Growth Disorders... Too Tall Too Small

Thomas M. Koroscil, M.D.-Ph.D.
Chief, Division of Endocrinology
Associate Professor of Medicine
Boonshoft School of Medicine

Introduction

Dwarfism, gigantism, and acromegaly are three rare but devastating growth disorders

This presentation will outline the main etiologies, manifestations, diagnostic modalities, and treatment options for these three conditions

Interlaced within the discussion are short bios of historical figures afflicted with one of these growth aberrancies

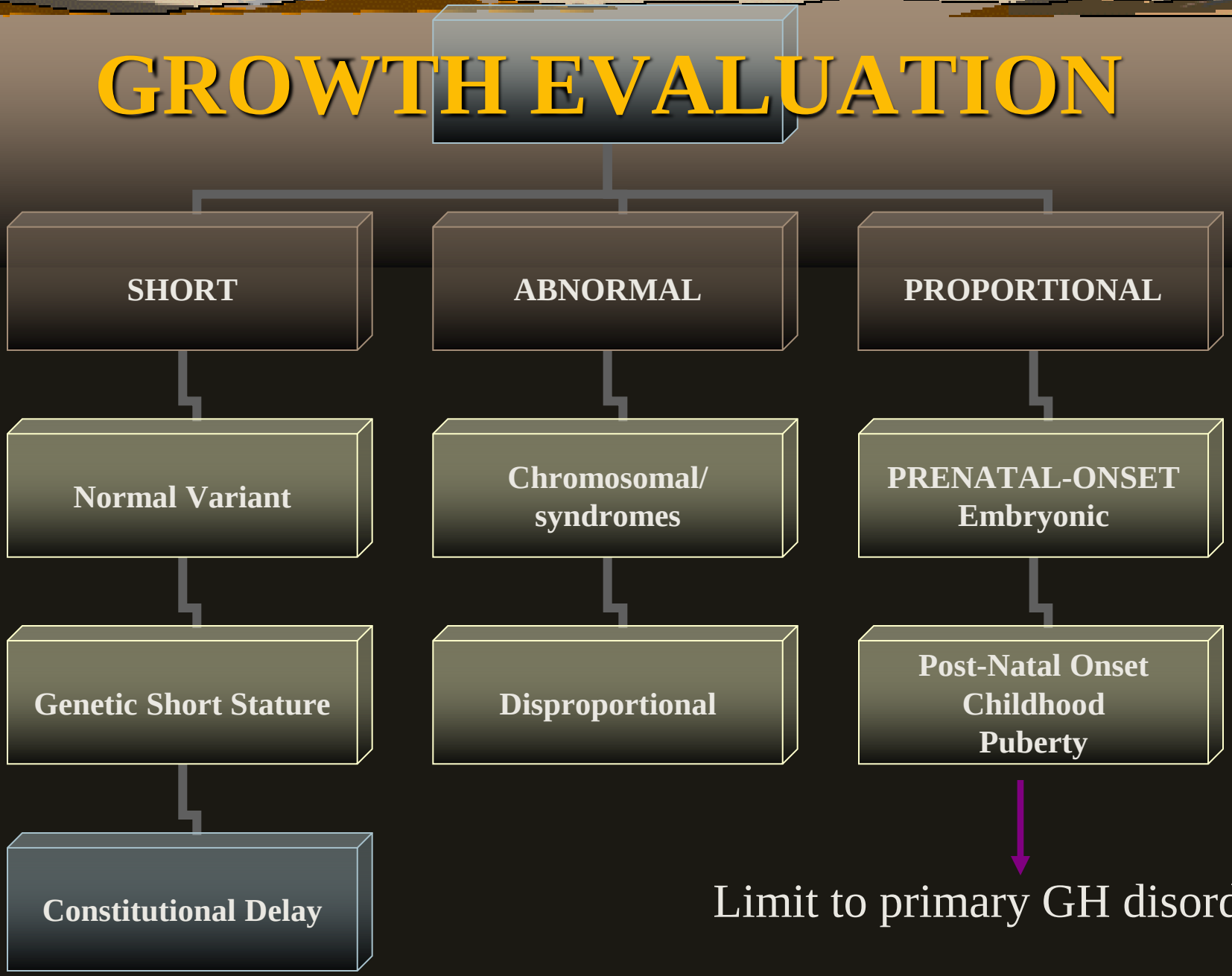
Normal Growth

- Results from the absence of chronic disease

  Proper interaction of:

  - Genetic
  - Nutritional
  - Metabolic
  - Endocrine factors

GROWTH EVALUATION



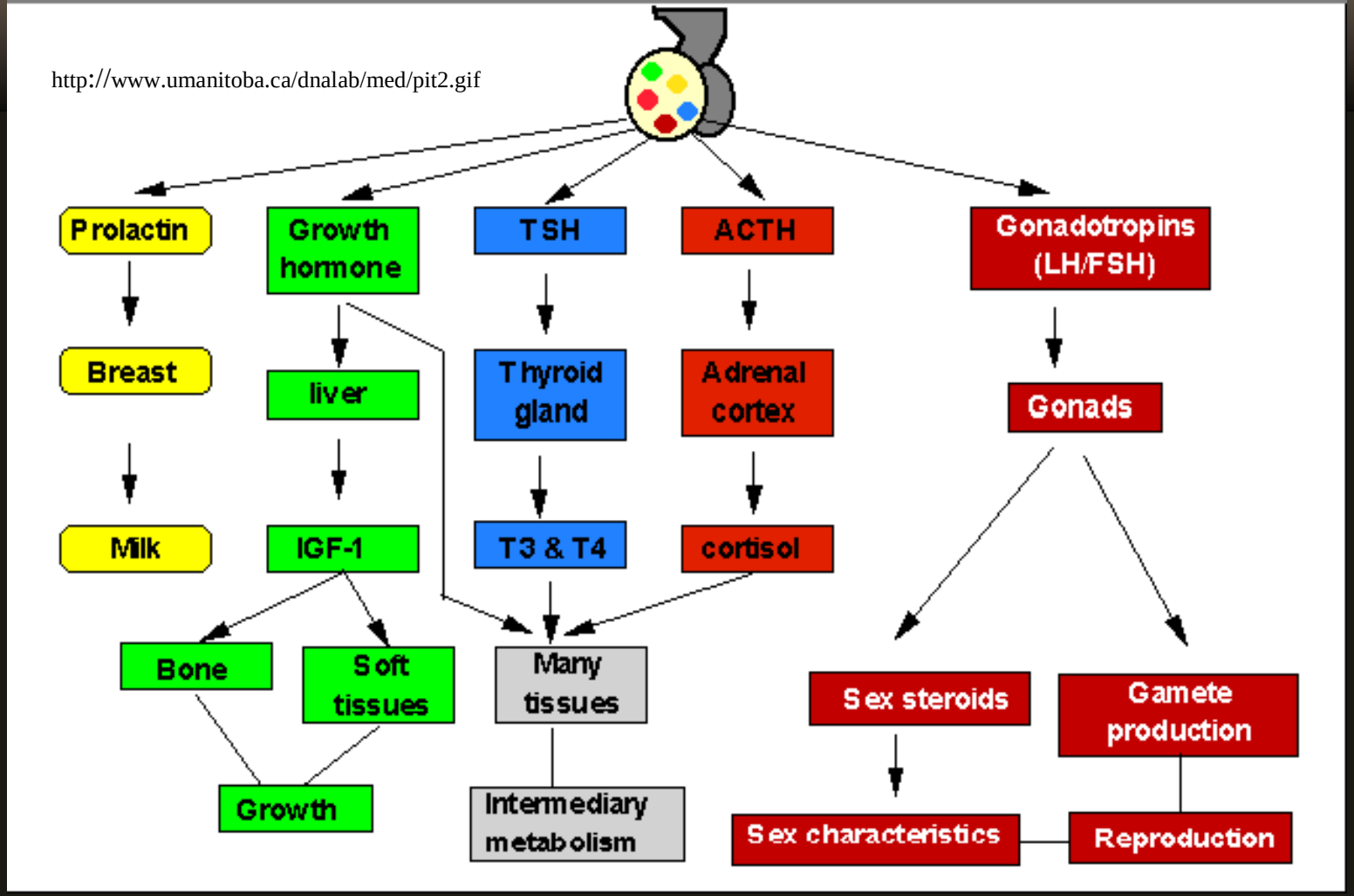
How Tall Will My Child Grow? Height calculations for your child.

