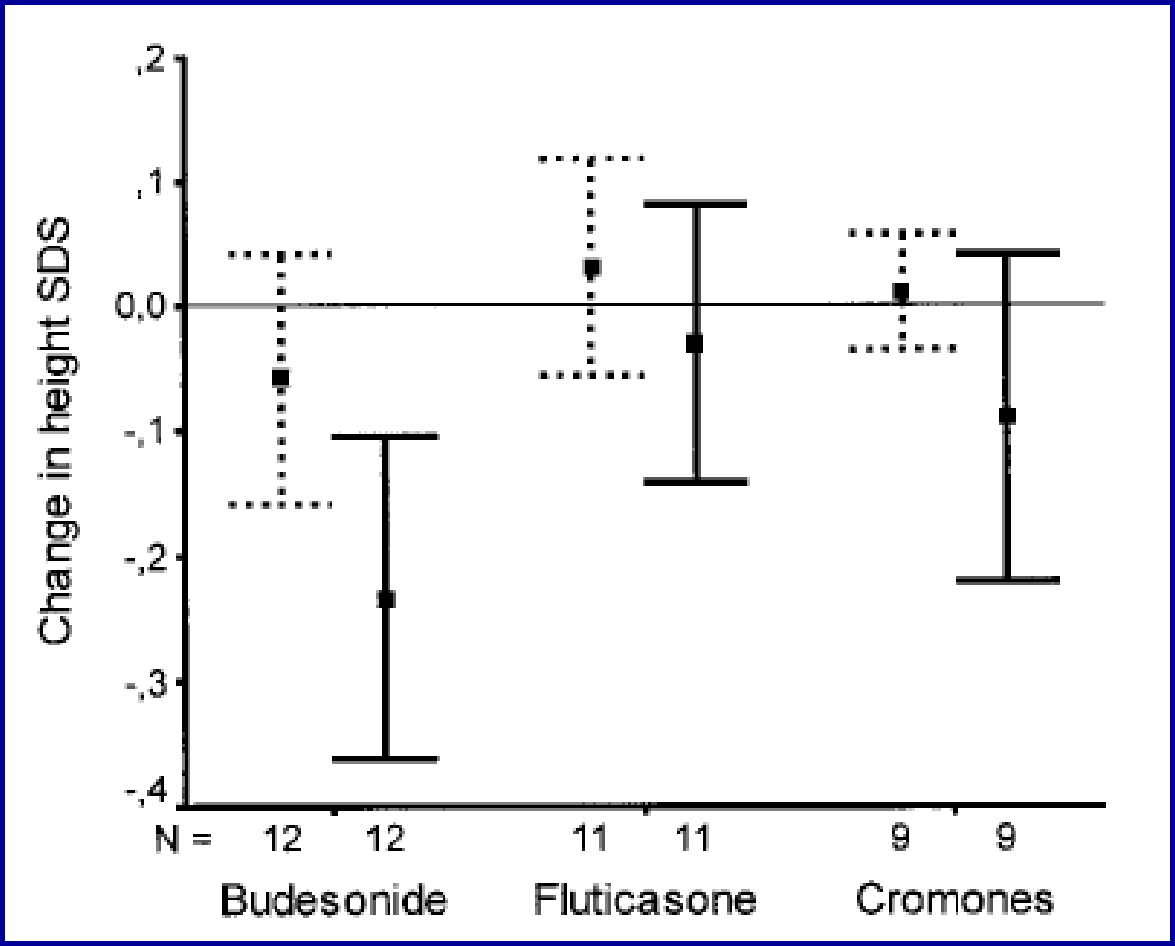
Mother 165 cm

Father accountant, mother lawyer

Youngest of three children

Is it likely that flixotide has affected his growth?

Fluticasone and growth suppression



75 asthmatic children
9.5 (5.5-14.7) yrs
Randomised to
Budesonide 200→400 μg/d
Fluticasone 500→200 μg/d
Na cromoglycate

Kannisto S J Clin Endocrinol Metab 2000; 85: 652-7

Fluticasone and HPA axis suppression

50 asthmatic children and adolescents (13.1 yrs)

Treated with >1000 µgm/m2/day for >6 mos

17% had HPA axis suppression

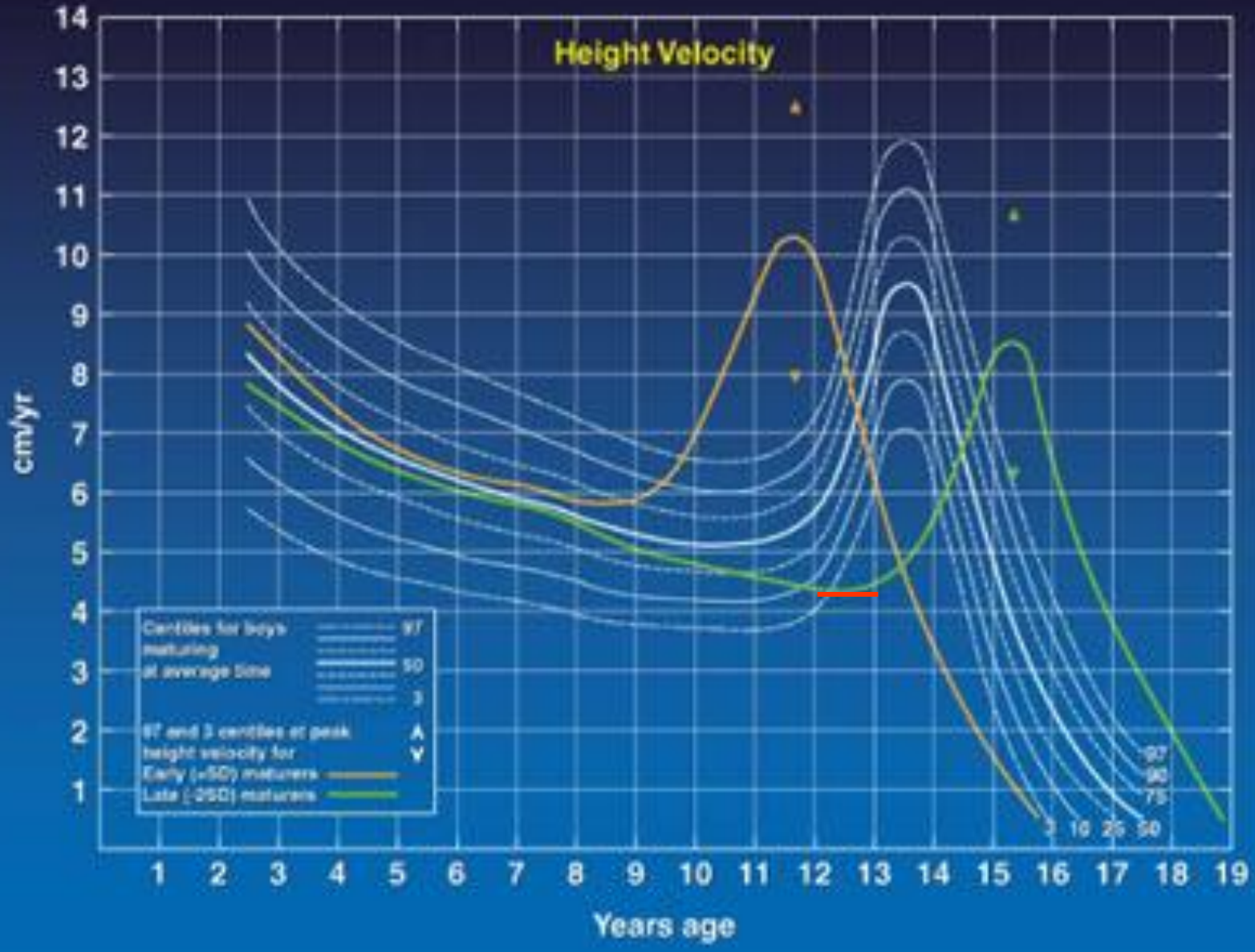
Sim D Eur Resp J 2003; 21: 633-6

Fluticasone and growth and HPA axis suppression

Only seen with high doses of fluticasone:

