25 Year Old Man with History of Growth Hormone Treatment

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HPI

- CC: 25yo WM - Management of osteoporosis and interest in resuming GH therapy for "IGF-1 deficiency"
- Born ~34 weeks, normal growth until 1 year when weight/length declined <3rd percentile
- 4 years: GH stimulation testing "didn't tolerate"
- 6 years: dx with asthma; frequent steroids age 7-13
- 10 years: saw our group, wt 4 kg below 3rd percentile
  ht 7cm below 3rd percentile
  saw OSH endo: started on GH
- 12 years: pubertal changes, Lupron age 13-17
- 18 years: GH stopped, felt to have achieved normal ht

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Chronic Renal Insufficiency
Congenital Adrenal Hyperplasia
Cushing's Syndrome
Growth Hormone Deficiency in Children
Growth Hormone Deficiency in Adults
Idiopathic Short Stature
Insulin-like Growth Factor Deficiency
Intrauterine Growth Restriction
McCune-Albright Syndrome / Fibrous Dysplasia
Panhypopituitarism/Tumors
Precocious Puberty
Russell-Silver Syndrome
Septo Optic Dysplasia / Optic Nerve Hypoplasia
Small for Gestational Age
Thyroid Disorders

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Is your child growing normally?

Healthy children grow a MINIMUM of 2 inches to 2 and a half inches EACH year
(after the age of 2 and before puberty).

If you are **Searching for reasons** why your child may not be growing well- click here- "What is normal growth?"

If you already have a diagnosis for your child, click on the diagnosis name on the left side or bottom of this page.

Online Growth Charts
Check your child's growth

Check on your child's height and weight with our online or other special growth charts.

Growth hormone deficiency and other growth disorders are a reflection of a child's overall health.

Children fail to grow for a variety of reasons. Growth hormone deficiency is only one possible cause. Other vital hormones such as thyroid, or insulin-like growth factor also play important roles in a child's growth. Genetics, sleep, nutrition and exercise are also factors for normal growth.

If a child is growth hormone deficient or failing to grow due to an underlying medical problem, his or her visible growth failure means that other more serious (non-visible) things are going on inside the body. Those "invisible" factors are our focus and concern. Height (too much at a young age or too little) is simply something we can see to warn us that something may be going wrong. It is natures early warning signal- an alarm for parents to take their child to the physician.

Many conditions which interfere with children's growth are treatable. Growth hormone, thyroid hormone, and now insulin-like growth factor (in the non-generic form) are medications which are as close to nature as possible. Children with a wide range of growth deficiencies (such as Turner Syndrome, Russell-Silver Syndrome, Intrauterine Growth Retardation - Small for Gestational Age just to name a few) have had wonderful results thanks to growth hormone and other treatments.

Each week we hear from parents about the short people in their family, and this is absolutely a factor to consider. However, scientists have now discovered a few genes which are responsible for growth failure. Therefore, as parents of affected kids ourselves (and yes some of us are short adults) we always tell worried parents- *the primary indicator as to if your child needs to be seen by a medical professional is how much he or she is growing each year*!

Parent's know their child better than anyone else in the world. Trust your instincts, be your child's strongest advocate. MAGIC is simply parents who have banded together- to help other parents. **You are not alone.**

Chronic Renal Prob. Failure to Grow Gen. Info.
Congenital Adrenal Hyperplasia (CAH)
Constitutional Growth Delay (late bloomers)
Failure to Thrive
Growth Hormone Deficiency in Children (hypopituitarism)
Growth Hormone Deficiency in Adults
Idiopathic Short Stature (ISS)
Insulin-like Growth Factor Deficiency (IGFD/IGF-1) Intrauterine Growth Restriction
McCune-Albright Syndrome / Fibrous Dysplasia
Optic Nerve Hypoplasia (deMorsier Syndrome)

Today's economic hardships really hurt non-profit charities for kids with rare conditions. Help us offset the soaring costs to provide programs for MAGIC families and children. Thank you! Donations are 100% tax deductible!

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Affected Adults- Educational Program Books now online!
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View details regarding this program.