- Add the mother's height and the father's height in either inches.
- Add 5 inches for boys or subtract 5 inches for girls.
- Divide by two.

- Another way to estimate a child's adult height is to double a boy's height at age 2 or a girl's height at age 18 months.

Overview of anterior pituitary hormone functions

http://www.umanitoba.ca/dnalab/med/pit2.gif



History of Growth Disorders

- 1921 – Growth promoting factor in the pituitary was first discovered
- 1944 – Bovine GH isolated
- 1960s – Children 1st Rx with cadaveric hGH
- 1985 – rhGH therapy becomes available

1. An adult patient is measured at a height of 4 feet tall. The appropriate term for this patient is which of the following?

A. Midget
B. Small-fry
C. Little person or little people
D. Munchkin
E. Muggle

Short Statue

- Little People of America (LPA)
- Define: Dwarfism
  - Medical or genetic condition
  - Adult height ≤ 4'10"
  - Disproportional
    - Achondroplasia – autosomal dominant – 1:15000-30,000
      - The *FGFR3* gene mutation: provides instructions for making a protein called fibroblast growth factor receptor 3.
    - Spondyloepiphyseal dyplasia – 1:95,000
    - Diastropic dyplasia – 1:110,000
    - Osteogenesis imperfecta (bone fractures and blue sclera)
  - Proportional
    - Growth hormone deficiency (absolute or functional)

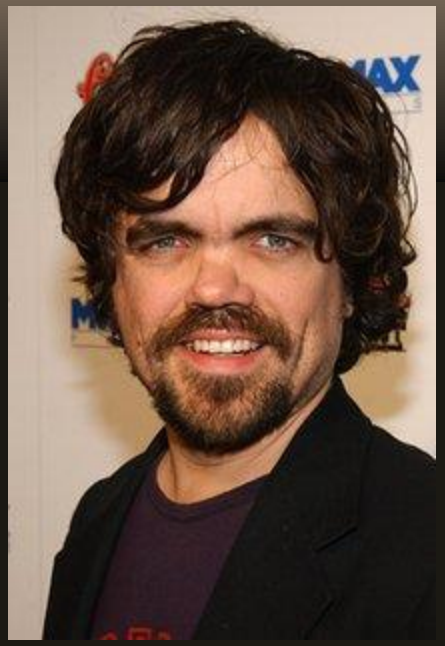
Short Statue

- Dwarfism – acceptable term
- What is a midget?
  - Unacceptable term
  - Term dating to times of “freak shows”
- Little People – acceptable term
  - LPAonline.org

The “Foos” family

Achondroplasia

Peter Dinklage was born in Morristown, NJ in 1969 of two normal sized parents. Which of the following characters has he portrayed?

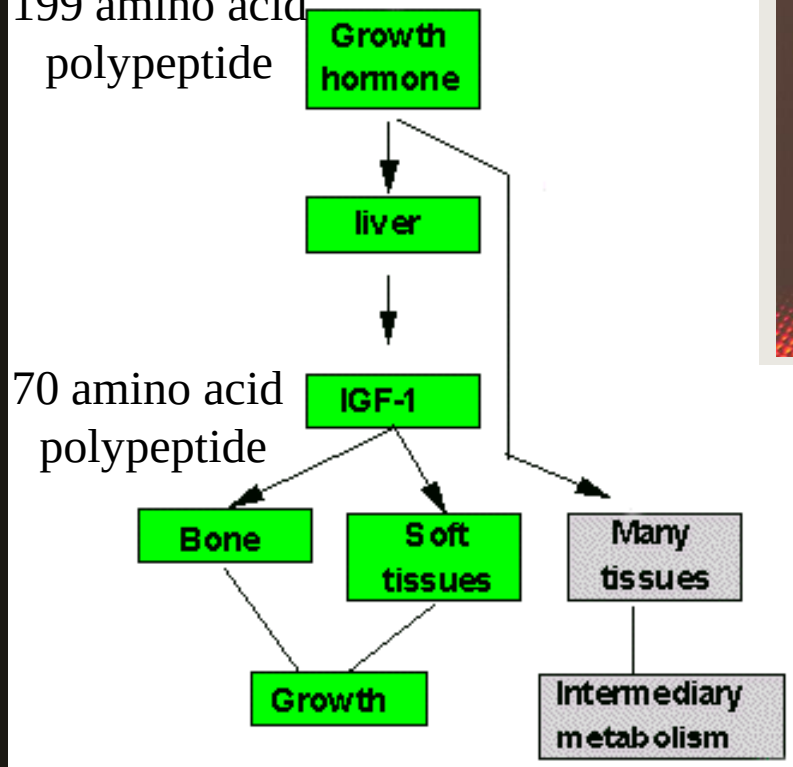


- 1. Tyrion Lannister
- 2. Theon Grayjoy
- 3. Jorah Mormont
- 4. Samwell Tary
- 5. Stannis Baratheon

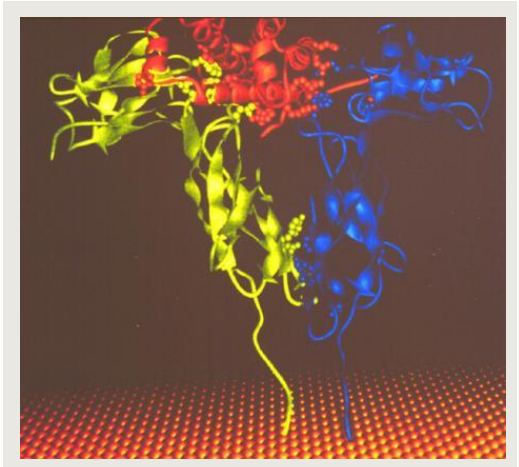
All people with achondroplasia have short stature. The average height of an adult male with achondroplasia is 131 centimeters (4 feet, 4 inches), and the average height for adult females is 124 centimeters (4 feet, 1 inch). Characteristic features 0f achondroplasia include an average-size trunk, short arms and legs with particularly short upper arms and thighs, limited range of motion at the elbows, and an enlarged head (macrocephaly) with a prominent forehead. Fingers are typically short and the ring finger and middle finger may diverge, giving the hand a three-pronged (trident) appearance. People with achondroplasia are generally of normal intelligence.