Approx >600 µgm/day younger children

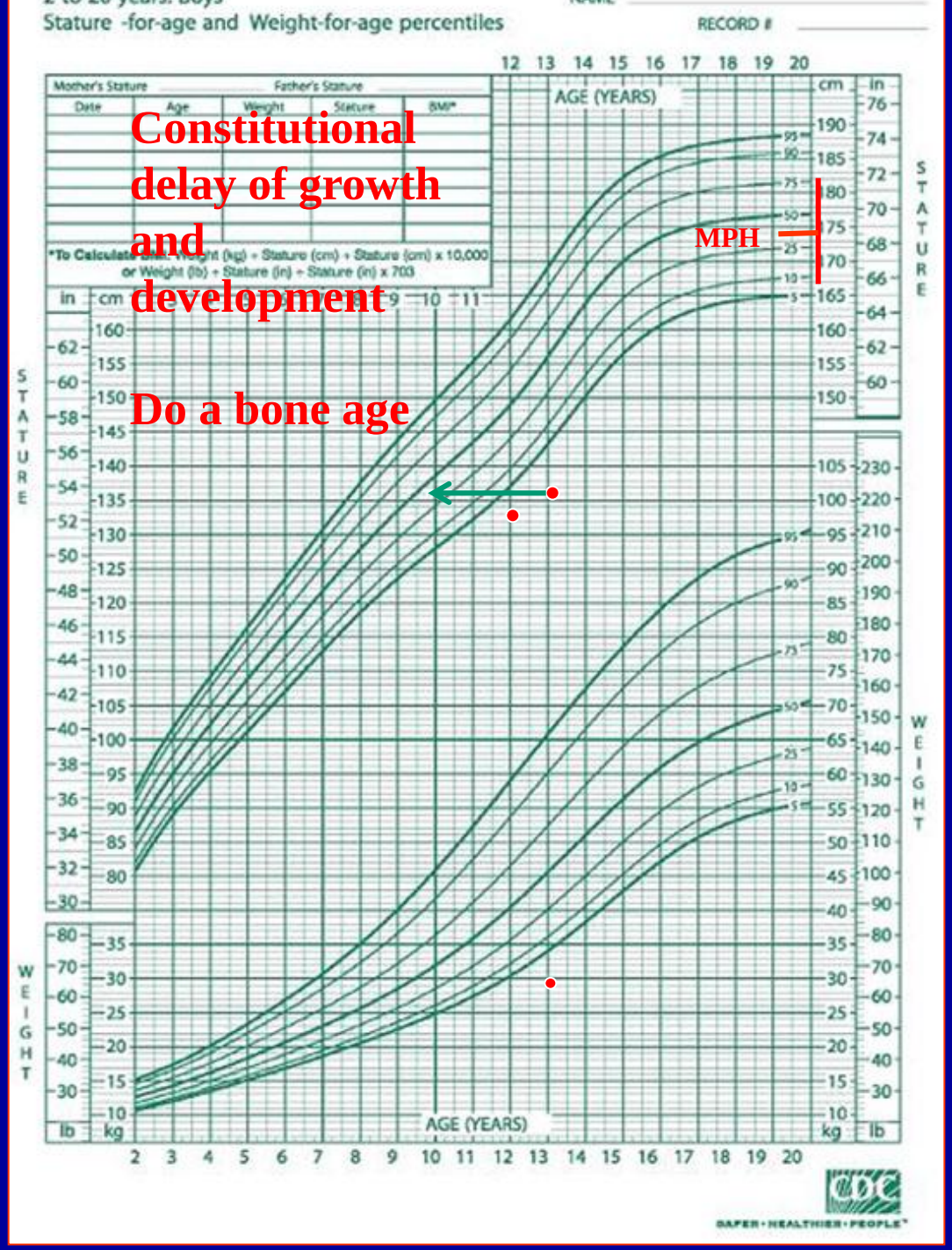
Approx >1,000 µgm/day older children


Height Velocity
cm/yr
Years age
14
13
12
11
10
9
8
7
6
5
4
3
2
1
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
Centiles for boys maturing at average time
97
50
3
97 and 3 centiles at peak height velocity for
A
V
Early (+SD) maturers
Late (-2SD) maturers
97
90
75
50
10
25

Case 2

What is the most likely diagnosis and how will you manage him now?

Case 2


Stature -for-age and Weight-for-age percentiles
RECORD #
Mother's Stature
Father's Stature
Date
Age
Weight
Stature
BMI*
Constitutional delay of growth and development
MPH
Do a bone age
AGE (YEARS)
STATURE
WEIGHT
cm
in
lb
kg
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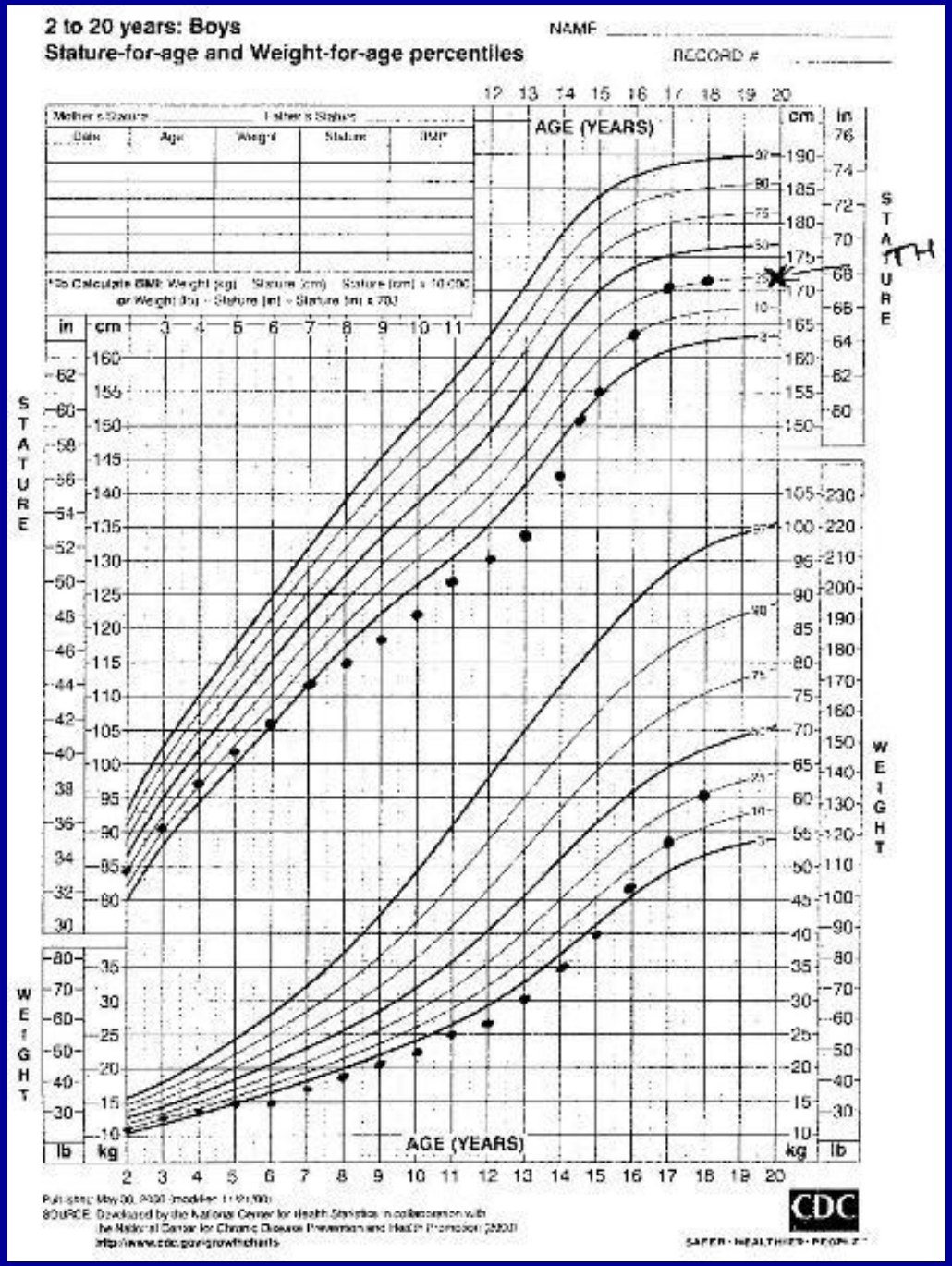
Case 2


2 to 20 years: Boys
Stature-for-age and Weight-for-age percentiles
NAME
RECORD #
AGE (YEARS)
STATURE
WEIGHT
cm
in
lb
kg
CDC

Height Percentile

Mother's Height

Father's Height

Simplified Calculation of Body Surface Area (BSA)

$$BSA\ (m^2) = \sqrt{\frac{Ht\ (cm) \times Wt\ (kg)}{3600}}$$

Reference: Mosteller, R.D. 1987, 'Simplified calculation of body surface area', *N. Engl. J. Med.*, 317:1098.

Supine Length (recommended up to the age of 3 so that there is overlap with standing height at 2 to 3) is taken on a flat surface, with the child lying on his back. One observer holds the child's head in contact with a board at the top of the table and another straightens the legs and turns the feet upward to be at right angles to the legs and brings a sliding board in contact with the child's heels.

Standing Height (recommended from age 2 onwards) should be taken without shoes, the child standing with his heels and back in contact with an upright wall. His head is held so that he looks straight forward with the lower borders of the eye sockets in the same horizontal plane as the external auditory meati (i.e. head not with the nose tipped upward). A right-angled block (preferably counterweighted) is then slid down the wall until its bottom surface touches the child's head and a scale fixed to the wall is read. During the measurement the child should be told to stretch his neck to be as tall as possible, though care must be taken to prevent his heels coming off the ground. Gentle but firm pressure upward should be applied by the measurer under the mastoid processes to help the child stretch. In this way the variation in height from morning to evening is minimised. Standing height should be recorded to the last completed 0.1 cm.

$C = M(1 + L.S.Z)^{1/L}$

Where C is the centile required, LMS are those parameters published by CDC and Z is the standard deviation equivalent to the centile required.

1st Centile calculated by Associate Professor Peter Davies, Children's Nutrition Research Centre, Brisbane.

Represents 50th centile height attained for an individual boy entering puberty at the average time based on longitudinal data. All other centiles are based on cross-sectional data.

Height

cm: 160, 155, 150, 145, 140, 135, 130, 125, 120, 115, 110, 105, 100, 95, 90, 85, 80, 75, 70, 65, 60

cm: 190, 185, 180, 175, 170, 165, 160, 155, 150, 145, 140, 135, 130, 125, 120, 115, 110, 105, 100, 95

in: 76, 75, 74, 73, 72, 71, 70, 69, 68, 67, 66, 65, 64, 63, 62, 61, 60, 59, 58, 57, 56, 55, 54, 53, 52, 51, 50, 49, 48, 47, 46, 45, 44, 43, 42, 41, 40, 39, 38

97 95 90 75 50 25 10 5 3 1

cm in

Penis Stage: 5+ 4+ 3+ 2+ — 97 90 75 50 25 10 3

Pubic Hair Stage: 5+ 4+ 3+ 2+ — 97 90 75 50 25 10 3

Testes Vol: 12mL 4mL — 97 90 75 50 25 10 3

cm: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

Age (years): 11 12 13 14 15 16 17 18

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

Case 2

How will you manage him now?

Is he distressed by his size and lack of pubertal development?

