

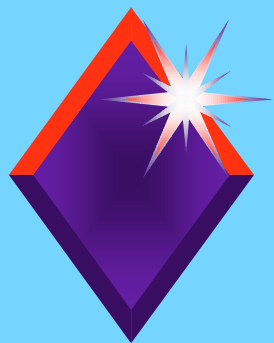
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Abnormalities of Growth & Development

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OBJECTIVES

To understand the

- ◆ determinants of normal growth
- ◆ common variations in normal growth
- ◆ diagnostic approach to a child with abnormal growth
- ◆ principles of management of a child with abnormal growth



OBJECTIVES

Topics **NOT** covered in today's discussion

- ◆ Sexual differentiation
- ◆ Ambiguous genitalia and disorders of sexual differentiation
- ◆ Pubertal development
- ◆ Disorders of pubertal development - delayed / precocious
- ◆ Physiology of hormone secretion / action

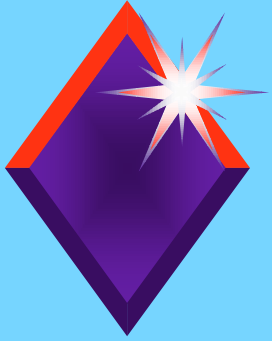


Determinants of Normal Growth

Normal growth is the aggregate of hormonal, environmental, nutritional, and genetic factors

Hormonal Factors

- ◆ Thyroid - essential for normal growth
 - hypothyroidism is a common cause of severe growth delay
- ◆ Sex steroids - bone maturation is dependent on estrogen
 - testosterone can enhance GH secretion
- ◆ Glucocorticoids - potent inhibitor of growth



GH/IGF-1 Axis

Image of GH/IGF-1 Axis removed



Determinants of Normal Growth

Hormone	Growth Rate cms/yr	Adult Height
Sex Steroids ↑	Increase	Diminished
Sex Steroids ↓	Normal	Increased
Thyroxine ↑	Normal/± incr	Normal
Thyroxine ↓	Decreased	Diminished
GH ↑	Increase	Increased
GH ↓	Decrease	Diminished
Cortisol ↑	Decrease	Diminished
Cortisol ↓	Normal	Normal



Normal Growth

Anthropometric parameters

- ◆ Weight
- ◆ Measurement of height - Stadiometer
 - less than 2yrs of age - length (supine)
 - greater than 2 yrs of age - height (erect)
- ◆ Head circumference
- ◆ Span
- ◆ Upper segment / lower segment ratio