Polypeptide hormones must be given by injection

199 amino acid polypeptide



70 amino acid polypeptide



http://www.umanitoba.ca/dnalab/med/pit2.gif
www.ghresearchsociety.org/

2. Which of the following statements regarding Tom Thumb is NOT true?

A. He was born in Bridgeport, Connecticut
B. He married a “normal” height woman
C. He had a low IGF-1 concentration
D. He had a low growth hormone concentration
E. He worked in the circus

General Tom Thumb
(1838-1883)

- Born Charles Sherwood Stratton
- Stood 3 feet, 4 inches tall
- Discovered by P.T. Barnum
- Toured the world
- Performed for many world leaders, including Abraham Lincoln, Queen Victoria of England, and Queen Isabella of Spain
- Became very wealthy through his years in show business

Drimmer, Very Special People, 1973

http://bullseyedesigns.com/sideshow

Dwarfism

Causes of Growth Hormone Deficiency

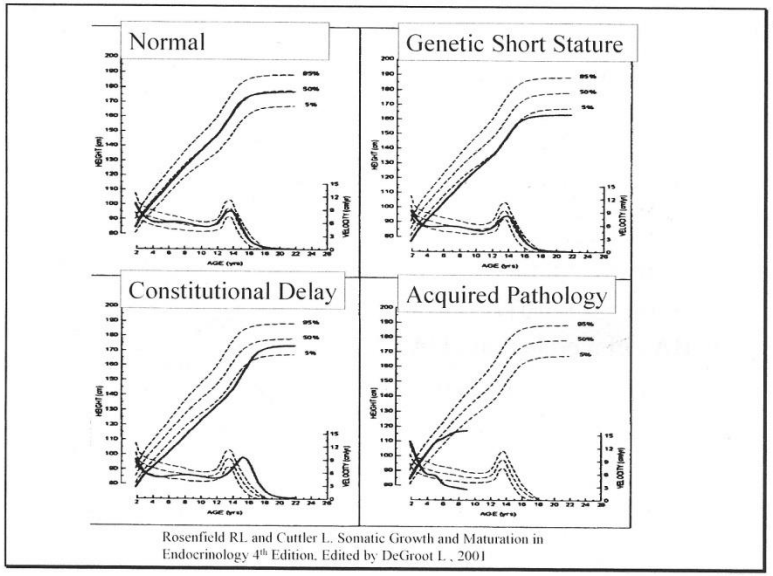
- Congenital (5-30% familial)
  - Several genetic mutations affecting gene transcription or affecting the GH molecule
- Pituitary/midline developmental anomalies
- Postnatally: acquired causes
  - Tumors
  - Radiation
  - Infiltrative
  - Autoimmune
  - Trauma
  - Granulomatous
  - Infectious
  - Idiopathic

Dwarfism
Growth Hormone Deficiency

- Manifestations:
  - Growth retardation – proportionate dwarfism
  - Hypoglycemia
  - Micropenis
  - Craniofacial abnormalities
  - "Chubby"
  - Retarded bone age
  - Delayed puberty

Syracuse Univ. Library, Special Collections

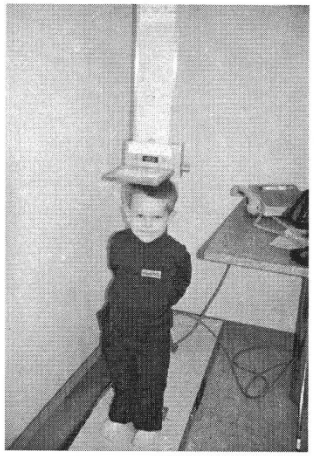
Tom Thumb married Livinia Warren in Feb 63.
She was 32" tall
Weight=29 pounds



Rosenfield RL and Cuttler L. Somatic Growth and Maturation in Endocrinology 4th Edition. Edited by DeGroot L. , 2001

Evaluation

- Accurate height
- Height / weight / proportions
- Height velocity
- Screening labs
  - CBC, ESR
  - Tissue trans-glutaminase
  - Chem Profiles
  - UA, urine Culture
  - Bone age
  - TFT (fT4 + TSH)
  - IGF1



Dwarfism: Growth Hormone Deficiency

Importance of Growth Charts
Objective Data

Additional labs/tests:
IGFBP-3
Karyotype: Down's, Turner's

Dwarfism: Growth Hormone Deficiency

- Diagnosis
  - Low IGF-1 and low IGFBP-3
    - Integrated concentration of secreted GH
  - Assess stimulated GH response (2 tests)
    - Arginine
    - Clonidine
    - Glucagon
    - Insulin tolerance test
  - Image the pituitary

Dwarfism
Growth Hormone Deficiency

- Treatment: Growth Hormone (Somatropin)
  - Recombinant DNA technology
  - Subcutaneous injection
  - Several commercial brands available
  - Indications: GH deficiency in children
    GH deficiency in adults
    Turner's syndrome
    Prader-Willi syndrome
    Idiopathic short statue
  - Cost: $200 per week (based on 40 pound child)

3. Which of the following statements is true regarding Laron Syndrome?

A. People with the disorder have low GH levels
B. People with the disorder have GH receptor defects
C. People with the disorder have disproportionate growth
D. People with this disorder paradoxically have elevated IGF-1 concentrations
E. Many people in the villages of Honduras have this syndrome.

Dwarfism
Growth Hormone Resistance

Laron Syndrome: Growth hormone receptor defect

- Due to growth hormone receptor mutation
- Approximately 30 mutations have been isolated
- Mountains of Ecuador 1/3 world's population of Laron Syndrome
- No diabetes, no cancer

Localization to receptor is supported:

- Clinical improvement with IGF-I administration
- No effect from GH administration

Resistance can be partial, with variance in clinical presentation

Hull, 1999

Dwarfism
Growth Hormone Resistance

Increased GH but decreased IGF-I

- Growth retardation
- Acromicria
- Micro-orchidism and pubertal delay
- Obesity
- Neurologic underdevelopment
- Laryngeal narrowing
- Disproportionately long torso
- Cholesterol abnormalities
- Osteoporosis
- Small heart

10 year old Laron Dwarf
Normal Intelligence

Laron, 1999

Dwarfism
Growth Hormone Resistance

Treatment: Injectable IGF-1

Decreases	Increases
Adiposity	Linear velocity
Cholesterol	Head circumference
Glucose intolerance	Sexual development
Morbidity	Renal function

Laron, 1999

Lucia Zarate
(1864-1890)

- At birth, weighed 8 oz; length of 7 inches
- As an adult, weighed less than five pounds; height of < 20 inches
- World's Shortest Woman

- In United States, made $20/hr !!

http://bullseyedesigns.com/sideshow

Dwarfism
Summary

Important to identify dwarfism early

Define etiology: GH deficiency
GH resistance

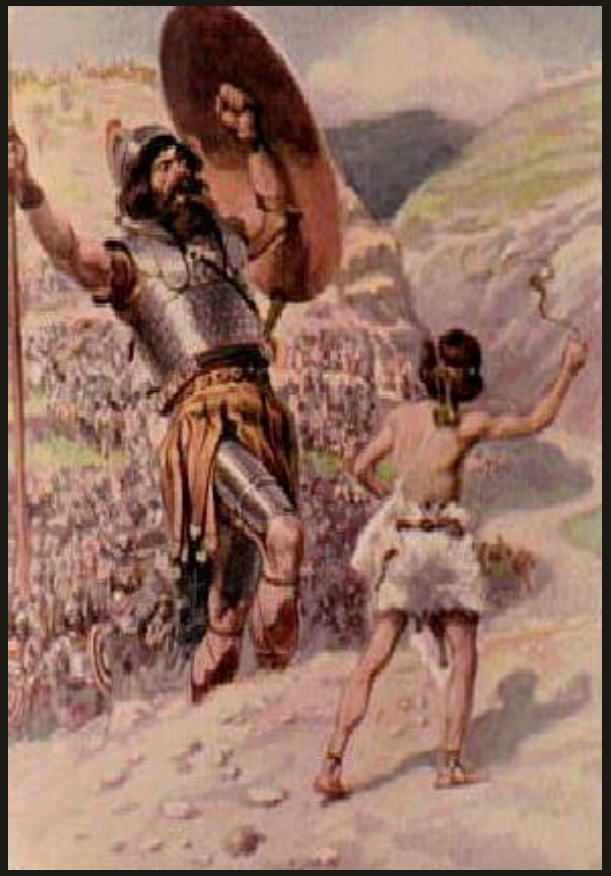
Effective treatments available which promote growth and decrease morbidity