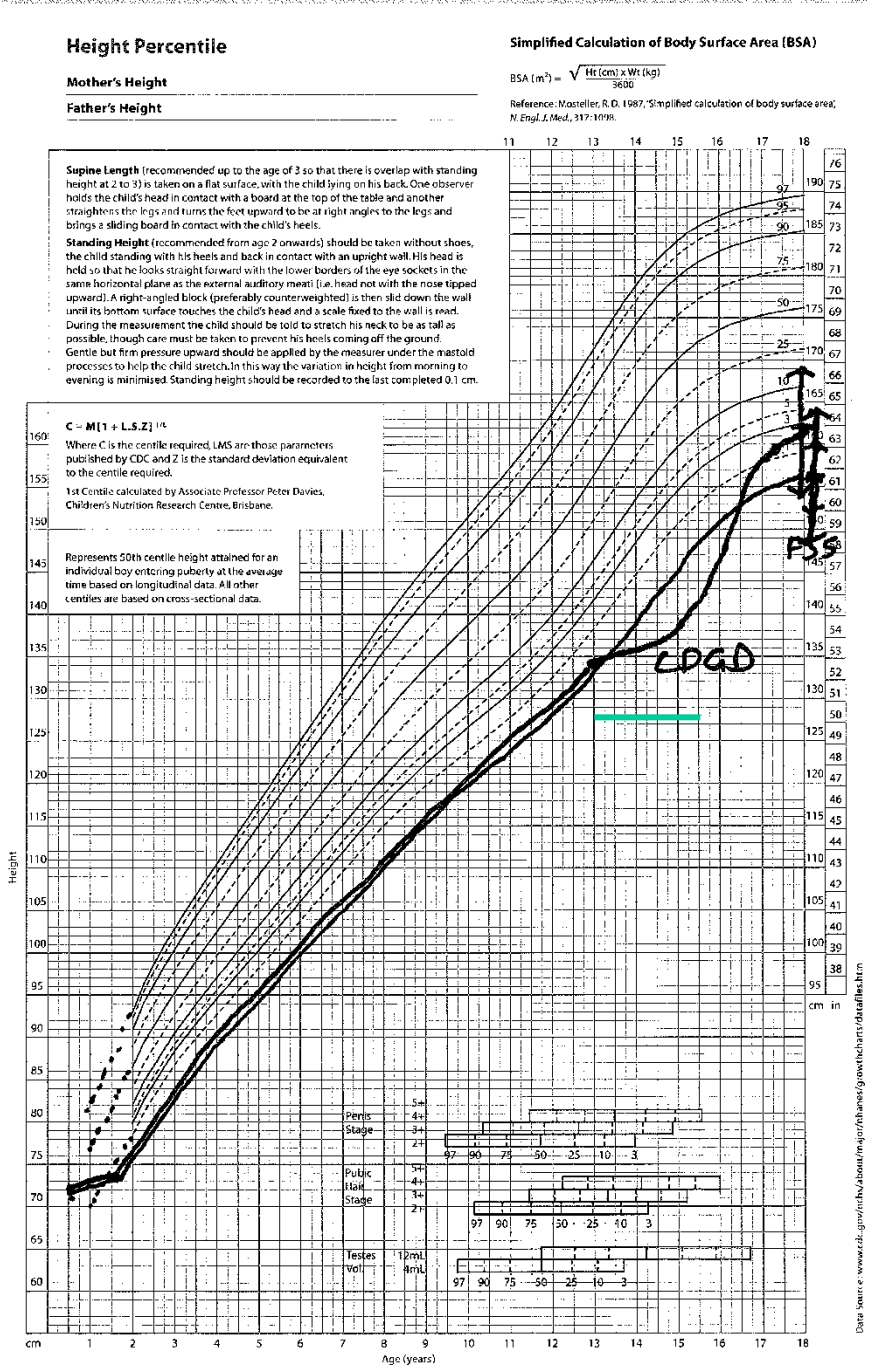
- May benefit from low dose testosterone
- panteston (testosterone undeconate) 40 mg/day x 6 mos
- Will not adversely affect final height and will give some pubertal development and height acceleration

Normal Variant Short Stature

	FSS	CDGD
Birthweight	Normal	Normal
Chronic illness	Absent	Absent
Family history	FSS	CDGD
Infant growth	X centiles	X centiles
Childhood HV	Normal	Normal
Late childhood HV	normal	slow

Normal Variant Short Stature

	FSS	CDGD
Bone Age	<1 yr from CA	>1 yr from CA
Puberty	On time	Delayed
Final Height	Short	Normal



Prepubertal slump

Case 3

A 12 year old girl presents with short stature. She is a keen netballer and is finding it difficult to compete.

Case 3

Recurrent otitis media all through early childhood (grommets)

No maternal pregnancy illnesses/drugs

Birth weight 3,200 gm

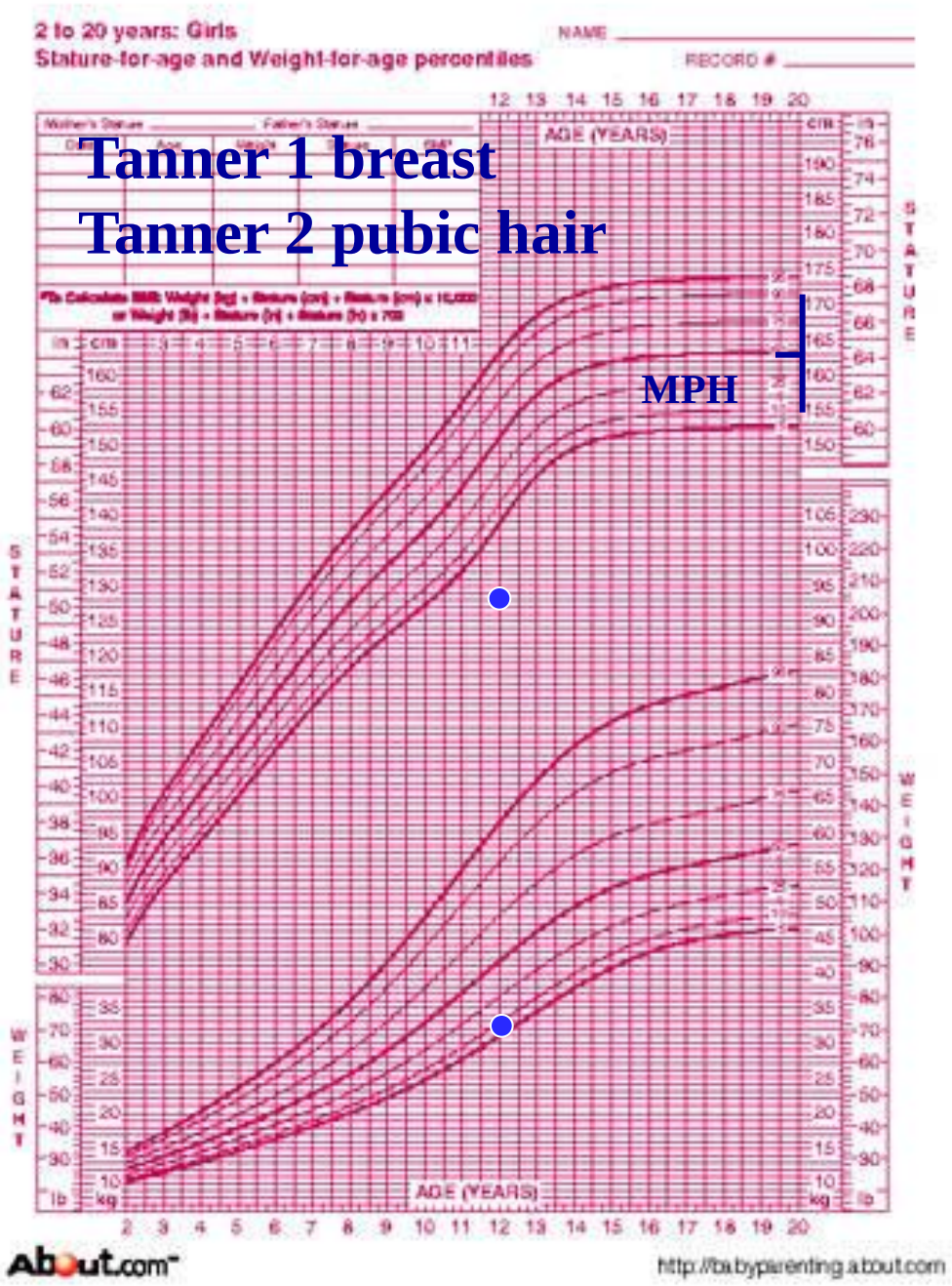
Father 181 cm, early developer

Mother 162 cm, menarche 12 yrs

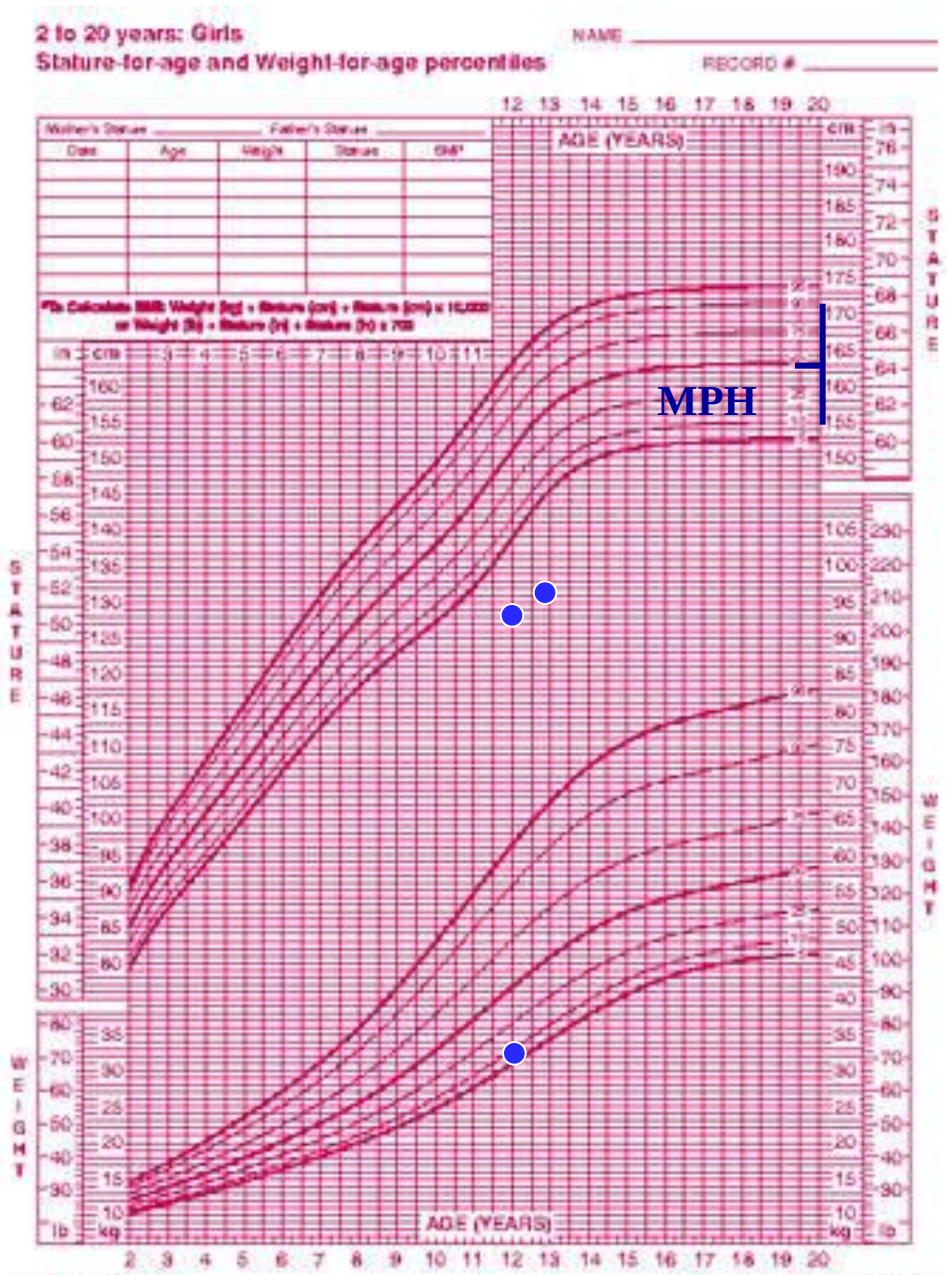
MPH 165 cm (50^{th} percentile)