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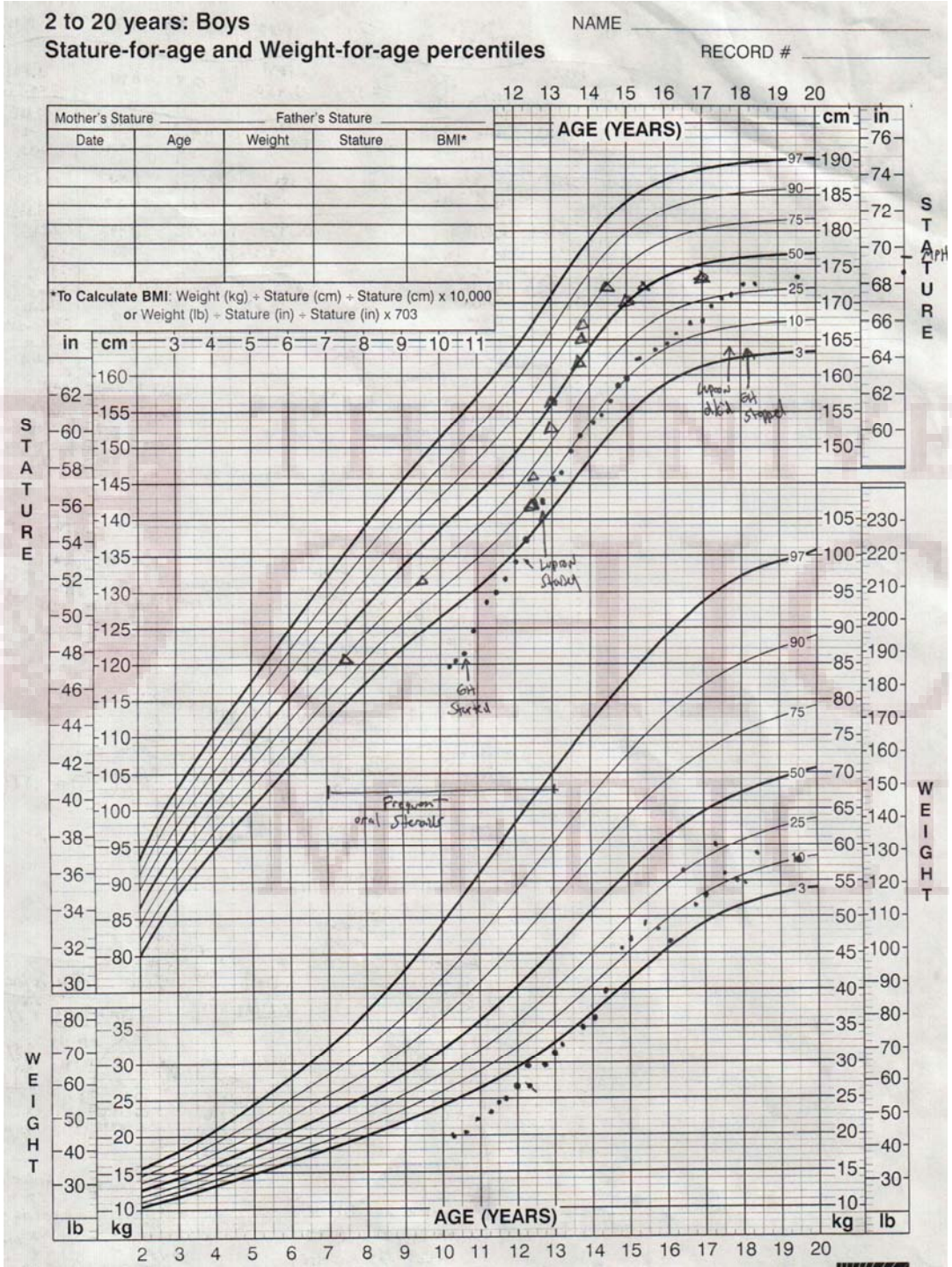


Growth Chart

HPI continued

- 18 years: dx with <u>osteoporosis</u> by DEXA, Ca+D

  -ibandronate (dizzy) → alendronate (stopped for esophagitis)

  -IV ibandronate x2yrs age 19-21

  -reports shoulder dislocation and neck/upper back injury with vertebral disc compression age 23 with "paralysis in the R arm and R leg"

  - age 24 dropped down stairs, fx multiple ribs; fractured his R humerus while transferring from wheelchair

- 22 years – Present: asthma worsened, systemic steroids ~50% of the time; typical 40-60mg/day, presently 10mg/d