Normal Growth

Anthropometric
parameters

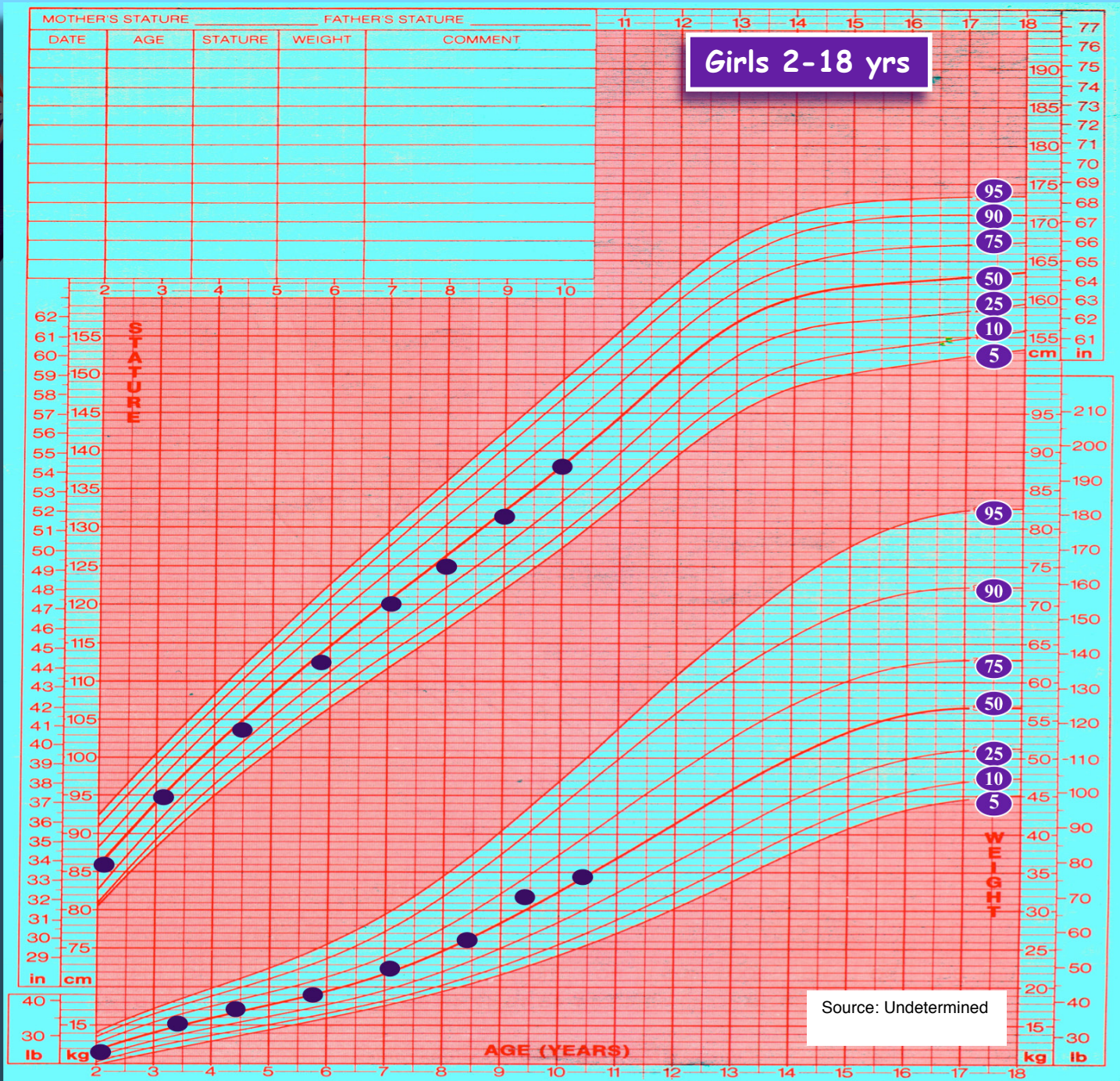
Upper / Lower Segment Ratio

Lower segment : symphysis pubis to floor

Upper segment : Ht (-) lower segment

Image of fetal and
post-natal growth
chart removed

2m	5m	Birth	2yr	6yr	12yr	25yr
Fetal		Post-natal				





Normal Growth

Growth Velocity

- ◇ measured in cms/yr
- ◇ should be measured over at least a 6-12 month period
- ◇ more the # of height points used to calculate GV -
more reliable is the interpretation
- ◇ assessment of pubertal status is critical
for interpretation of GV
- ◇ Normal GV - is a strong argument **AGAINST** a
significant hormonal abnormality

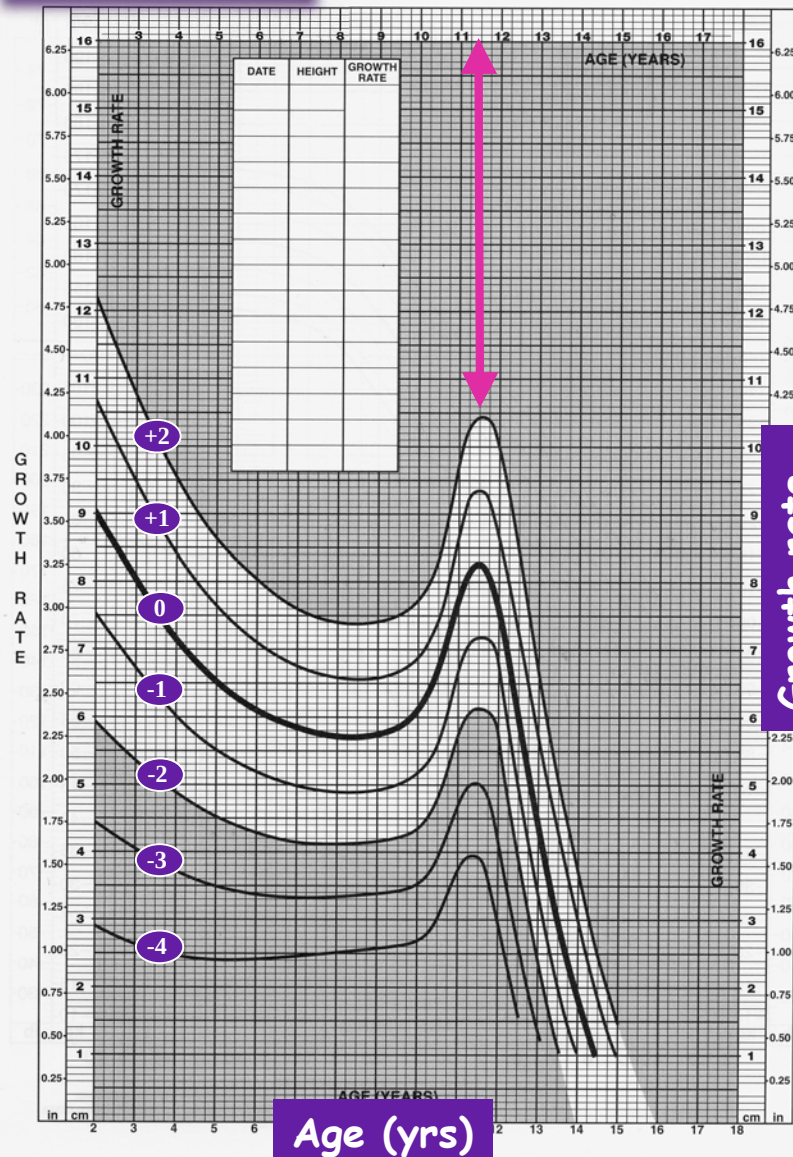
Girls 2-18 yrs

ons

NAME _____

RECORD #

DATE OF BIRTH



**Growth rate
(cms/yr)**

This plot is for the average maturing child. For early and late maturers, see J.M. Tanner, et al., *J. Pediatr.* 107:317-329, 1985 and J.M. Tanner, et al., *Arch. Child.* 41:613-635, 1966.

Source: JM Tanner, et al.

Source: JM Tanner, et al.