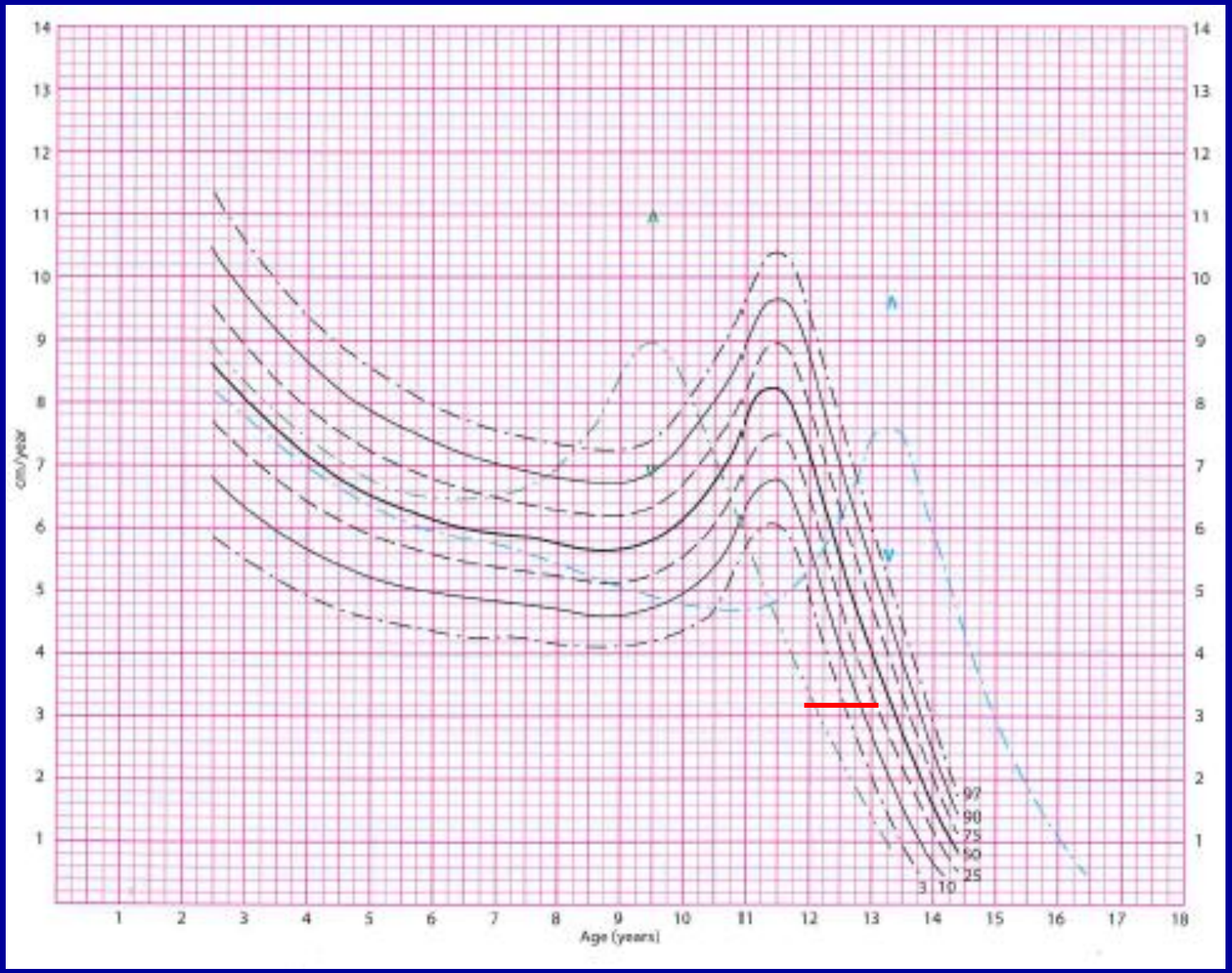
Father bus driver, mother house wife

Oldest of two children (brother 6 yrs old, tall)


2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles
NAME
RECORD #
AGE (YEARS)
STATURE
WEIGHT
Tanner 1 breast
Tanner 2 pubic hair
MPH
About.com
http://babyparenting.about.com

Case 3
Aged 7 yrs


2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles
NAME
RECORD #
Mother's Stature
Father's Stature
Date
Age
Weight
Stature
BMI*
AGE (YEARS)
STATURE
WEIGHT
MPH
About.com
http://babyparenting.about.com


cm/year
Age (years)
97
90
75
50
25
10
3

Case 3

Are further investigations required?

Case 3

Are further investigations required?

Karyotype

TFTs

FBC+ESR

Electrolytes and renal function

Case 3

Are further investigations required?

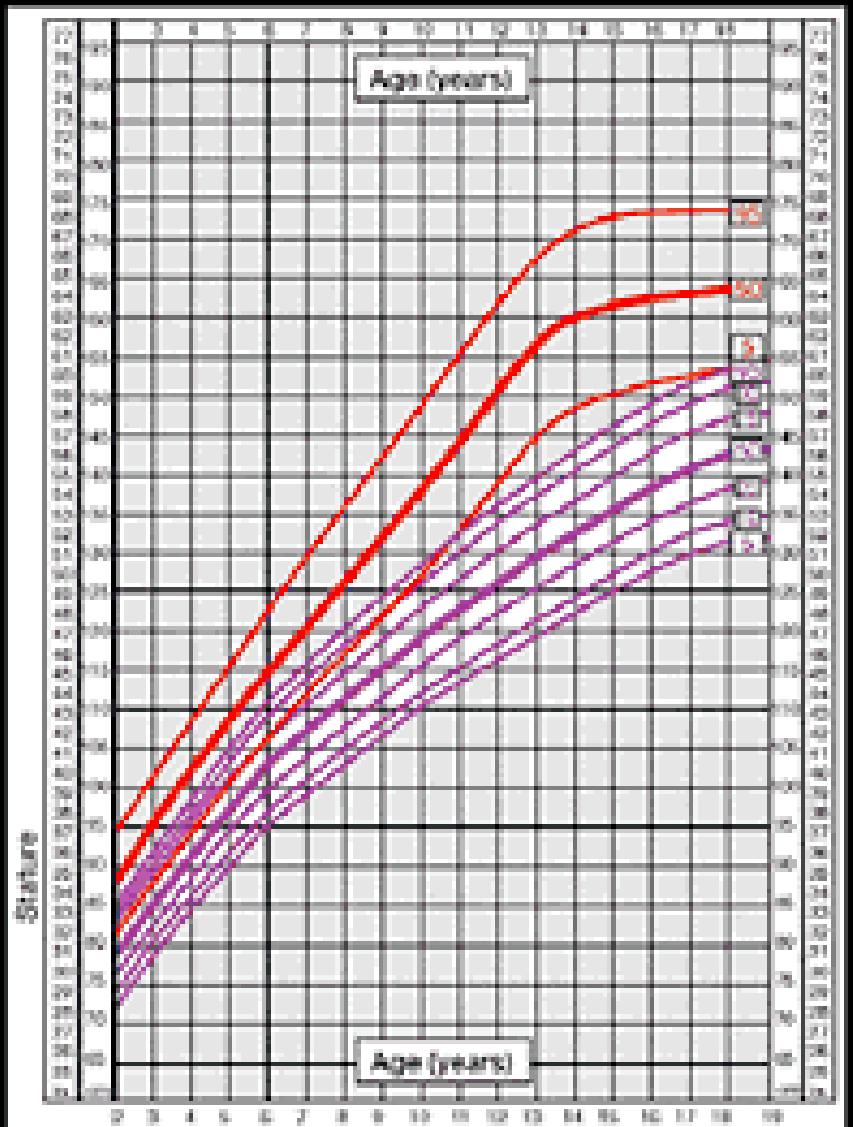
Karyotype: XO

TFTs

FBC+ESR

Electrolytes and renal function

Growth Chart: Girls With Turner Syndrome



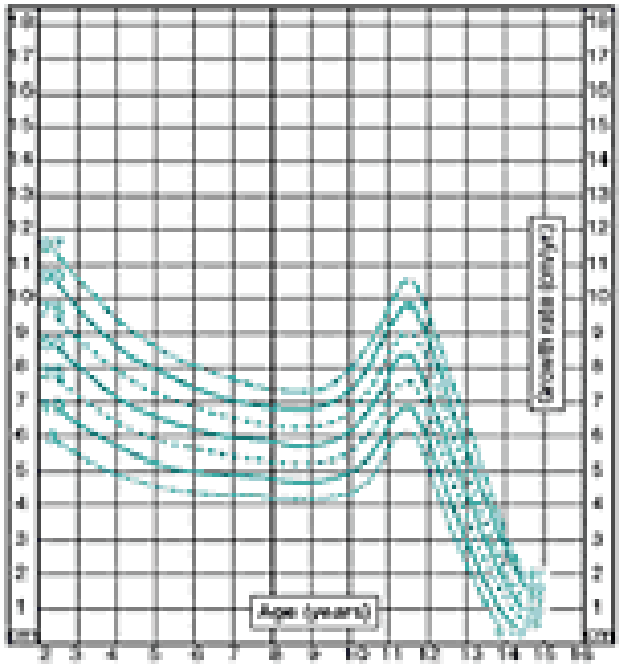
Height Velocity: Normal vs Turner Syndrome