- 24 years – discussed restarting GH with OSH endo to help strength/bone health; restarted on self-pay basis

  recently found out that OSH Endo could not keep following him

ROS

- Weakness, wheel-chair dependent
- Diffuse joint pains
- Chronic SOB/wheezing
- Spells of shaky/sweaty 2x/wk for 2-3 years
- Headaches
- Blurry vision
- Increase in urine output and thirst x2-3 wks
- Chronic constipation, recent diarrhea
- Temperature instability
- Shaving, +spont erections with ejaculation and normal libido

PMH and ROS

PMH

- Osteoporosis with rib/humerus fx's
- "IGF-1 deficiency" with SS
- Asthma
- GERD
- Viral myocarditis
- Coronary vasospasm
- Neck/back injury with ? R arm/leg paralysis
- Juvenile arthritis
- ? connective tissue disorder
- Fe deficiency anemia
- Hypersomnia
- Vit D/B1 deficiency
- Hx of pneumonia
- Hx of anaphylaxis

ALLERGIES: 11 meds

MEDICATIONS

- GH 0.4mg/d
- Prednisone 10mg/d
- Vit D 50,000 IU/d q2wks x1 yr
- Caltrate 500mg bid
- Calcitonin 200 IU spray qd x3mo
- Sucralfate
- Ranitidine
- Esomeprazole
- Ondansetron
- ASA 81 mg qd
- Diltiazem CD 120mg qd
- Nitroglycerin SL prn
- Allegra
- Albuterol nebs + MDI
- Pulmicort nebs
- MVI, Vit C, Zinc
- EpiPen

Family and Social History

Family

- Italian
- Mother 61, 5’2”, breast Ca, COPD, menarche 9
- Father 65, 6’0”, CAD/stent, pre-DM, vietnam vet
- Brother 16, dx “IGF-1 deficiency” age 14, Rx’d IGF-1 x3yrs, 5’10”

Social

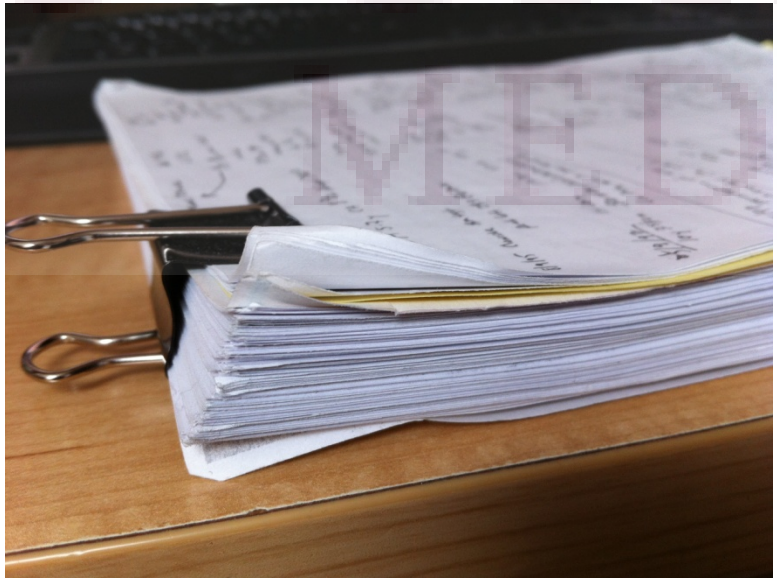
- Lives with parents, finished HS and some college courses
- EMT training x1 year
- Dependent for feeding, dressing, bathing, toilet
- Denied abuse, recalled being bullied in school

Physical Exam

VSS Wt 148lbs, Ht 67.6 inches, BMI 22.8
Gen: Awake, alert, non-cushingoid, non-acromegalic
Head/Face: Nondysmorphic
Neck: no thyromegaly, no acanthosis
Resp: Clear bilaterally, unlabored
CV: RRR no m/r/g
Abd: Soft, scaphoid, non-tender, no masses
GU: Testes 8-10mL volume bilaterally, no gynecomastia
Musc: No bony deformities, holding R arm close to body, could not abduct, + internal/ext rotation; decreased R grip strength; unable to flex R quadricep; sensation intact, hypersensitive R arm/leg; no atrophy; Spine aligned normally
Neuro: CN 2-12 intact, DTRs 2+/symm bilaterally
Derm: no acne, + facial hair