Goliath
The Philistine Giant

- Height of six cubits and a span
- Translates to roughly three meters, or over nine feet
- Armor weighed 125 lbs
- The iron point of his spear weighed 15 lbs

Story of David and Goliath

I Samuel 17:4-7, Holy Bible, NIV



www.orura.com/cards/p35.jpg

Gigantism and Acromegaly

Gigantism denotes an environment of excessive growth hormone prior to closure of epiphyseal growth plates (before puberty)

Proportionate growth

Probable etiology in patients >7'4"

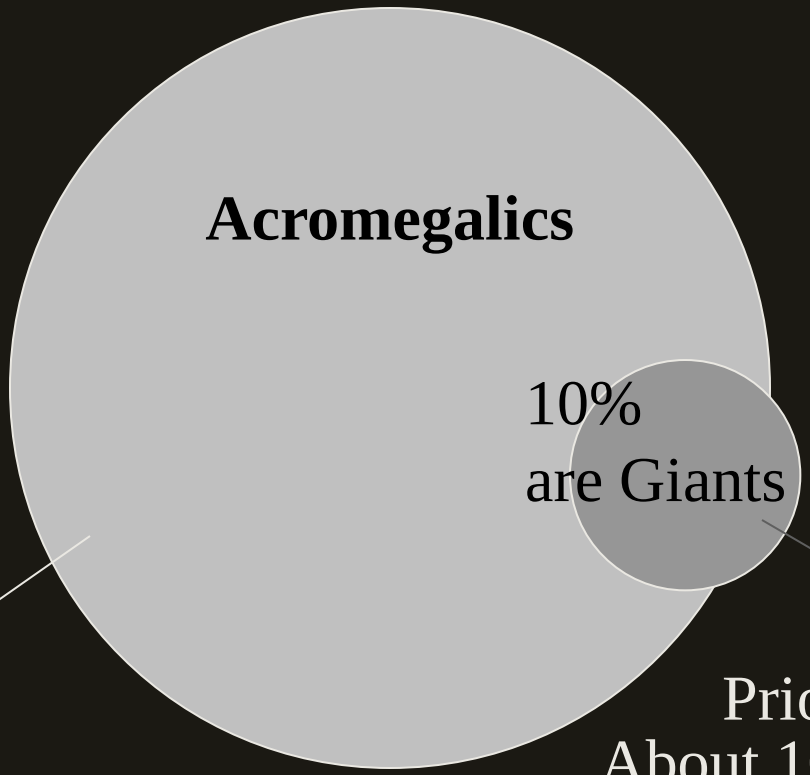
Acromegaly excessive growth hormone after closure of epiphyseal growth plates

Disproportionate growth

Eugster, 1999
Sotos, 1996

Gigantism and Acromegaly

Typical physician sees only a few in his/her career



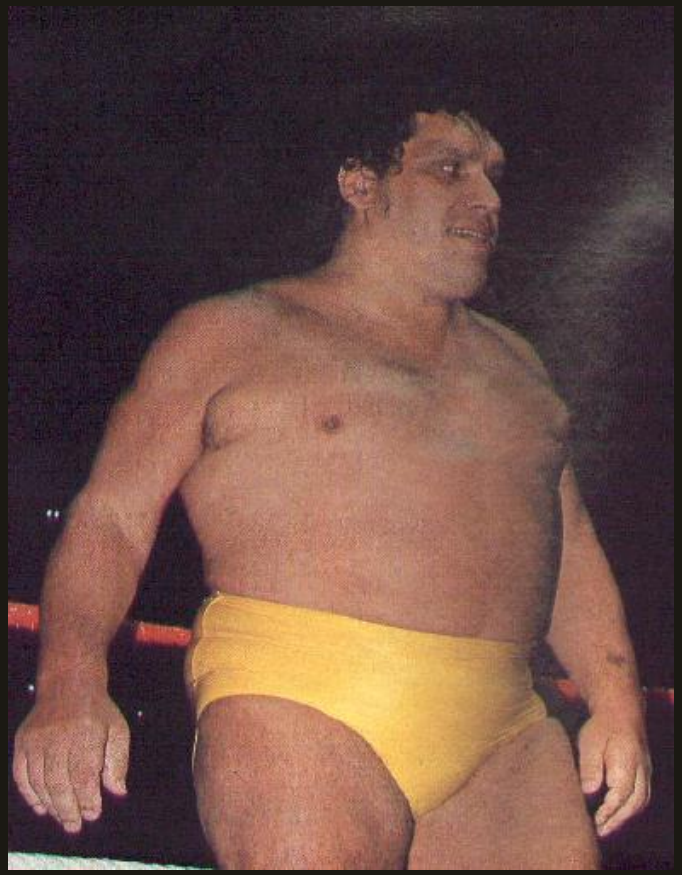
Incidence

3rd decade
3/million/yr

Prior to closure of plates
About 100 cases documented

Eugster, 1999
Maugans, 1995
Sotos, 1996

Andre the Giant
(1946-1993)



members.tripod.co.uk/Bryvoski/ Bryvoski-net/Gallery/andre.jp

- Born Andre Rousimoff in Grenoble, France
- 1988 – briefly the WWF champion
- 1989 – WWF tag team champion with Haku
- (as part of the Colossal Connection)
- Final height of 7’4”
- Top weight of 520 lbs

http://www.puroresu.com/wrestlers/andre/

http://www.angelfire.com/al/andrethegiant/bio.html

Andre the Giant

Fezzik in The Princess Bride (1987)

http://www.geocities.com/Hollywood/Makeup/6353/andre.html

http://www.puroresu.com/wrestlers/andre/

4. Which of the following is the most common source of ectopic GHRH associated with acromegaly or gigantism?

A. Pheochromocytoma
B. Germ cell tumors
C. Pancreatic islet cell tumors
D. Carcinoid
E. Teratomas

Gigantism and Acromegaly

Hypersecretion of Growth Hormone

Pituitary Source (Primary)

Pituitary adenoma

(98%)