Adolescent growth

- General population average – 13 cm
- Turner syndrome average – 6.5 cm

General population girls

Yearly growth rate

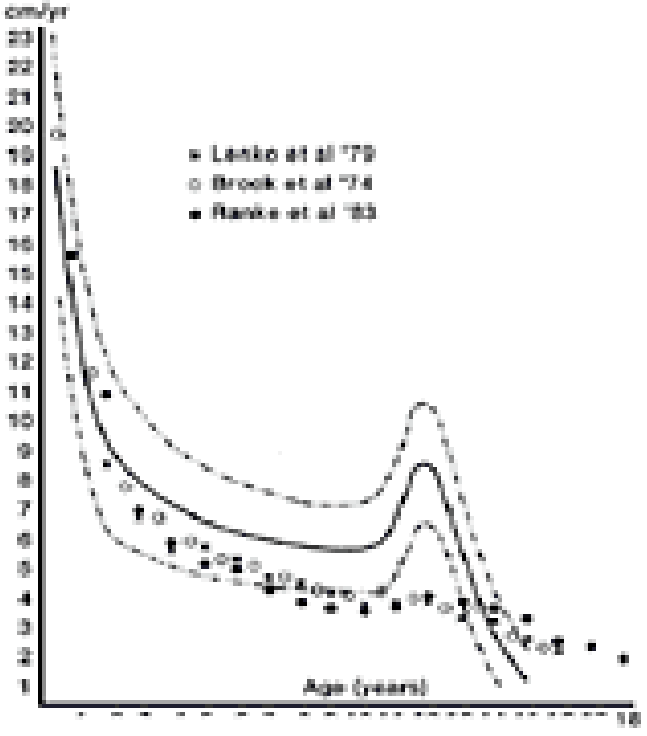


3, 10, 25, 50, 75, 90, 97 percentiles are shown

Redrawn with permission from standard growth chart provided by Castlemead publications.

Turner syndrome

Height velocity



1983;141(2):81-88.

Ranke MB, et al. *Eur J Pediatr.* 1983;141(2):81-88.

Turner Syndrome

Consider in all girls with unexplained short stature or Ht below MPH range.

Commonest feature is short for MPH (100%).

50% will only have short stature as clinical feature.

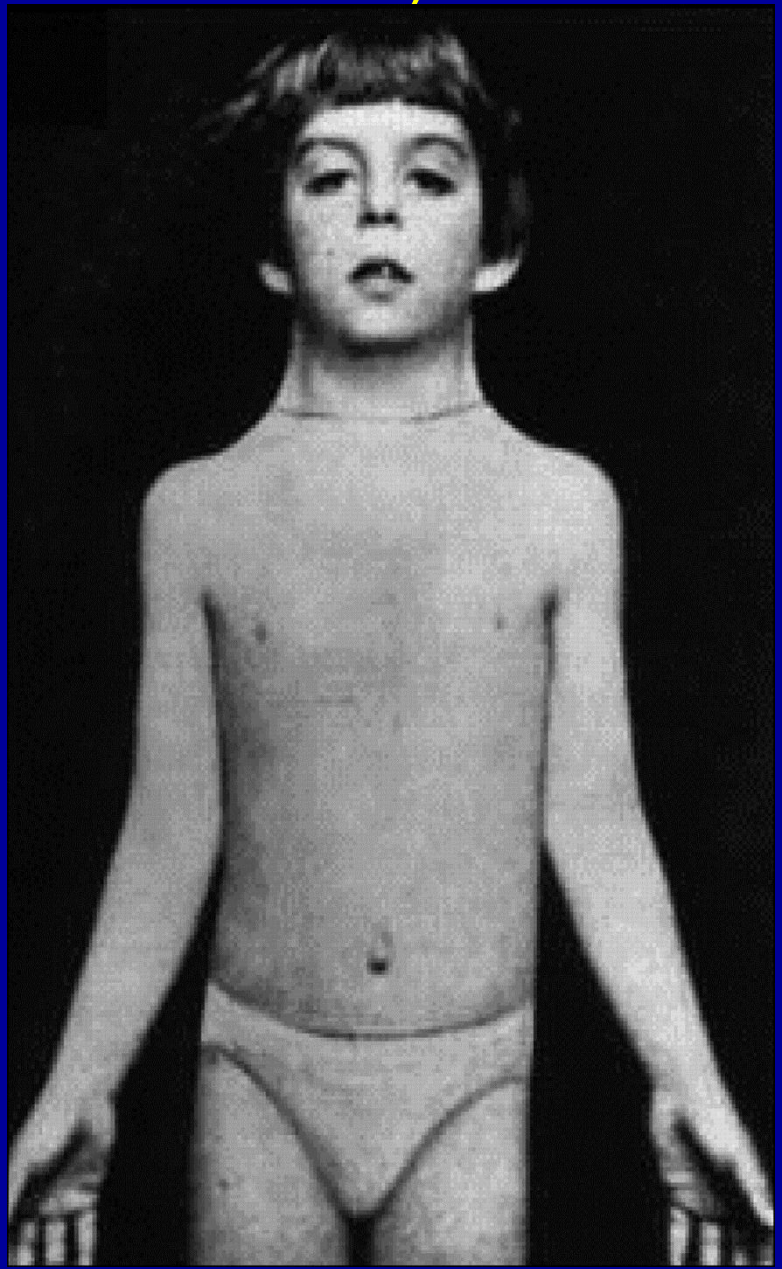
Present with short stature, poor HV or delayed puberty.

Management:

Growth hormone therapy for short stature

E_2 for puberty and beyond

Turner Syndrome



Case 4

An 8 yr old boy presents with short stature.