Normal Growth

- ◇ Chronological age
- ◇ Dental age
- ◇ Bone Age (skeletal maturation)

beyond the neonatal age - X-ray of L wrist

comparison with published standards (Greulich & Pyle)

Usefulness - prediction of final height

- age of onset of puberty closely linked to bone age
- corroborates diagnosis, but is never diagnostic

Caveats - imprecise / ethnic variability



SHORT STATURE

- ◆ Definition
- ◆ Classification
- ◆ Etiology
- ◆ Evaluation / Diagnostic Approach
- ◆ Treatment



SHORT STATURE

Definitions

- ◆ Short Stature
height < 3rd percentile
- ◆ Growth Retardation
growth velocity < 3rd percentile



SHORT STATURE

Definitions

- ❖ Short Stature
height < 3rd percentile
- ❖ Growth Retardation
growth velocity < 3rd percentile

Etiology

Normal Variant



Pathological



SHORT STATURE

Normal Variant

Familial / Genetic

final ht appropriate for parental ht
normal size at birth

GV may be $\downarrow$ in 0-3 yrs of age

BA = CA

Constitutional Delay of Growth & Puberty "Late Bloomer"

family history
normal size at birth
normal GV

delayed puberty

BA < CA

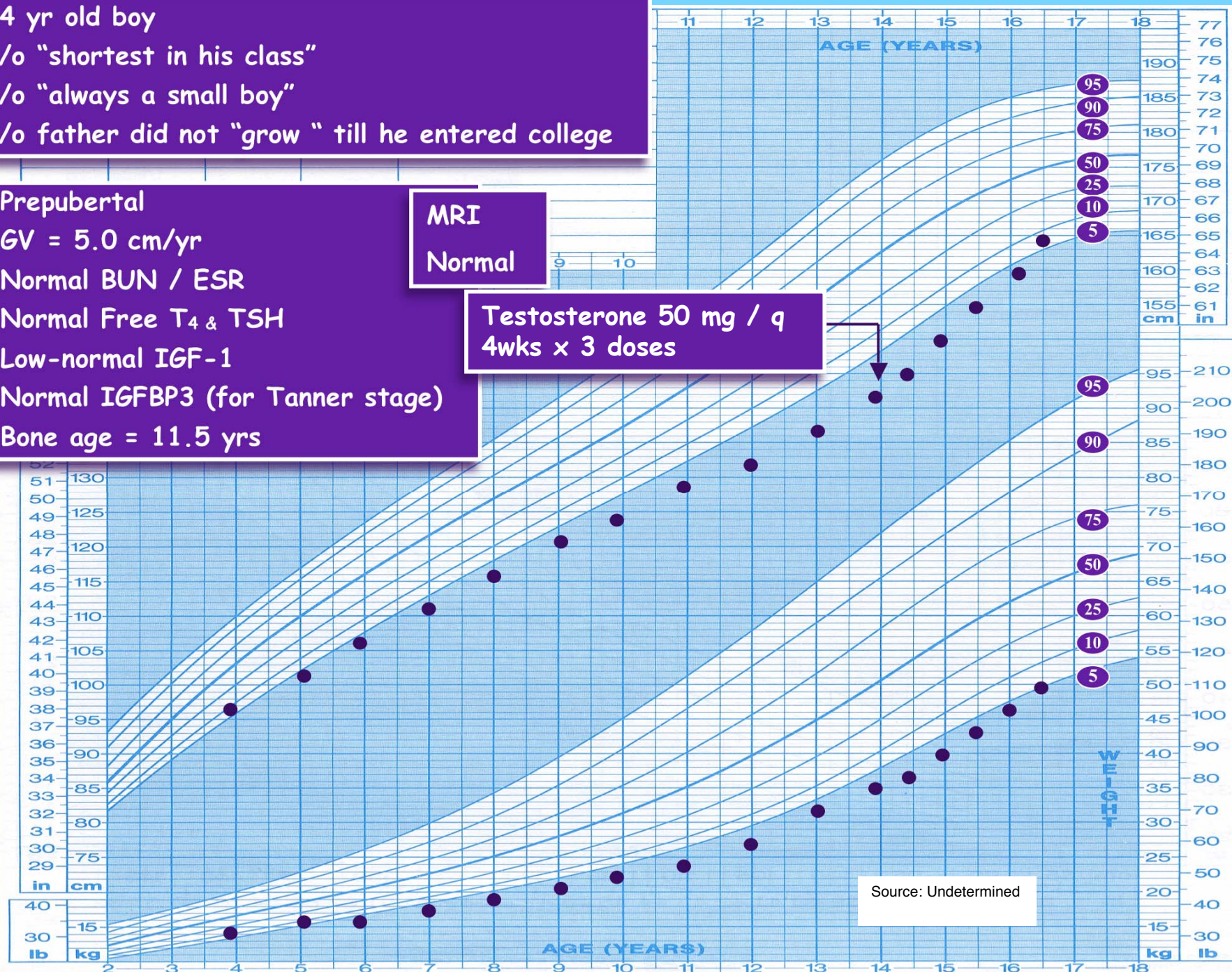
BA = bone age
CA = chronological age

14 yr old boy
 h/o "shortest in his class"
 h/o "always a small boy"
 h/o father did not "grow " till he entered college

Prepubertal
 GV = 5.0 cm/yr
 Normal BUN / ESR
 Normal Free T₄ & TSH
 Low-normal IGF-1
 Normal IGFBP3 (for Tanner stage)
 Bone age = 11.5 yrs

MRI
 Normal

Testosterone 50 mg / q
 4wks x 3 doses



Source: Undetermined



SHORT STATURE

Definitions

- ❖ Short Stature
height < 3rd percentile
- ❖ Growth Retardation
growth velocity < 3rd percentile

