Growth & Obesity

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25TH May 2010

Factors affecting longitudinal growth:

• Nutrition
  • affected by general health, hormone balance (leptin/insulin/gut hormones etc)
• General Health
• Normal skeleton
• GH/IGF1 axis
• Insulin
• Sex steroids
• Adrenal function
• Thyroid status

Infant growth – predominantly nutritionally driven
Childhood growth – predominantly GH/IGF axis dependent
Considerable overlap...
Pubertal growth – androgen/oestrogen dependent

Measuring...

• <2 – supine table with 2 measurers
• >2 – stadiometer – mastoid elevation
• Proportions – arm span to height (=1)
  • Upper:Lower segments
    – 1.7 as a neonate
    – 1.4 by 4-5 years
    – 1.0 by 10-12 years

Importance of monitoring...

Specific charts for Turner’s, Down’s syndrome and achondroplasia
Other charts that have recently become available
BMI
Waist circumference
Recently published body fat reference charts

Guide to Accurate Measurement
IGF System

Mid-parental height

- Boys: \((\text{Mother's height} + 10) + \text{Father's height}) / 2\)
- Girls: \((\text{Mother's height} + 10) + \text{Father's height}) / 2\)
- Target height range: 10 for boys, 9 for girls

Height Velocity

- Measurement of rate of growth
- Inaccurate if interval of less than one year
- Difference in height (cm) / interval (y)

Short stature

Genetic Short Stature

- Determine parental target height
- Growth velocity
- Not an absolute diagnosis
  - If the parents are short and the child is short then may be due to the inheritance of a genetically transmitted disorder
  - Eg endocrine causes (pseudohypoparathyroidism, thyroid problems), osteochondrodysplasias, renal disease, blood disorders such as thalassaemias etc
- Cause may not yet be discovered – GH/IGF Axis abnormalities
CDGP
• Exclusion of other causes of SS along with late maturation
• FH delayed puberty is often present
• Parental anxiety/Distress to child should not be underestimated

Pathological Growth Failure
• ENDOCRINE
• P sychosocial
• I atrogenic
• C hromosomal
• N utritional
• I ntrauterine
• C hronic Disease
• S keletal

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Endocrine
a. Hypothyroidism
b. Cushing Syndrome
c. Pseudohypoparathyroidism
d. Rickets
e. IGF deficiency
   a. GH deficiency due to hypothalamic dysfunction
   b. GH deficiency due to pituitary GH deficiency
   c. GH insensitivity (Primary or Secondary)
   d. Primary defects in IGF synthesis
   e. Primary defects in IGF transport/clearance
   f. IGF resistance
      a. Defects of the IGF-1 receptor
      b. Post-receptor defects

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Pathological Growth Failure

- ENDOCRINE
- P sychosocial
- I atrogenic - Steroids/Radiotherapy
- C hromosomal
- N utritional
- I ntrauterine
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Pathological Growth Failure

- ENDOCRINE
- P sychosocial
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Turner Syndrome

- XO or mosaic
- Gonadal dysgenesis
- Hypogonadism
- Short stature
- Female genitalia
- Pubertal failure
- Increased carrying angle
- Web neck

Pathological Growth Failure

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Pathological Growth Failure

- ENDOCRINE
- P sychosocial
- I atrogenic - Steroids/DXRT
- C hromosomal - Turner
- N utritional
- I ntrauterine
- C hronic Disease eg. Diabetes, CF, Asthma
- S keletal
Pathological Growth Failure

- ENDOCRINE
- Psychosocial
- Iatrogenic
- Chromosomal
- Nutritional
- Intrauterine
- Chronic Disease
- Skeletal

Osteochondrodysplasias
Over 100 conditions
Achondroplasia is the commonest AD but 90% are new mutations
FGFR mutation
Achondroplasia growth curves available

Baseline investigations

- Clinical judgement – not every Ix is needed!!
  - May be just a Bone Age

- Clinical features suggesting Ix’s may be warranted;
  - Extreme short stature
  - Height significantly below target height
  - Subnormal height velocity
  - History of chronic disease
  - Obvious dysmorphic syndromes (Turner’s/Noonan’s)
  - Precocious or abnormally delayed puberty
  - Extreme parental concern

Baseline investigations

- FBC, ESR
- Electrolytes
- Ca/PO4/Vit D status
- LFTs
- Ferritin
- Coeliac screen
- Karyotype (girls)
- Thyroid function
- Cortisol
- Prolactin