Completely asymptomatic

No medications, no hospitalisations

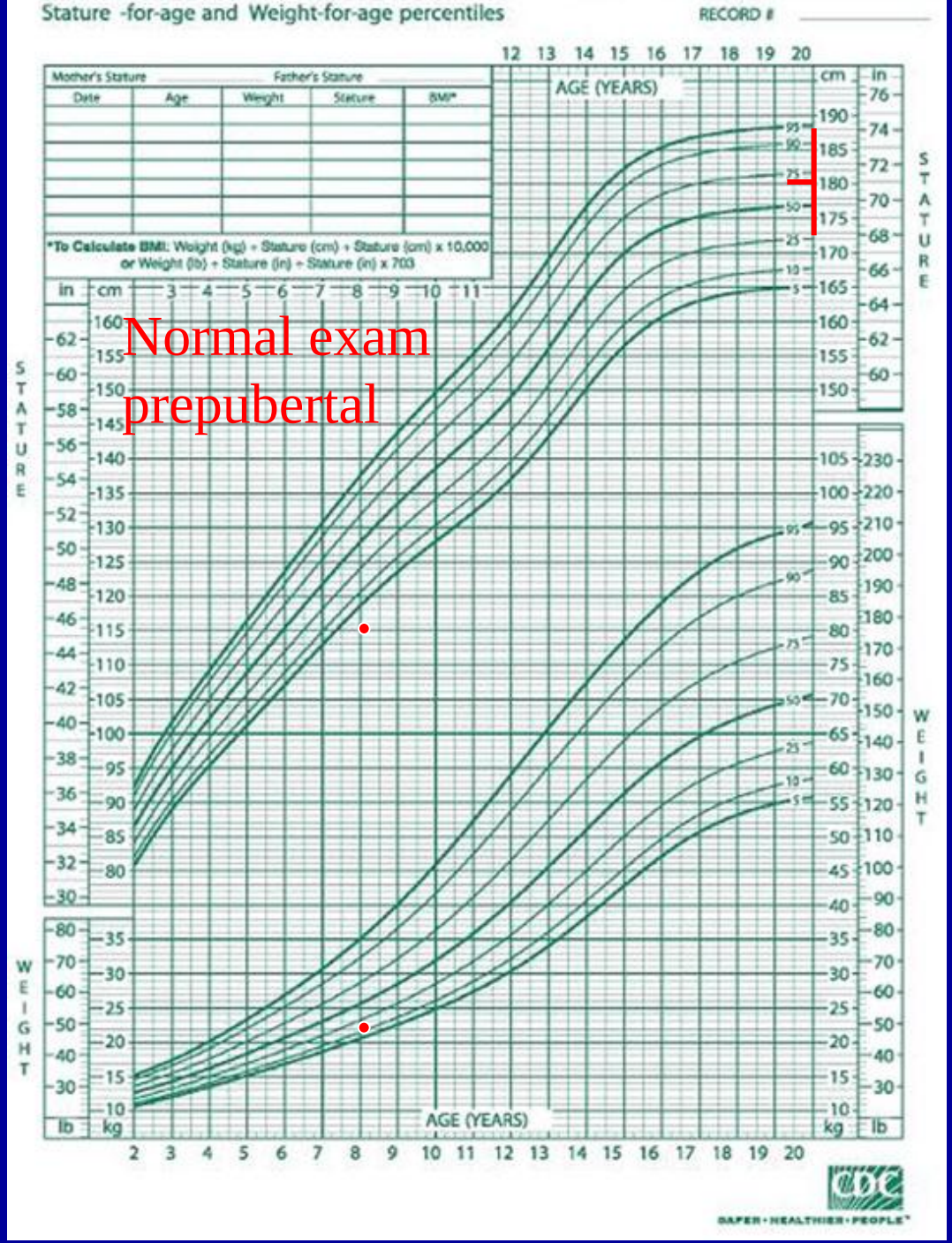
No family history of note

Born at term, 3,400 gm

Father 182 cm, puberty history unknown

Mother 163 cm, menarche 12 yrs

Case 4


Stature -for-age and Weight-for-age percentiles
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
AGE (YEARS)
STATURE
WEIGHT
Normal exam
prepubertal
cm
in
lb
kg
95
90
75
50
25
10
5
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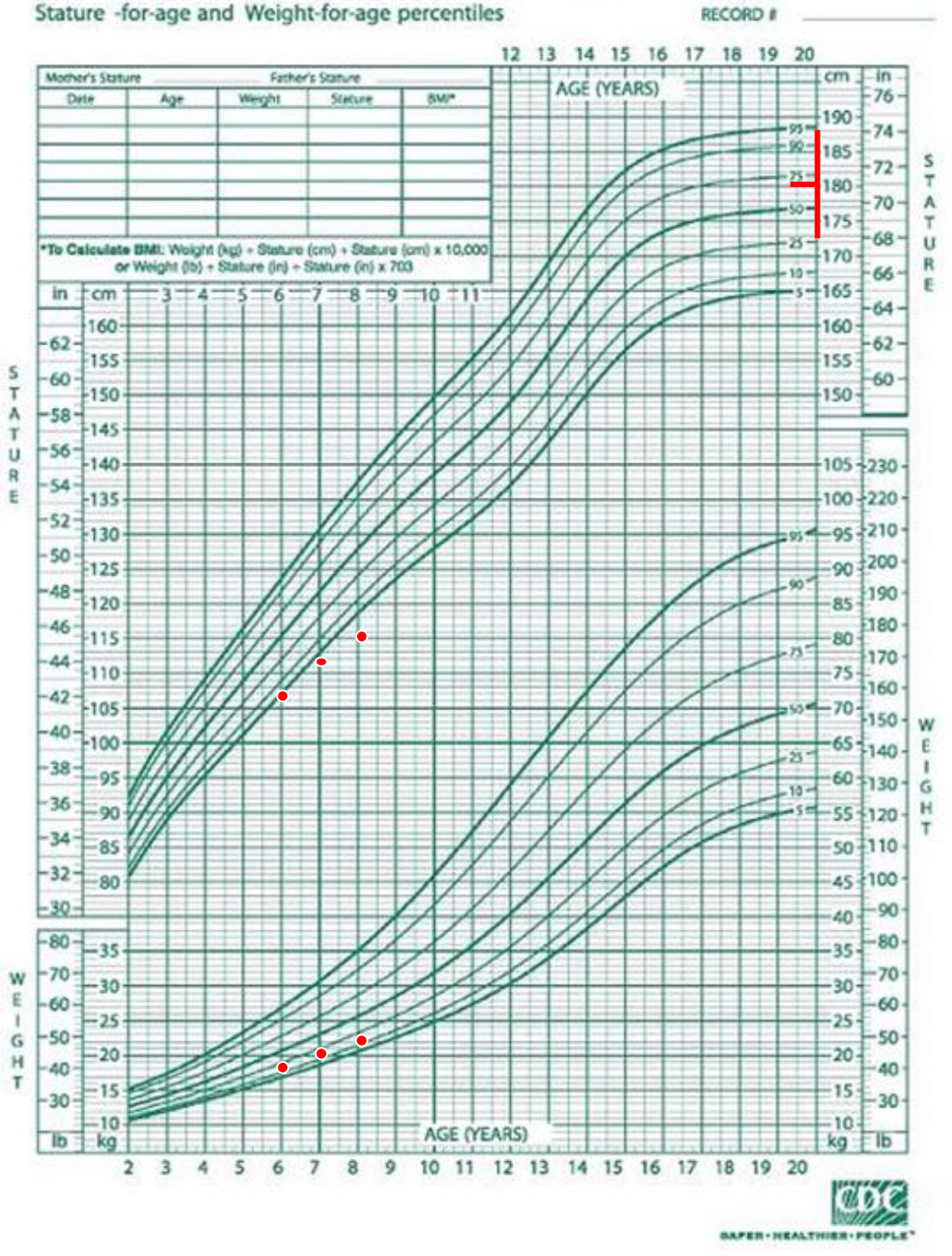
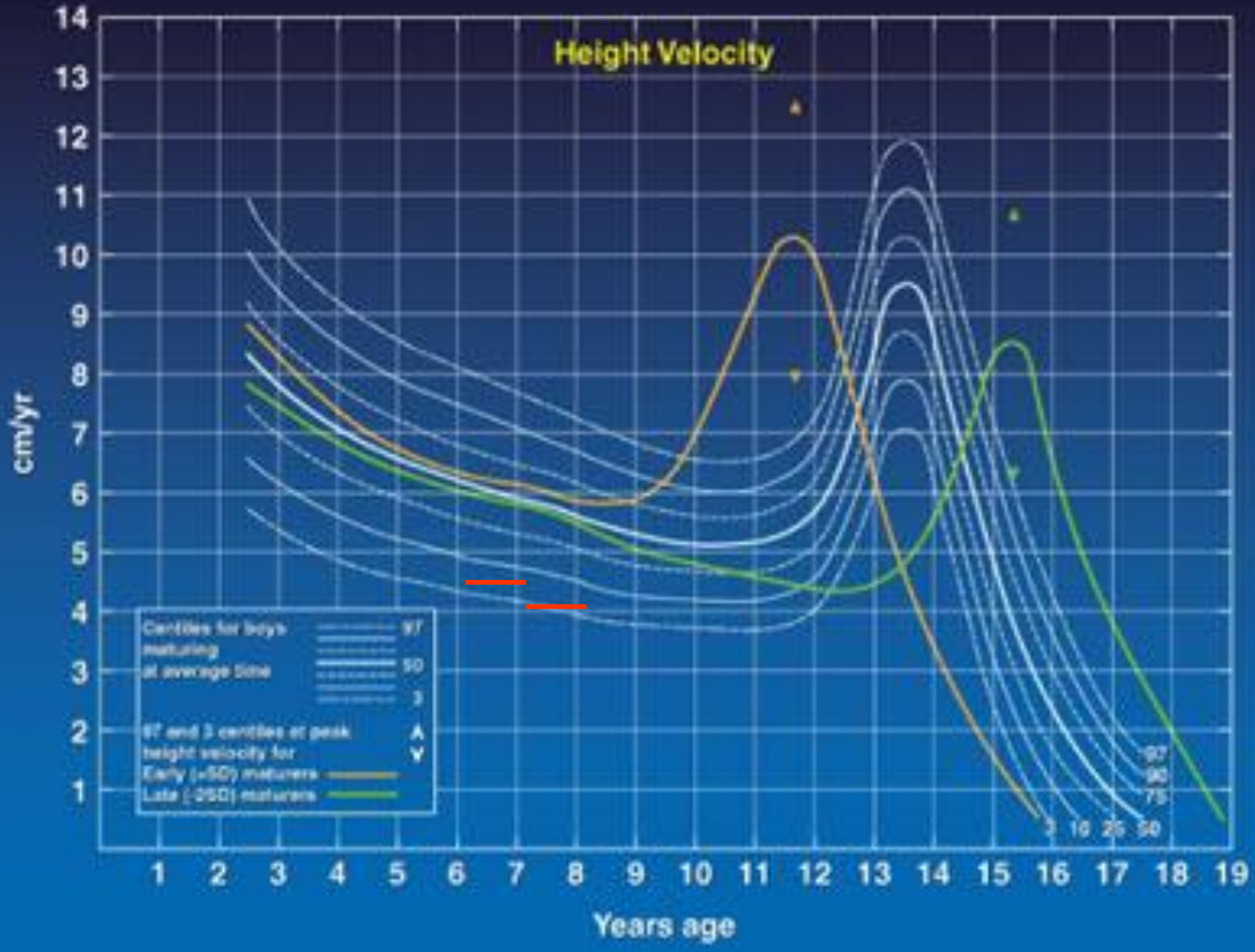
Case 4


Stature -for-age and Weight-for-age percentiles
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
AGE (YEARS)
STATURE
WEIGHT
cm
in
lb
kg
95
90
75
50
25
10
5
CDC
SAFER·HEALTHIER·PEOPLE™


Height Velocity
cm/yr
Years age
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
1 2 3 4 5 6 7 8 9 10 11 12 13 14
97
90
75
50
25
10
3
50
3
A
V

Initial investigations

Hb 125 g/l MCV 62 WBC 6.4 (N differential)

ESR 4

Urea 2.3 mmol/l Na 141 mmol/l K 4.1 mmol/l

Case 4

What is the most likely diagnosis?

Case 4

What is the most likely diagnosis?

Coeliac disease:

(high titres of endomyseal and tissue transglutaminase Abs)

Hypothyroidism

GH deficiency

Chronic renal insufficiency

Coeliac disease (CD)

In young children GI symptoms predominate

Older children often asymptomatic

50% of children with CD asymptomatic

Short stature without GI symptoms 2-8% CD

Csizmadia CGDS et al. Lancet 1999;353:813–14.

Voss LD et al. BMJ 1992;305:1400–2.

Ahmed ML et al. Arch Dis Child 1993;69:361–5.

Coeliac disease (CD)

Microcytosis

Low Haemoglobin

Low serum iron

Delayed bone age

Case 5

A mother is worried that her 8 yr old son is not gaining weight.

He has ADHD treated with concerta 36 mg/day for the past 18 months.