Etiology

Normal Variant



Pathological

Proportionate

Disproportionate



SHORT STATURE

Pathological
Proportionate

Endocrinopathies

Hypothyroidism
GH deficiency
Cushing's syndrome

GI

Malabsorption
Inflammatory bowel disease
Celiac disease

Renal

Chronic renal failure
Renal tubular acidosis

Chronic Systemic Illness

Cardiac
Pulmonary
Liver
Infection

IUGR

Malnutrition

Psychosocial Dwarfism
Emotional Deprivation Syndrome

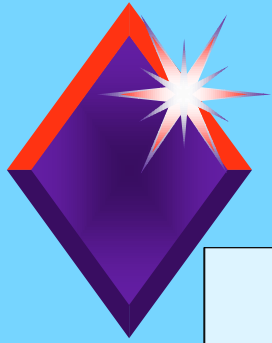


Image of one year
old boy removed

Ht age = 1 yr old

Image of one year
old boy removed

4 yr old boy

Voracious appetite / drinks urine - toilet bowl

Withdrawn / flat affect

No dysmorphic features

Chaotic home situation - abusive father

All lab tests normal

4 yr old boy

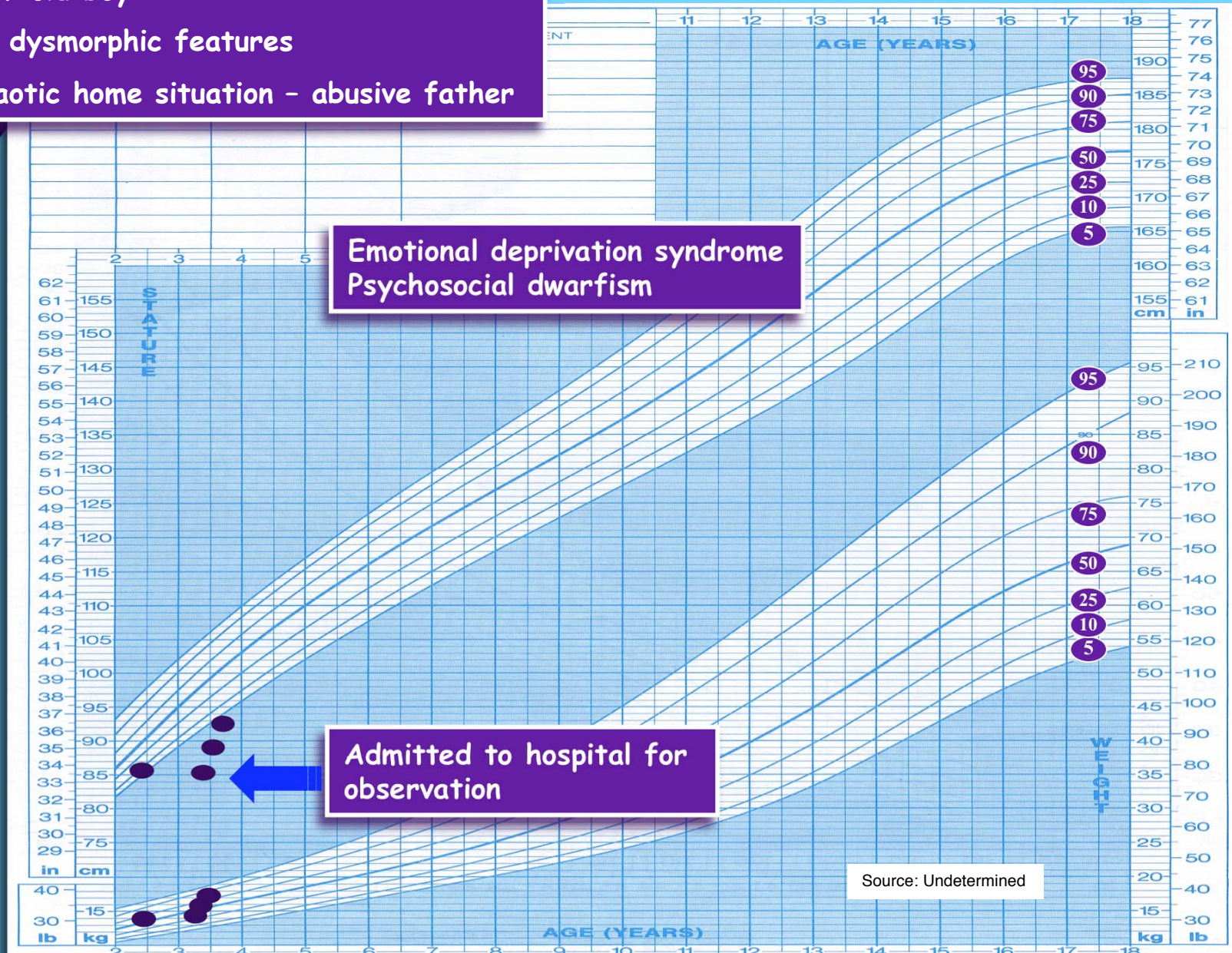
No dysmorphic features

Chaotic home situation - abusive father

Emotional deprivation syndrome
Psychosocial dwarfism

Admitted to hospital for
observation

Source: Undetermined



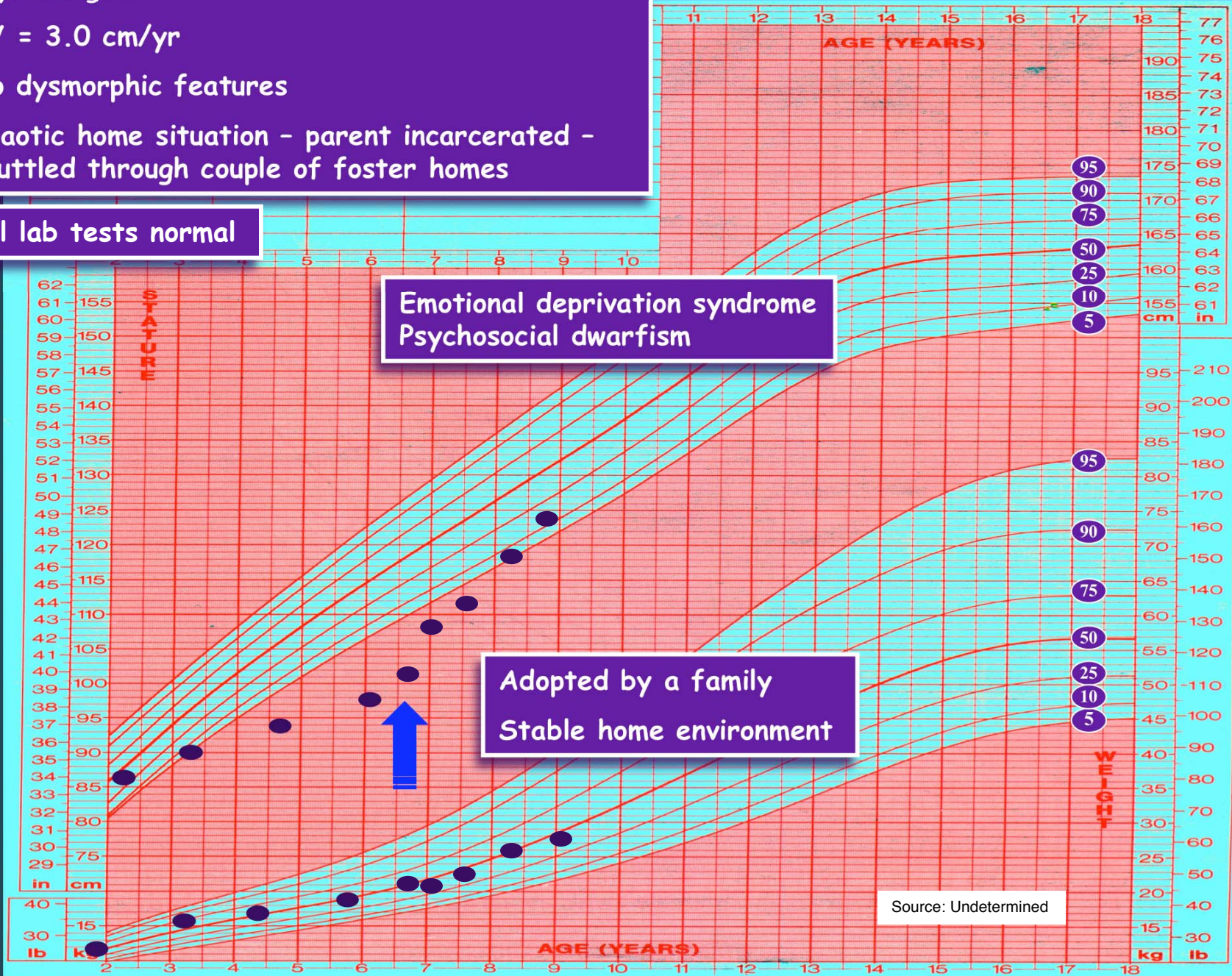
6 yr old girl

GV = 3.0 cm/yr

No dysmorphic features

Chaotic home situation - parent incarcerated -
shuttled through couple of foster homes

All lab tests normal





SHORT STATURE

Pathological
Disproportionate

Skeletal Abnormalities

Dysplasia
Achondroplasia
Rickets
Vertebral anomalies

Dysmorphic Syndromes

Turner

Down
Russell-Silver
Prader-Willi