Extra-pituitary Source

Hypothalamic GHRH hypersecretion with resulting pituitary hyperplasia

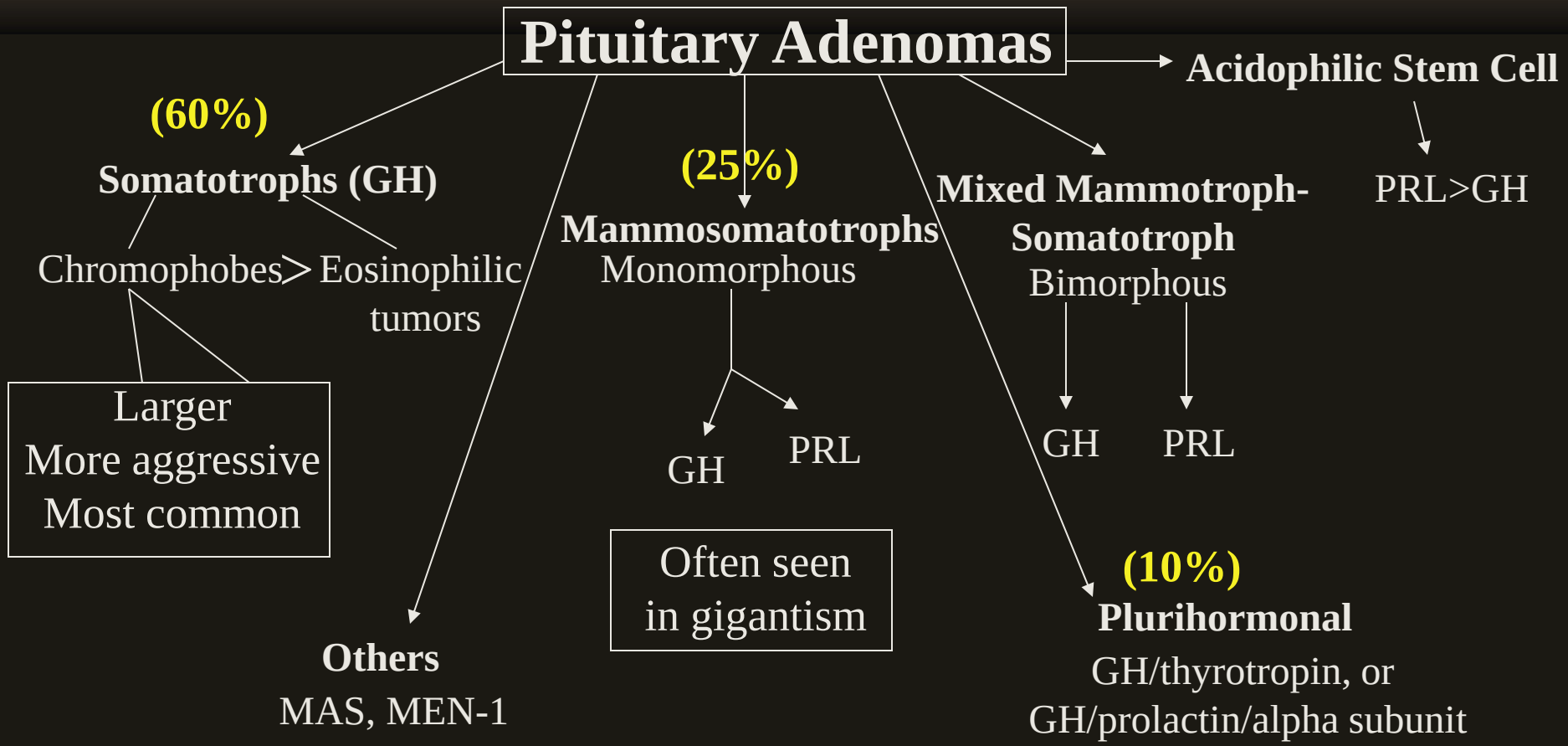
Intracranial GHRH secreting tumor

Ectopic sources GHRH (eg: carcinoid)

Ectopic GH secretion: pancreatic lesions

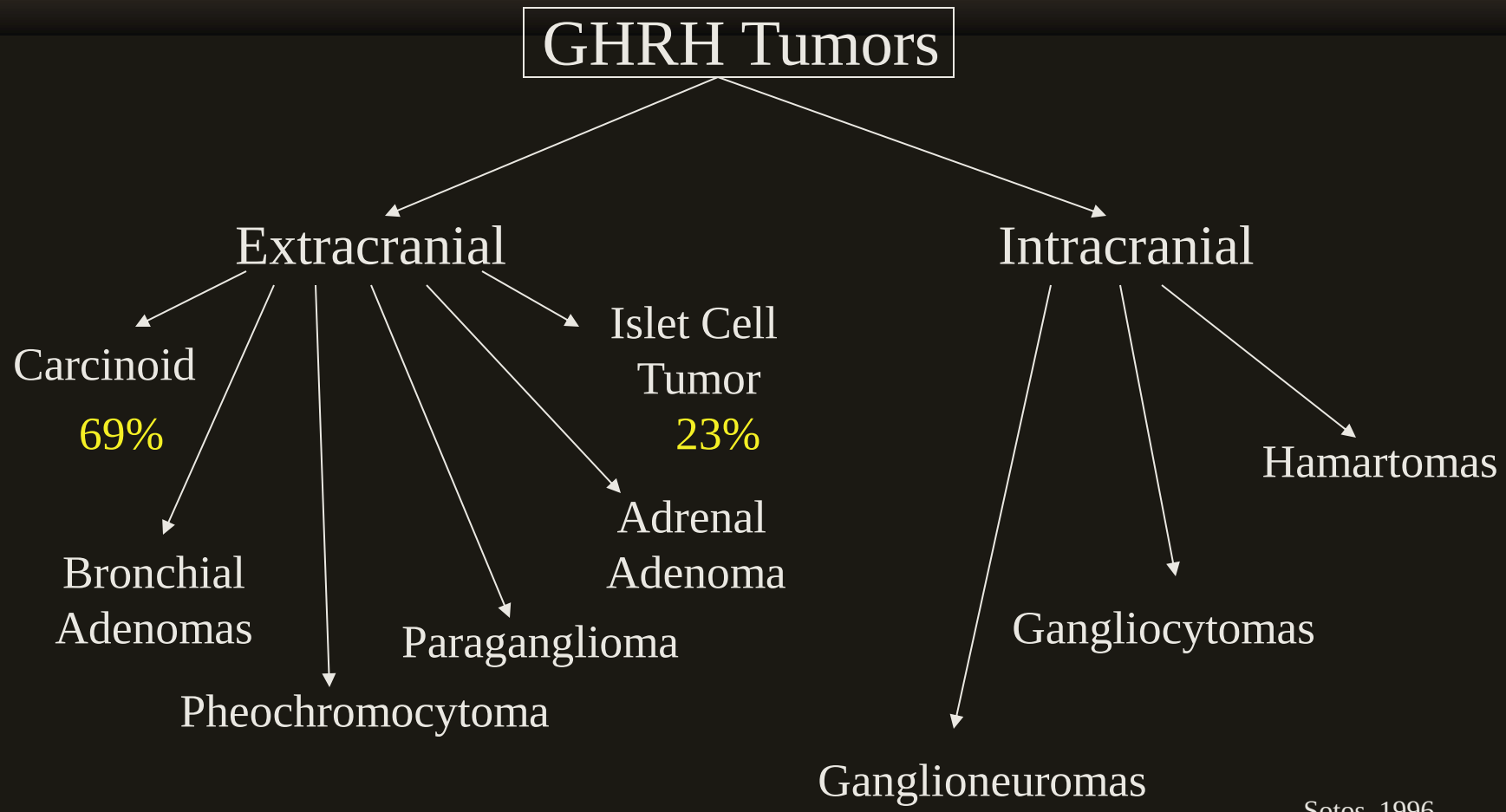
Eugster, 1999

Gigantism and Acromegaly



Sotos, 1996

Gigantism and Acromegaly



Sotos, 1996

Chang Woo Gow (1841-1893)

The Chinese Giant

- Final height of nearly eight feet (recorded at 7’8 ½ ”)
- Reported that he had a taller sister !
- Spoke six languages
- Art collector
- Displayed his collection at his home

http://www.ashleighhotel.co.uk/chang.html

http://bullseyedesigns.com/sideshow

Chang Woo Gow (1841-1893)

The Chinese Giant

http://www.ashleighhotel.co.uk/chang.html

Gigantism and Acromegaly

Clinical Manifestations

George Auger
1883-1922

The Welsh Giant

Most common:

- -Growth of soft tissue
- -Thickening of bones
- -Acral growth
- -Sinus enlargement
- -Cardiomegaly
- -Increases in height
- -Cholelithiasis
- -Headache

Maugens, 1995
Sotos, 1996

Gigantism and Acromegaly

Clinical Manifestations

	Gigantism	Acromegaly
Linear Acceleration	100%	14-19%
Acral Growth	40-100%	100%
Soft-tissue Enlargement	100%	100%
Bone Thickening	100%	100%
Headache	Common	75-87%
Cardiomegaly	Frequent	Frequent