Bone-age
Skeletal survey in dysmorphic children

GH insufficiency

1 in 3500-4000

- Mild
  - Unlikely to present before puberty
  - Less severe SS
  - Subnormal height velocity over 12m
  - Isolated GH insufficiency

- Severe
  - Usually presents before age 3
  - Obvious SS
  - Subnormal height velocity from birth
  - Hypothyroidism
  - Microcephaly
  - Possible associated pituitary defects
  - Excess subcut fat
  - Mid-facial hypoplasia in extreme cases
  - Possible features of septo-optic dysplasia
  - Delayed skeletal maturation

Causes of GH insufficiency

- Idiopathic multiple anterior pit hormone deficiencies
- Genetic (e.g. ++ +)
  - GH-1 gene mutations (recessive, dominant, X-linked types)
  - GH receptor mutations
  - rh transcription factor deficiencies
  - GH resistance
- Congenital
  - GH deficiency (endocrine isolated GH insufficiency) (rare genetic)
  - Structural defects (e.g. optic atrophy, agenesis of the pituitary, hypogonadism)
  - Intrauterine infection
- Acquired
  - CNS tumours (e.g. glioma, meningioma, optic nerve glioma)
  - Hypothyroidism (with SS)
  - Cranial irradiation
  - Head injury
  - Inflammatory/pneumococcal diseases
  - Transplant
    - Psychosocial depression
    - Post-pubertal
- Hypothyroidism

Diagnosis of GH insufficiency

- Auxology
  - Short stature
  - Height inappropriate for target height
  - Subnormal height velocity

- Biochemical
  - STH and IGF1 (reflect GH status as long as GH receptor function is normal; considerable overlap between normal and SS (GH deficiency = impressive and different diseases))
  - GH Stimulation tests (Pulsatile – peaks every 3 hours)
    - Document normal TSH and cortisol before undertaking
    - Priming may be required in older children
  - Different options
    - Glucose test
    - Clonidine
    - TRH
  - Results
    - GH
    - What level of GH required? >20ml/L
    - Number of tests required?
Failure to grow with GH therapy

- Technical problems
  - Measurement errors
  - Poor compliance
  - Improper preparation / handling / storage
  - Incorrect injection technique
  - Incorrect GH dosage

- Other conditions
  - Subclinical hypothyroidism
  - Chronic Disease or poor nutritional status
  - Glucocorticoid therapy for any reason
  - His of irradiation of the spine
  - Previous epiphyseal fusion

- Failure of GH effect
  - Anti GH antibodies
  - GH Resistance Syndromes
  - Incorrect diagnosis and child not actually GH deficient

Tall stature

“COMMON” CAUSES:

- Idiopathic
  - Familial (tall parents) (normal GV and bone age)
  - Early puberty
  - Obesity
- Thyrotoxicosis
- Early Puberty
- Obesity
- Klinefelter

“Rare” causes: overgrowth syndrome (eg Soto’s, Marfan’s, BW)
GH secreting pituitary tumour

Investigations

- If physical examination normal, no intellectual delay and tall family – none
- Otherwise consider;
  - Bone age
  - Karyotype, Thyroid function, IGF-1
  - If GH secreting pituitary tumour suspected (rare!) then examine visual fields + do OGTT for GH secretion +/- MRI

MANAGEMENT

- Treat specific cause
- Counselling
- Rarely accelerate puberty in boys or girls with either testosterone or oestrogen respectively

BUT potential risks and therefore rarely used
Obesity Trends* Among U.S. Adults
BRFSS, 1985
(*BMI ≥ 30, or ~ 30 lbs overweight for 5’4” person)

No Data | <10% | 10%-14%

Obesity Trends* Among U.S. Adults
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Obesity Trends* Among U.S. Adults
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Obesity Trends* Among U.S. Adults
BRFSS, 1988
(*BMI ≥ 30, or ~ 30 lbs overweight for 5’4” person)

No Data | <10% | 10%-14%
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## Obesity Trends* Among U.S. Adults

**BRFSS, 2001**

(*BMI ≥ 30, or ~ 30 lbs overweight for 5' 4" person)

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## Obesity Trends* Among U.S. Adults

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## Obesity* Trends Among U.S. Adults

**BRFSS, 2003**

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