Pseudo-hypoparathyroidism



SHORT STATURE

Evaluation
Clinical History

Prenatal maternal infection, alcohol

Pattern of growth birth wt and length

Family History
Nutrition onset of puberty

Systemic Disease

Drugs steroids

Neurological headache, vision,
enuresis

Psychosocial



SHORT STATURE

Evaluation
Physical Exam

Anthropometric ht, wt, head circ., arm span, U/L ratio

Nutritional state

Tanner Staging for Pubertal Development

First sign of puberty on PE:

♀ breast dev / ♂ incr in testicular volume

Dysmorphic Features

Neurological exam

Thyroid Gland



SHORT STATURE

Evaluation
Diagnostic Approach

Target Height (in cms)

$$\text{girl} = \frac{[\text{father's ht} + \text{mother's ht}] - 13}{2}$$

$$\text{boy} = \frac{[\text{father's ht} + \text{mother's ht}] + 13}{2}$$

normal range is ± 8 cms



SHORT STATURE

Evaluation
Diagnostic Approach

Key Parameter - Growth Velocity

Normal GV

Familial
Constitutional

Impaired GV

Malnutrition
Chronic systemic illness
IUGR
Psychosocial
Chromosomal abnormalities
Endocrine
Malabsorption
Bone dysplasias



SHORT STATURE

Evaluation
Laboratory Tests

Screening Tests

CBC, ESR, BUN
FT₄, TSH
IGF-1, IGFBP3
Tissue Transglutaminase ab

KARYOTYPE

- ◆ in girls to exclude TURNER
- ◆ dysmorphic features

RADIOLOGICAL

- ◆ bone age
- ◆ skeletal survey



SHORT STATURE

Growth Hormone Deficiency
(GHD)