Adapted from Sotos, 1996, Table 2. Pg 583

Gigantism and Acromegaly

Clinical Manifestations

Diabetes/glucose intolerance

Thyroid Goiter/Nodules

Weight Gain

Hirsutism

Polydipsia

Osteoporosis

DI

Cholelithiasis

CHF

Paresthesias

Sellar Enlargement

Visual Changes

HTN

Alterations in Libido

Kyphosis

Hyperpigmentation

Sixth Nerve Palsy

Skin tags

Carpal Tunnel Syndrome

Arthralgias

OSA

Increased Metabolism

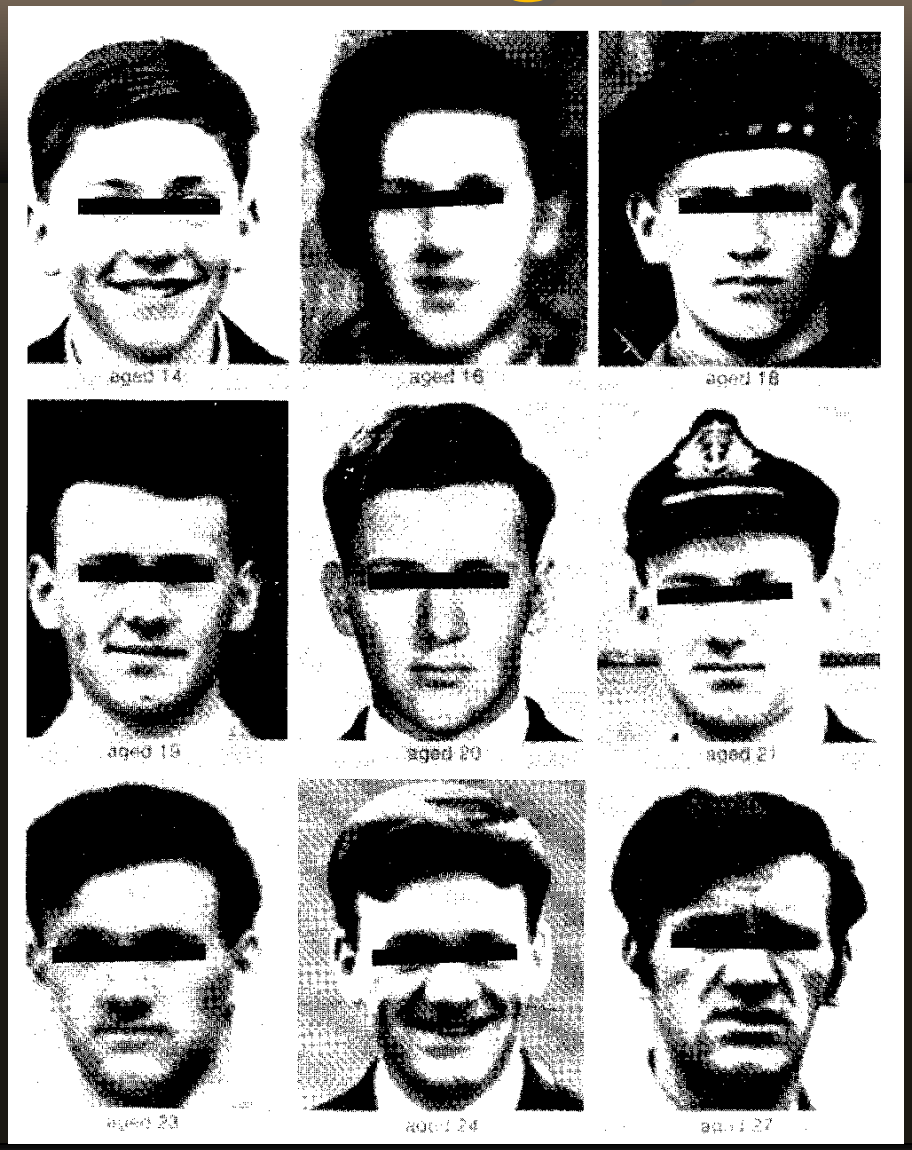
Increased Perspiration

Weakness

Enlarged Organs

Maugins, 1995
Sotos, 1996

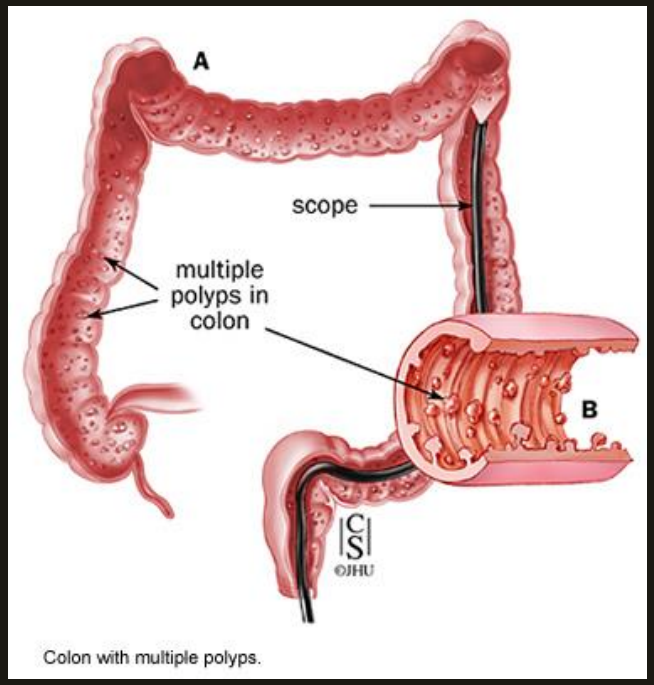
Acromegaly


aged 14
aged 16
aged 18
aged 19
aged 20
aged 21
aged 23
aged 24
aged 27

Acromegaly

Gigantism and Acromegaly

Malignancy



www.msnbc.com/news/602102.asp

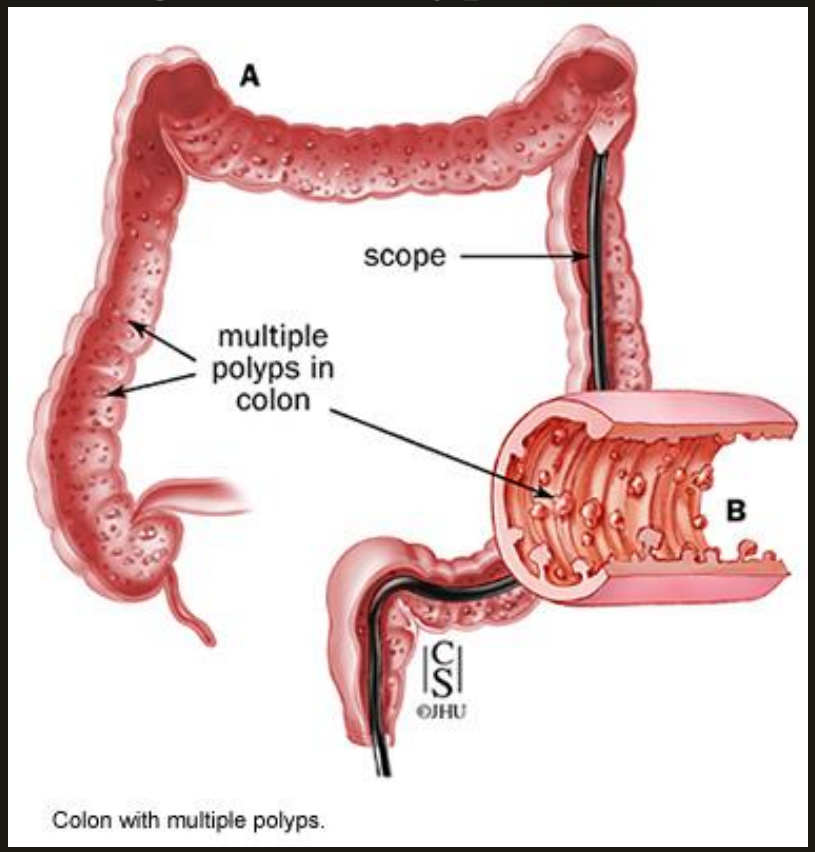
http://www.coloncancer.org/KF_01.jpg

www.enteract.com/~rosa/ prostatedrawing.html

Gigantism and Acromegaly

Malignancy

Skin Tags ⟶ Polyps



Colon with multiple polyps.

http://www.coloncancer.org/KF_01.jpg

- Conclusive evidence of correlation between acromegaly and increased colon cancer risk (RR of 13.4)
- Colonic polyps
  - Right-sided predominance
  - Increased prevalence, size
  - Multiplicity
  - Increased dysplasia
  - Increased transformation
- IGF-I can trigger transcription of c-myc
- Screen acromegalic patients as high-risk
  - First colonoscopy at age 40
- If polyps found, polypectomy and increased surveillance

Jenkins, 2001

Gigantism and Acromegaly

Diagnosis

History and Physical !!!