He has a reasonable appetite and is very active

No other interval history

Born at term at 3600 gm

Case 5

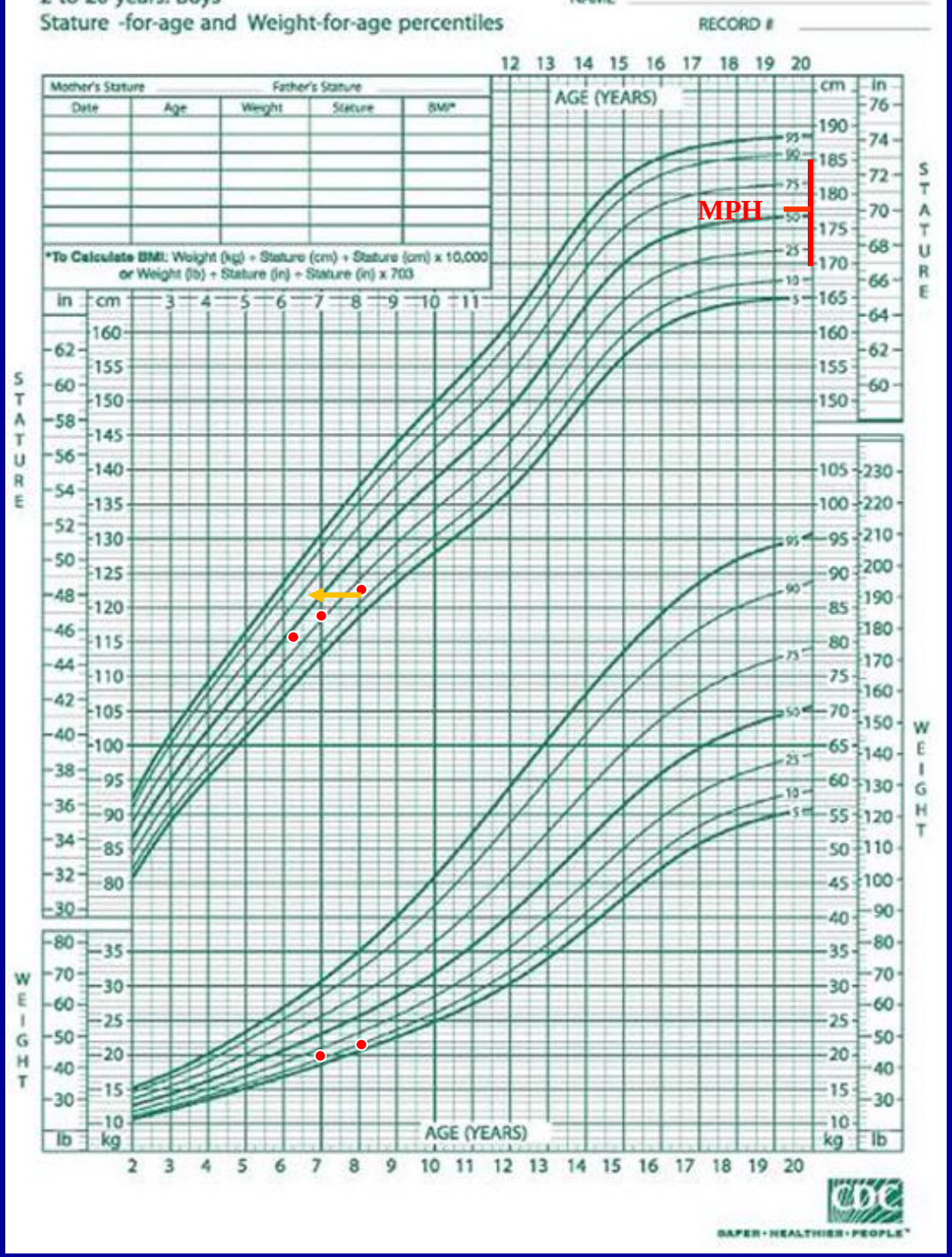
Mother 165 cm, 64 kg

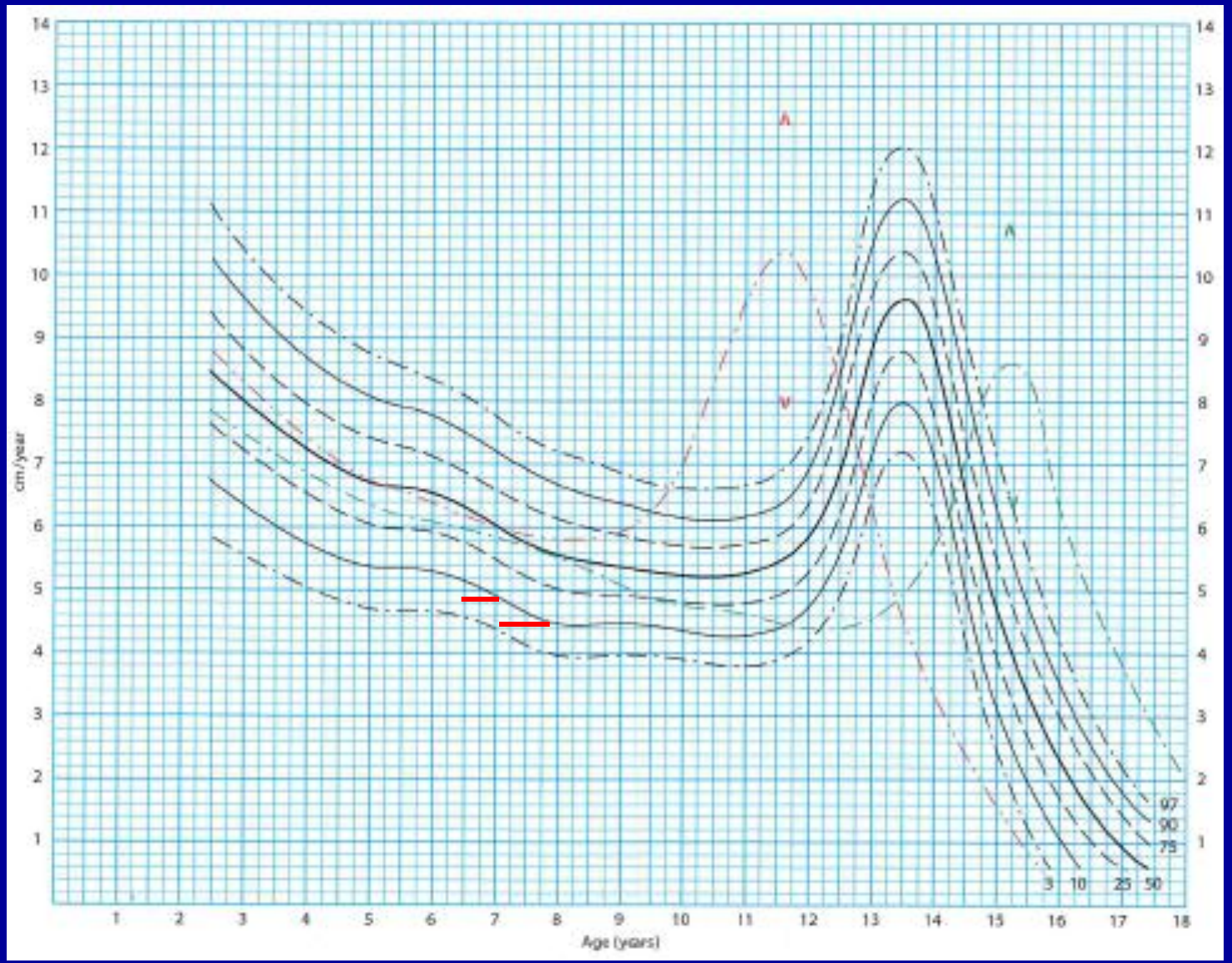
Father 180 cm, 70 kg

MPH 179 cm (50-75th PC)

Older brother who is slim

Case 1


Stature -for-age and Weight-for-age percentiles
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
AGE (YEARS)
STATURE
WEIGHT
MPH
95
90
75
50
25
10
5
cm
in
lb
kg
SAFER · HEALTHIER · PEOPLE™


cm/year
Age (years)
97
90
75
50
25
10
3

Case 5

What are the possible explanations for his poor growth?

Case 5

What are the possible explanations for his poor growth?

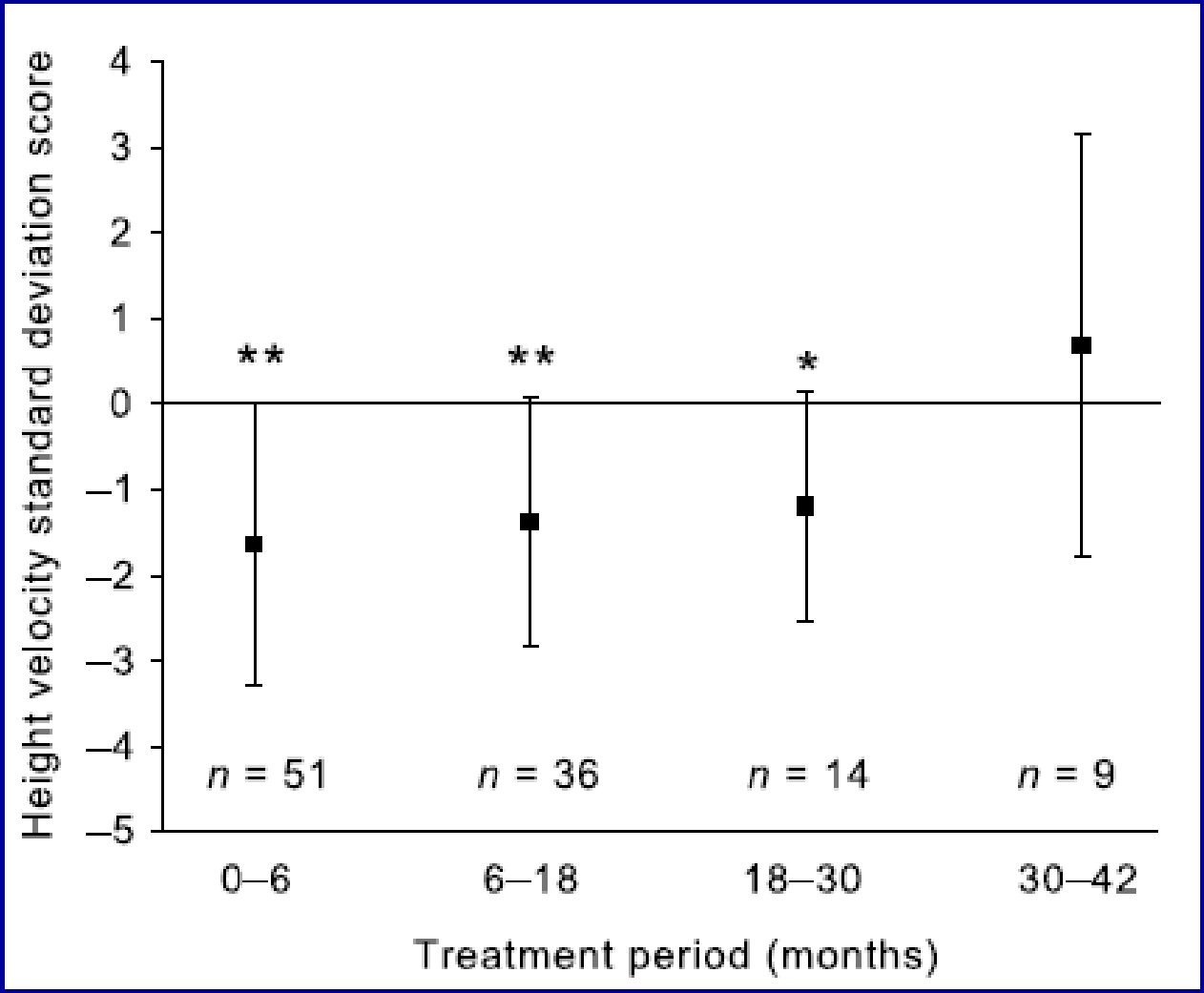
He has a poor height velocity

Pathological short stature, NOT normal variant short stature

Methyl phenidate most likely, hoiwever chronic illness screen should still be done:

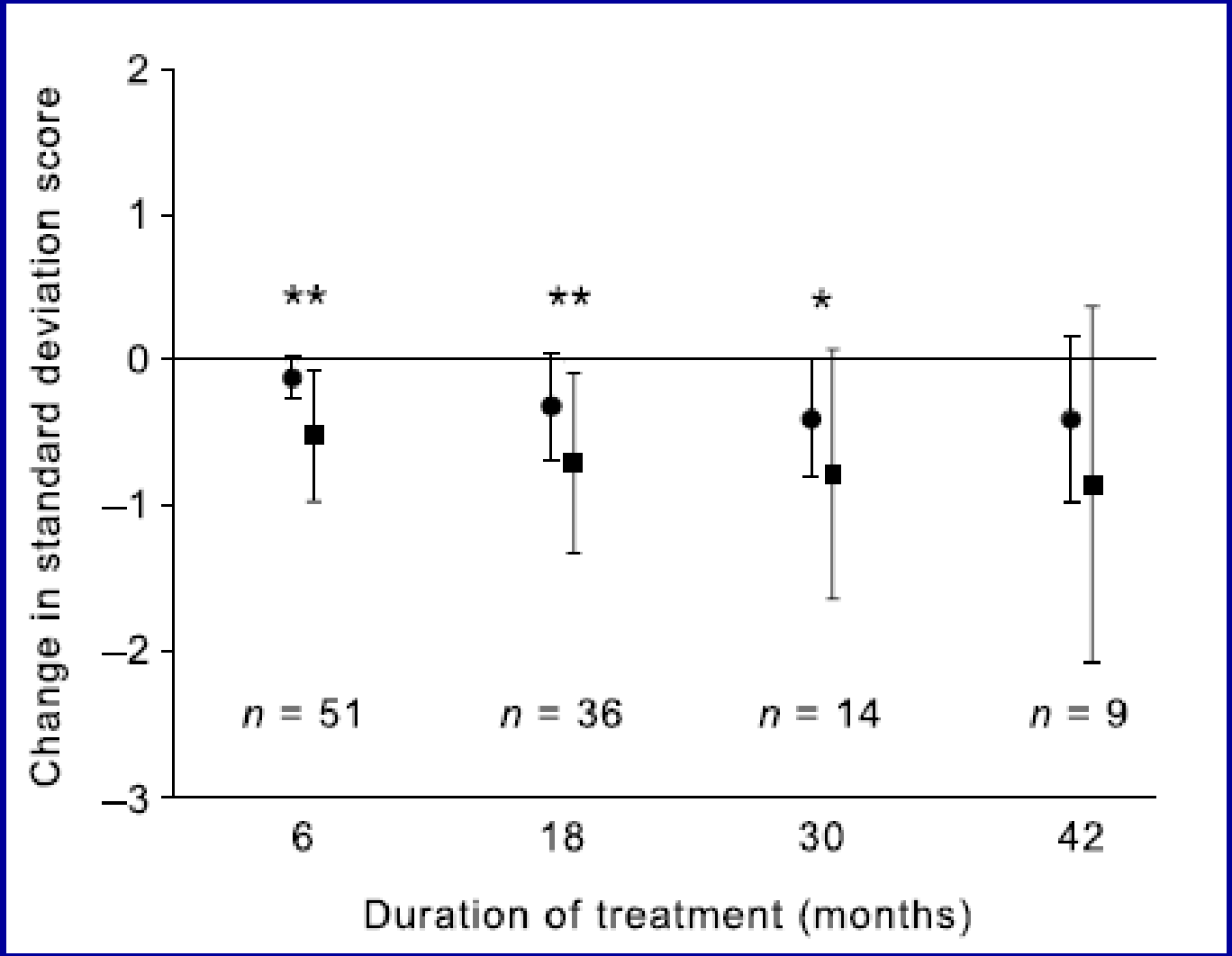
FBC, ESR, Renal function, LFTS, TFTs, urinalysis

Impact of methyl phenidate on childhood growth



Poulton A et al J Paediatr Child Health 2003; 39: 180-5

Impact of methyl phenidate on childhood height and weight gain



Poulton A et al J Paediatr Child Health 2003; 39: 180-5

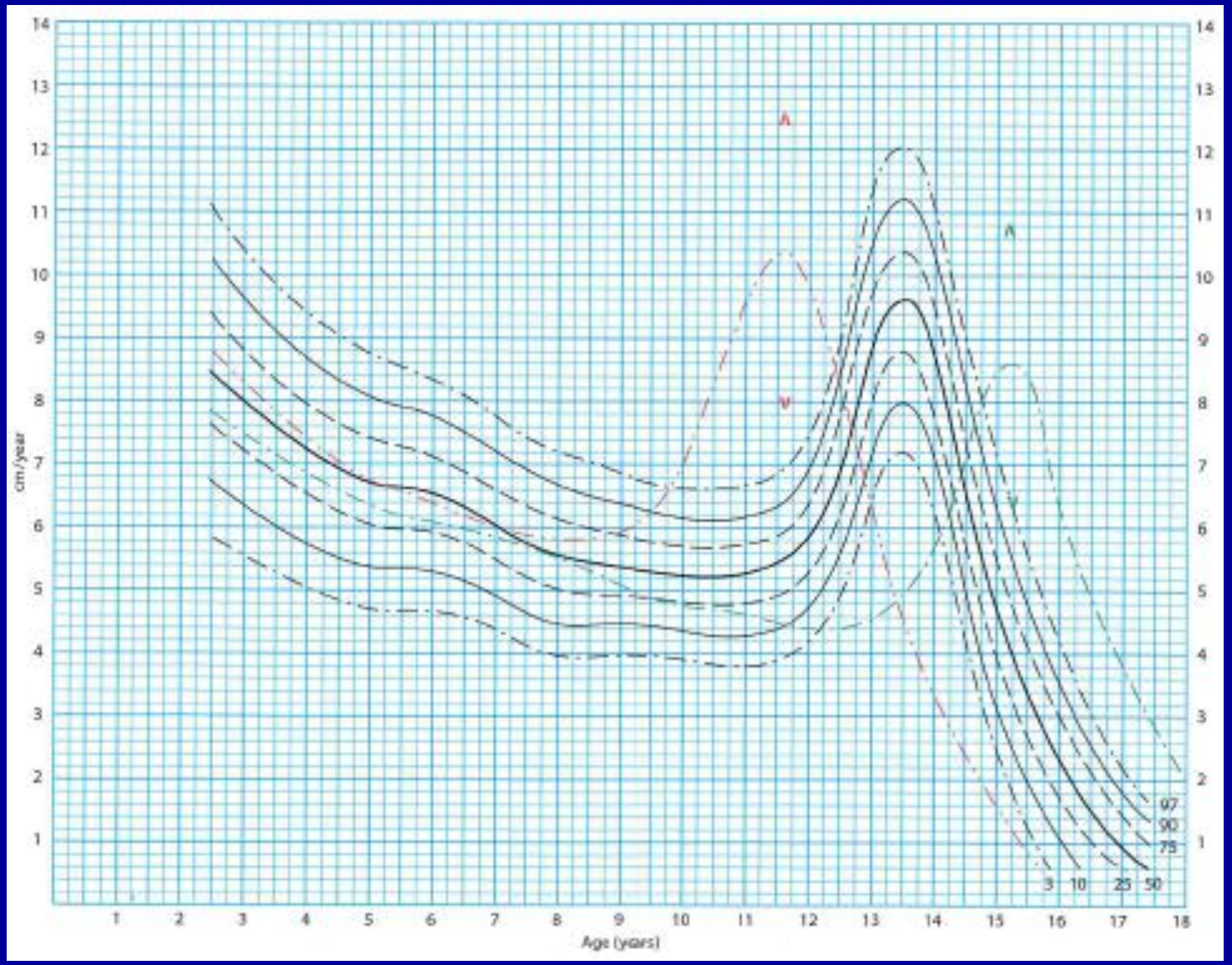
ADHD and stimulants

Poor growth may be a component of ADHD

Normal final height achieved suggesting stimulants (and/or ADHD) slow biological maturity

Not a contraindication to stop stimulants

And that's all!


cm/year
Age (years)
97
90
75
50
25
10
3

Height Percentile

Mother's Height

Father's Height

Simplified Calculation of Body Surface Area (BSA)

$$BSA\ (m^2) = \sqrt{\frac{Ht\ (cm) \times Wt\ (kg)}{3600}}$$

Reference: Mosteller, R.D. 1987, 'Simplified calculation of body surface area', *N. Engl. J. Med.*, 317:1098.

Supine Length (recommended up to the age of 3 so that there is overlap with standing height at 2 to 3) is taken on a flat surface, with the child lying on her back. One observer holds the child's head in contact with a board at the top of the table and another straightens the legs and turns the feet upward to be at right angles to the legs and brings a sliding board in contact with the child's heels.

Standing Height (recommended from age 2 onwards) should be taken without shoes, the child standing with her heels and back in contact with an upright wall. Her head is held so that she looks straight forward with the lower borders of the eye sockets in the same horizontal plane as the external auditory meati (i.e. head not with the nose tipped upward). A right-angled block (preferably counterweighted) is then slid down the wall until its bottom surface touches the child's head and a scale fixed to the wall is read. During the measurement the child should be told to stretch his neck to be as tall as possible, though care must be taken to prevent his heels coming off the ground. Gentle but firm pressure upward should be applied by the measurer under the mastoid processes to help the child stretch. In this way the variation in height from morning to evening is minimised. Standing height should be recorded to the last completed 0.1 cm.

$$C = M(1 + L.S.Z)^{1/L}$$

Where C is the centile required, LMS are those parameters published by CDC and Z is the standard deviation equivalent to the centile required.

1st Centile calculated by Associate Professor Peter Davies, Children's Nutrition Research Centre, Brisbane.

Represents 50th centile height attained for an individual boy entering puberty at the average time based on longitudinal data. All other centiles are based on cross-sectional data.