SHORT STATURE

GH Deficiency (GHD)
Signs & Symptoms

- ◆ Neonatal - normal size / hypoglycemia / jaundice / micropenis / midline defect
- ◆ Decreased growth velocity
- ◆ Delayed dentition / mid-facial hypoplasia
- ◆ Increase in adiposity



SHORT STATURE

GH Deficiency (GHD) Causes

- ◆ Tumor - craniopharyngioma
- ◆ Trauma - surgery / irradiation
- ◆ Idiopathic
- ◆ Congenital Aplasia / Hypoplasia / Septic-optic dysplasia
- ◆ Genetic Defects -
 - Isolated Growth Hormone Deficiency (IGHD)
 - PROP1 / POU1F1 (*Pit1*)



SHORT STATURE

GH Deficiency Diagnosis

Criteria for diagnosing GH deficiency

Clinical (NOT laboratory) diagnosis

- ◊ $GV < 2\ SD$
- ◊ Low IGF-1 & IGFBP-3
- ◊ Provocative GH Level $< 7-10\ ng/ml$

Corroborative evidence

- ◊ Delayed BA
- ◊ Related pathology



SHORT STATURE

GH Deficiency Diagnosis

Measurement of GH

- ◆ Spontaneous pulsatility of GH
precludes random measurement
- ◆ Provocative test after overnight fast
 - Insulin induced hypoglycemia is the "Gold standard"

IGF-1 / IGFBP3

- ◆ Altered by nutritional status
- ◆ Normal range related to age & pubertal status



SHORT STATURE

Treatment Indications for GH Therapy

- ◆ Growth hormone deficiency
- ◆ Turner syndrome
- ◆ Renal disease, before transplant
- ◆ Small for gestational age
- ◆ Prader-Willi syndrome
- ◆ Idiopathic short stature



SHORT STATURE

Treatment
GH Replacement Therapy

s/c injection
7days/wk

Side Effects

- ◆ Secondary/tertiary hypothyroidism
- ◆ Worsening of scoliosis
- ◆ Slipped capital femoral epiphysis
- ◆ Pseudotumor cerebri