History and Physical !!!

History and Physical !!!

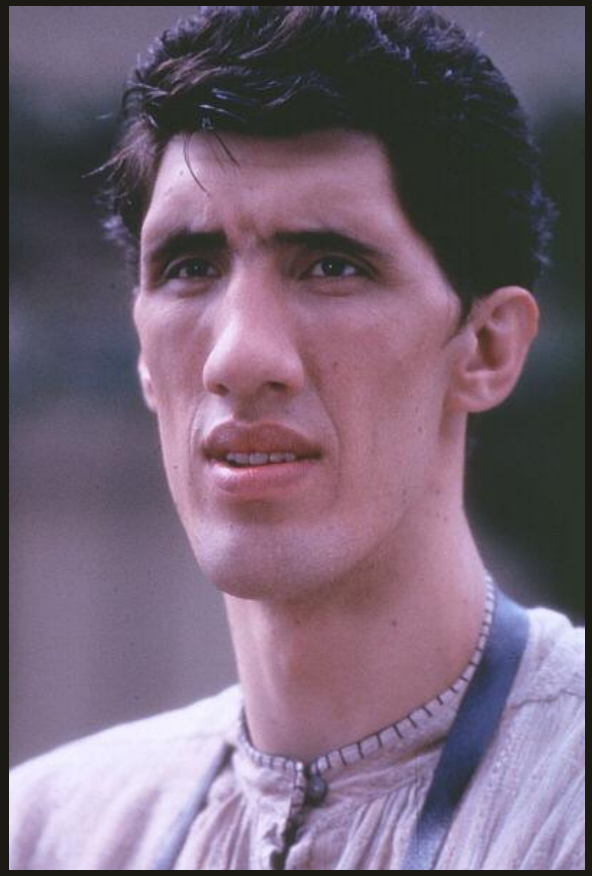
History and Physical !!!

History and Physical !!!

History and Physical !!!

Maugans, 1995

Gheorghe Muresan
Tallest NBA Player



movieweb.com/movie/mygiant

- 7 foot 7 inches tall
- Born in Romania, 1971
- Started playing basketball at age 14
- On Romanian National Team by age 16
- To NBA in 1994, played 6 years
- Professional highlight was staring in “My Giant” with Billy Crystal

www.guinnessworldrecords.com

Gheorghe Muresan
Tallest NBA Player

With Billy Crystal

My Giant

movieweb.com/movie/mygiant

5. The most appropriate screening test for a patient with suspected acromegaly is which of the following?

A. Measurement of IGF-1 concentrations
B. Oral glucose tolerance test with measurement of IGF-1 concentrations
C. Measurement of an early morning GH concentration
D. Measurement of a late night salivary GH concentration
E. MRI sella

Gigantism and Acromegaly

Diagnosis

GH is pulsatile (random level inadequate, though GH is < 1ng/ml for half of the day in normal adult individuals)

IGF-I (somatomedin C) is non-pulsatile

-Must be compared with age/gender

-Preferred over GH

-High IGF-I is very specific for acromegaly (unless pubescent or pregnant)

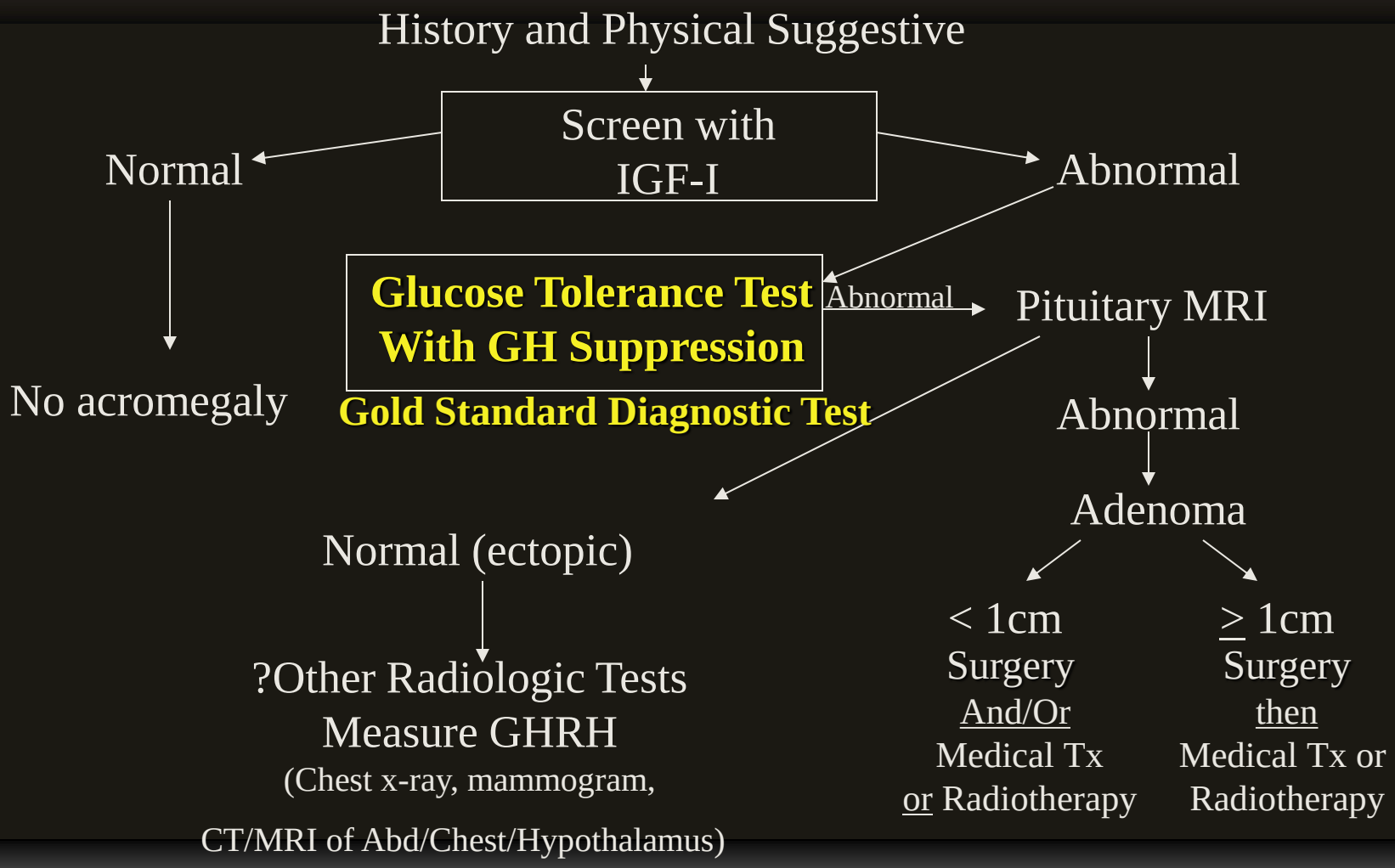
-IGF-1 is the screening test for acromegaly