Assessment and Evaluation

1) Chronic glucocorticoids with osteoporosis and fx, back injury ? paralysis
2) Short stature with normal adult height after GH and GnRH agonist therapy; ? of IGF-1 problem
3) Acute polyuria/polydipsia



Laboratory and Radiologic Eval

-CMP with Na 141, K 2.9

-Repeat 2wks later after K replete, Na 142, K 3.9
  Sosm 288, Uosm 578

-TSH 0.8, fT4 1.47

-5:50pm LH 9.2 mIU/mL (2-6.8)
  FSH 6.2 mIU/mL (1.2-8)
  Ttest 569 ng/dL (240-950) ftest 23 ng/dL (9-30)

-IGF-1 381 ng/mL (116-358)

-25-D 42 ng/mL, PTH 47 pg/mL, Ca 9.5 mg/dL, alb 4.3

-XR of T/L-spine: no compression fx

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Review of Records

Growth Hormone-Related

- Age 8: IGF-1 66 ng/mL, bone age 5.7 yrs

  Clonidine stimulation test: GH peak 24.9 ng/mL
- Age 10: OSH Endo started GH on basis of constitutional delay + growth suppression related to steroids
- Age 14-17: high dose GH used (0.7mg/kg/wk),

  IGF-1 levels as high as 1135 ng/mL (202-957)
- Age 19: 15mo off GH, IGF-1 204 ng/mL (126-382)
- Age 22: IGF-1 normal x1, low x1
- Age 24: IGF-1 normal x2

Review of Records

Bone-Related

- Age 18: lumbar L1-4 z-score -3.5
- Age 21: lumbar L1-4 z-score -0.7
- Age 24: lumbar L1-4 z-score -2.9

- Most recent exam: 3 months ago

  Fem neck Left -1.9, Right -1.0

  Total hip Left -1.6, Right -2.2

Re-Assessment/Plan

- <u>"IGF-1 deficiency"</u>

  - no evidence for a primary IGF-1 problem on the basis of normal growth response and supraphysiologic levels of IGF-1 while on GH; poor growth was likely related to GCs

  - did not feel that benefit > risk for treatment and advised against continuing GH

- <u>Osteoporosis</u>

  - glucocorticoid-driven; no evidence of vertebral fx

  - pulm referral to help manage off steroids; continue Ca + D

  - ? paralysis → referred to our neurology dept

Clinical Questions

1) How do you diagnose IGF-1 disorders?

2) What is the proper management of children with glucocorticoid-related growth suppression?

3) Is there a role for GH therapy in patients with glucocorticoid-induced osteoporosis?

“GH Insensitivity Syndromes”

- Primary – bio-inactive GH molecules
  - defect in GH-R (Laron dwarfism)
  - defect in GH- signal transduction
  - defect in synthesis/action of IGF-1
- Secondary – illness, malnutrition, inhibitors of GH action such as glucocorticoids

- Diagnosis: extreme short stature, decreased IGF-1, increased GH, inability to generate IGF-1 in response to GH

Glucocorticoids and Growth Suppression

- Exogenous and endogenous glucocorticoid excess profoundly suppresses growth
- Short-term growth velocity improvement seen using GH in GC-treated conditions like IBD, asthma, JIA, but longer-term efficacy/safety data lacking, so considered *experimental*
- Management:

  1) Use alternate therapy

  2) Lower daily steroid dose

  3) Switch pt to alternate-morning GC therapy

  4) Switch pt to topical/inhaled therapy

GH and GC-Induced Osteoporosis

- GH/IGF-1 anabolic effects on bone: ↑ osteoblast
- GCs - bone loss: ↑ osteoclast ↓ osteoblast

- No RCTs found looking at GH therapy in GIO in non-GH deficient patients
- 1999 (Berneis)– combined GH and IGF-1 used in healthy individuals administered short term GCs reversed negative bone effects
- 2002 (Manelli) – pts on chronic GCs given GH had increases in osteocalcin, C1NP

Take Home

- IGF-1 disorders, known as “GHI insensitivity syndromes”, are characterized by extreme short stature, low IGF-1, elevated GH, and poor IGF-1 response to GH therapy

- The use of GH in children with growth suppression secondary to glucocorticoid use is considered *experimental*

References

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