Monitor

GV, Free T₄, IGF-1, IGFBP3

8½ yr old girl

h/o poor growth x 12-18 months

recent h/o vague headaches

school performance has recently deteriorated

recent episodes of enuresis

Prepubertal

GV = 1.5 cm/yr

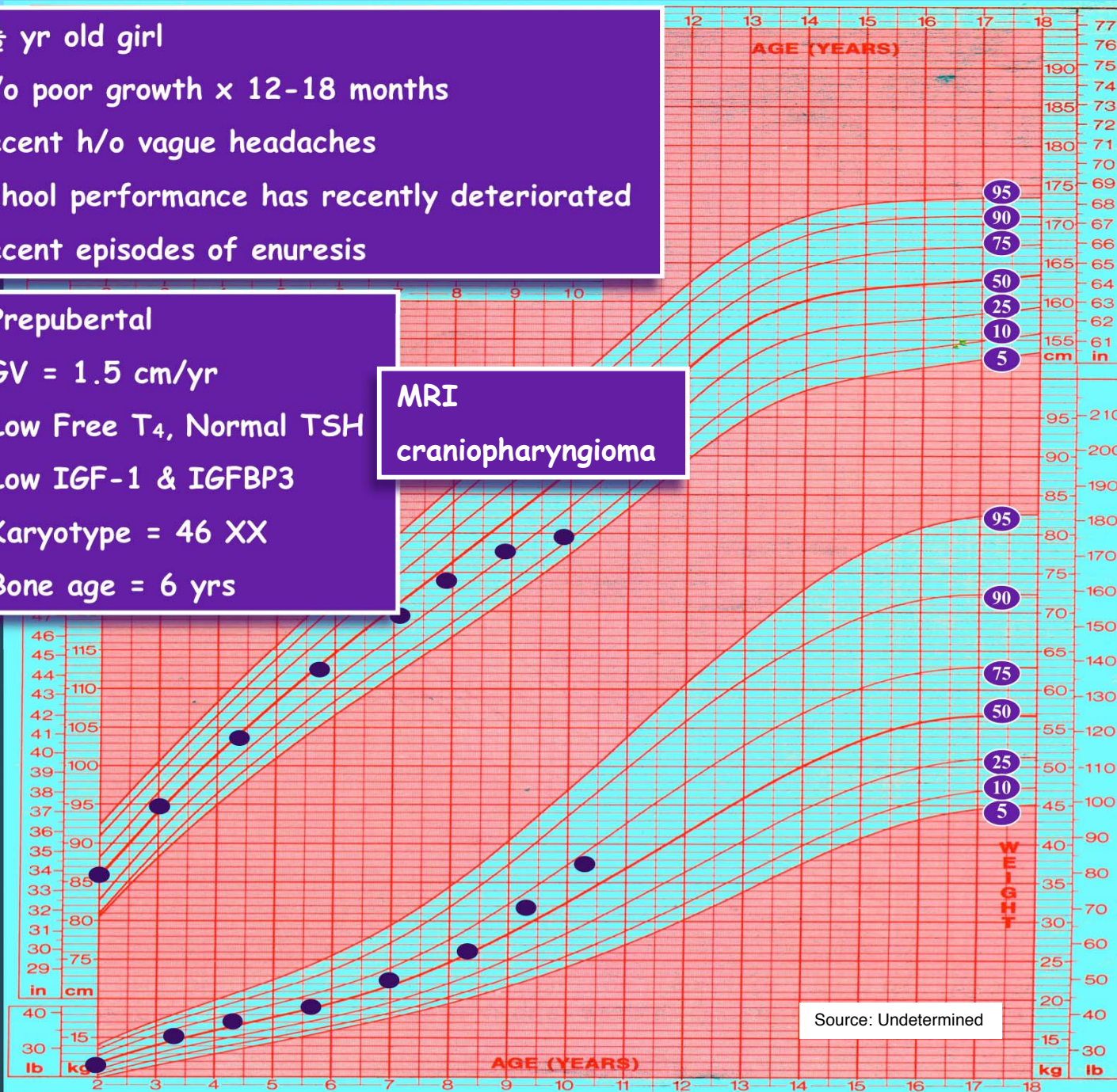
Low Free T₄, Normal TSH

Low IGF-1 & IGFBP3

Karyotype = 46 XX

Bone age = 6 yrs

MRI
craniopharyngioma



Source: Undetermined

8½ yr old girl

h/o poor growth x 12-18 months

h/o vague abdominal discomfort

Prepubertal

GV = 2.5 cm/yr

Normal Free T₄ & TSH

Low IGF-1

Normal IGFBP3

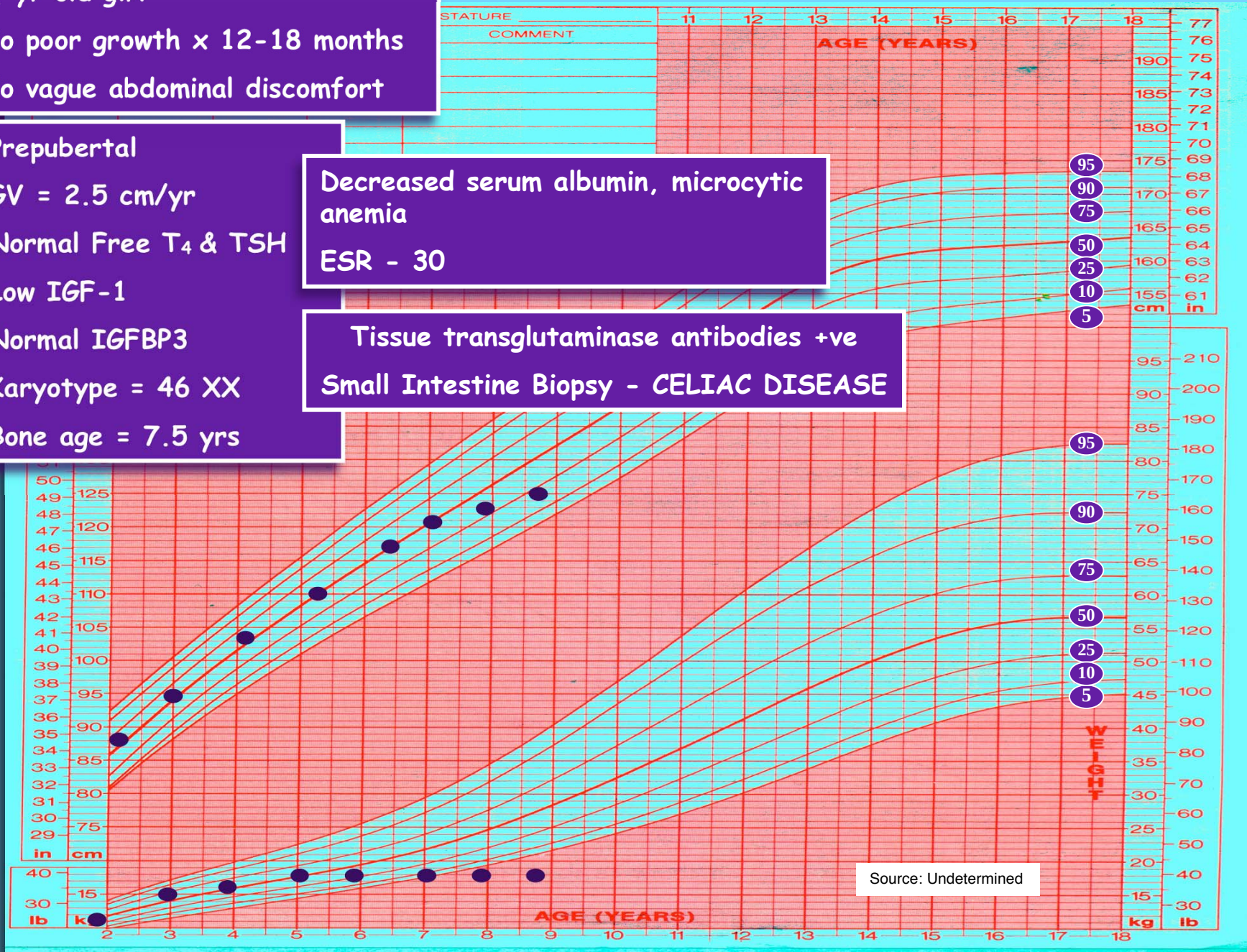
Karyotype = 46 XX

Bone age = 7.5 yrs

Decreased serum albumin, microcytic anemia

ESR - 30

Tissue transglutaminase antibodies +ve
Small Intestine Biopsy - CELIAC DISEASE



5 yr old girl

GV = 3.0 cm/yr

subtle dysmorphic features - clinodactyly,
webbing of neck $\pm$, $\uparrow$ carrying angle

GV = 3.0 cm/yr

Normal Free T₄ & TSH

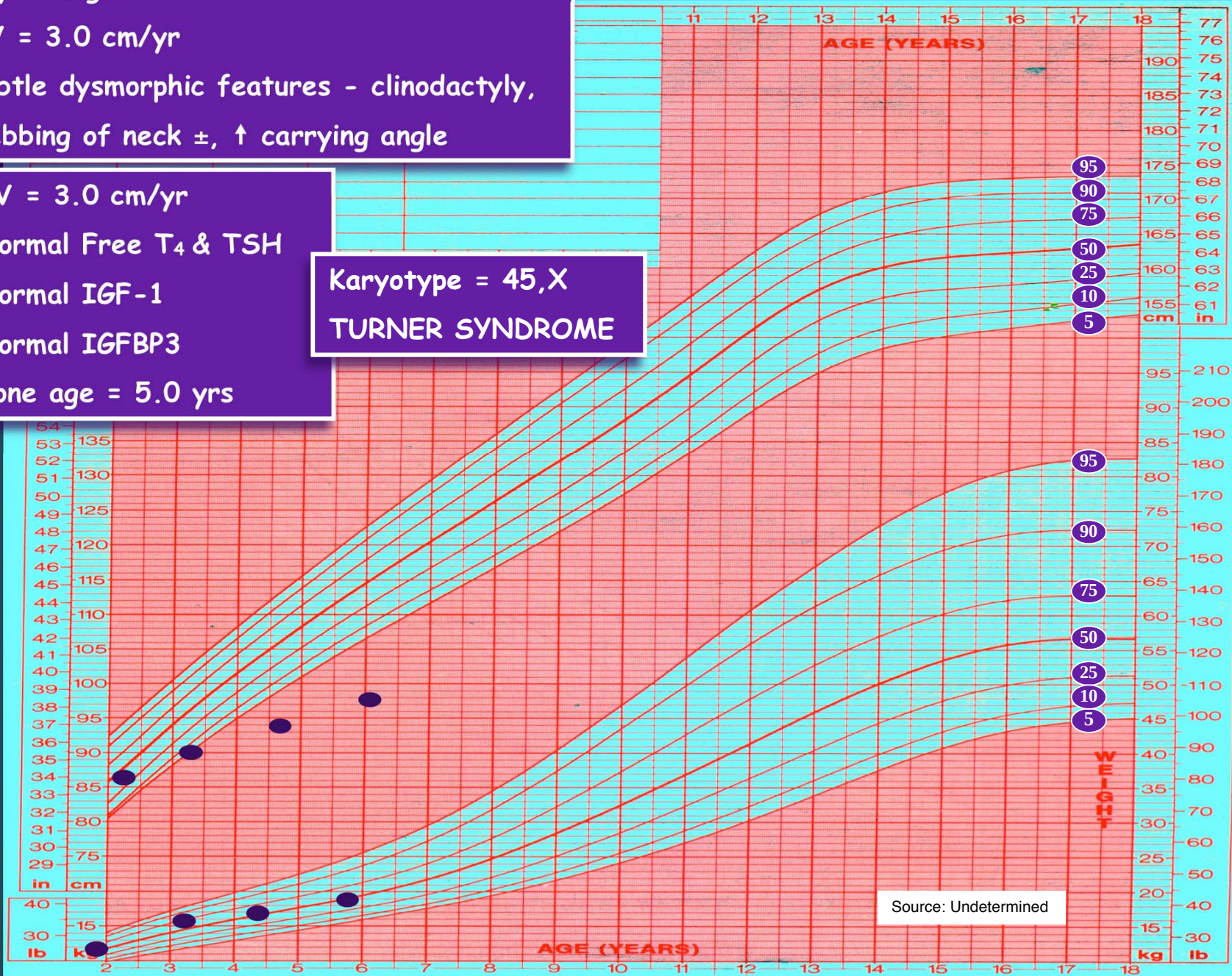
Normal IGF-1

Normal IGFBP3

Bone age = 5.0 yrs

Karyotype = 45,X

TURNER SYNDROME





Turner Syndrome



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[BY: Johannes Nielsen, et al.](#)



Turner Syndrome

- ❖ Described in 1938 by Dr. Henry Turner
- ❖ Most common sex chromosomal abnormality in females -- X chromosome
- ❖ Frequency 1:1500 to 1:2500 in live born infant girls
- ❖ 15% of spontaneous abortions = TS



Turner Syndrome

Karyotype 45, X

Image of Turner
Syndrome
Karyotype
removed



Turner Syndrome

Clinical Features - Postnatal

- | | |
|--------------------------------|---------|
| ❖ Growth Failure | 80-100% |
| ❖ Gonadal Dysgenesis | 80-100% |
| ❖ Inverted/ widespaced nipples | 60% |
| ❖ Nail dysplasia | 60-80% |
| ❖ High narrow palate | 60-80% |
| ❖ <u>Cardiac malformation</u> | 40-60% |
| ❖ <u>Renal dysplasia</u> | 40-60% |
| ❖ Low hairline/webbing | 30-40% |
| ❖ Pigmented nevi | common |



Turner Syndrome



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[BY: Johannes Nielsen, et al.](#)



Turner Syndrome



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Lymphedema

- ❖ Lymphedema at birth is highly correlated with 45,X karyotype and congenital heart abn



If you slept through this lecture...the 4 points to remember

- ◆ Growth velocity (and NOT height)
is the key anthropometric parameter
- ◆ Normal growth velocity virtually
excludes a pathological cause for short stature
- ◆ Always exclude Turner's synd in a girl with short stature
- ◆ Diagnosis of a child with growth problems is made
more on CLINICAL and less on laboratory criteria