Maugens, 1995

Melmed, 1998

Gigantism and Acromegaly

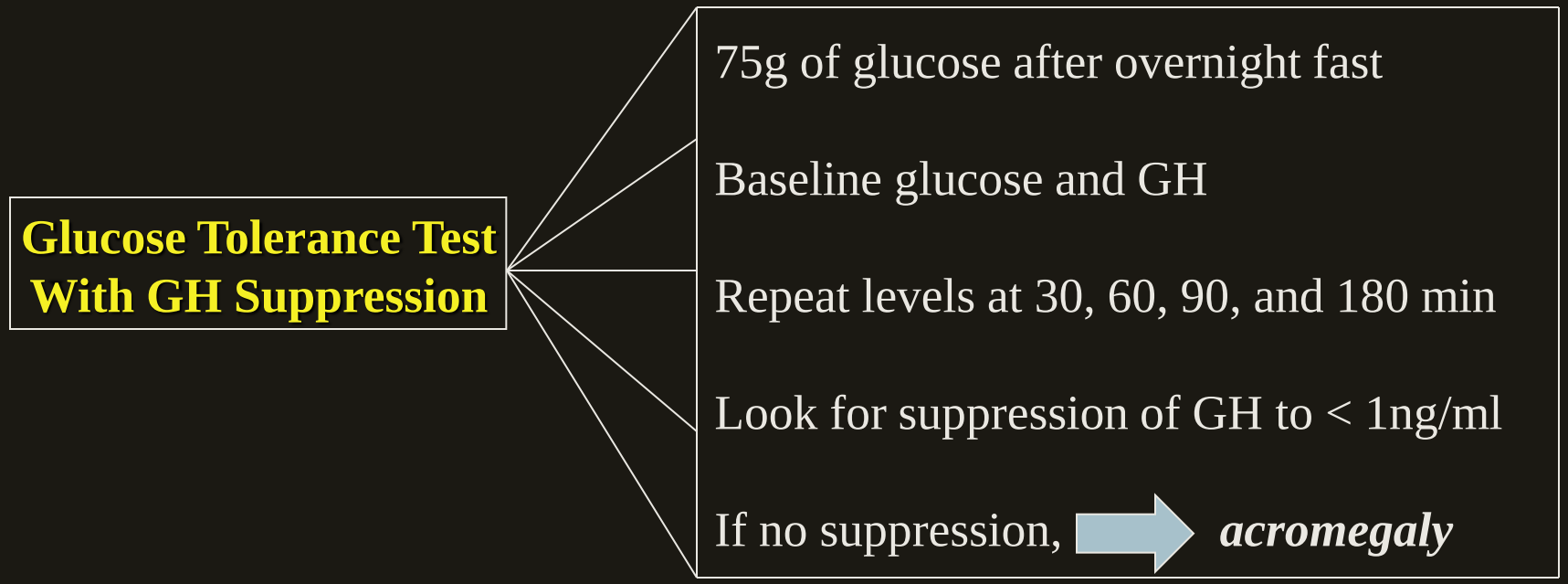
Diagnosis



Gigantism and Acromegaly

Diagnosis

Gold Standard Diagnostic Test



Guistina, 2000
Maugens, 1995

Gigantism and Acromegaly

Diagnosis

Pituitary MRI

Sandy Allen (1955-2008)
Former Tallest Woman

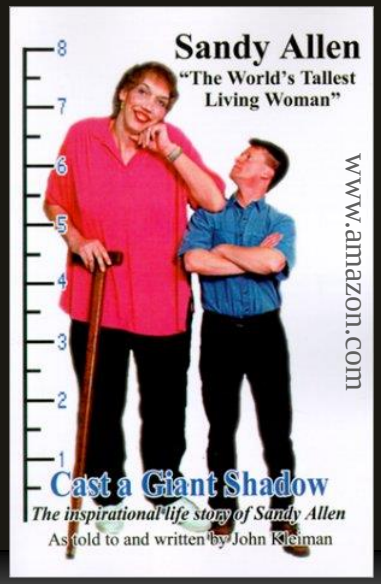
www.globalmark.com/sandy/diff02.jpg

Height of 7' 7 ¼"

Pituitary surgery in 1977

Lived in Indianapolis, IN

www.guinnessworldrecords.com



De-Fen Yao

http://www.tallwomen.org/tallest/

- Tallest living woman
- Reported height of 7’ 8 ½”
- Lives in China
- Now recognized by
  - Guinness Book of World Records

Gigantism and Acromegaly
Treatment

Goals of Therapy

Elimination of mass effect of tumor

Normalization of GH and IGF-I levels

GH<1 and normal IGF-1 for age/sex

Improve morbidity and mortality

-No control…3.5X mortality

-Appropriate control…normal mortality Guistina, 2000

6. When surgical intervention fails to cure acromegaly, which of the following WOULD NOT be an appropriate adjuvant treatment?

A. Gamma knife surgery
B. Sandostatin LAR
C. Lanreotide
D. Teraparatide
E. Repeat surgical intervention

Gigantism and Acromegaly
Treatment

Five Main Treatment Options

Surgery

Somatostatin Analogs

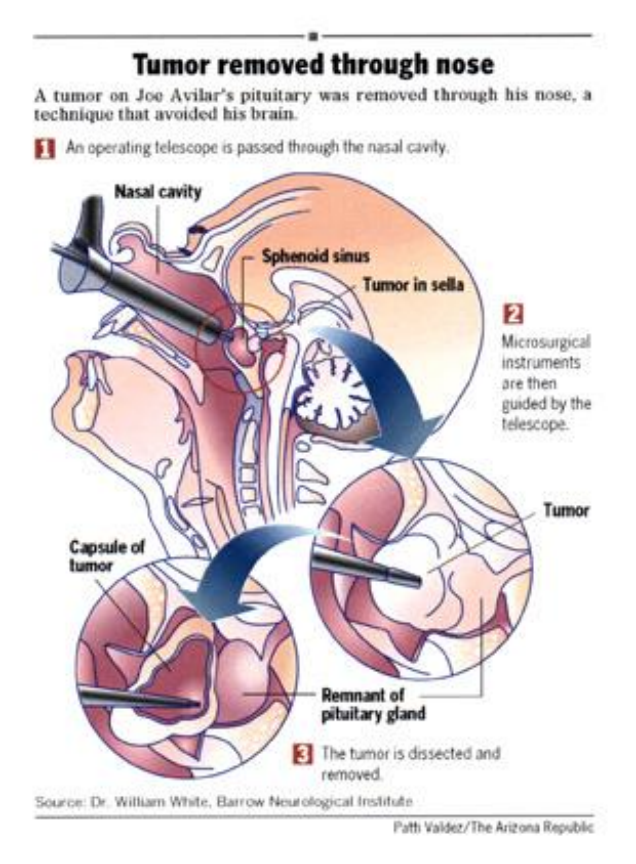
Radiotherapy

Dopamine Agonists

Growth Hormone Receptor Blockers

Melmed, 1998

Gigantism and Acromegaly
Treatment



http://www.thebni.com/index.asp?catid=au&pg=au_giant

Surgery

Preferred option if possible

70-90 % cure of disease in patients with microadenomas

20-50 % cure of disease in patients with macroadenomas

GH decrease is rapid post-op

IGF-1 decrease is delayed

> 40% of all surgical cases, however, result in inadequate control (GH> 5ng/ml)

Giustina, 2000
Melmed, 1998

Gigantism and Acromegaly

Treatment

Somatostatin Analogs: octreotide and lanreotide

- Longer lasting than somatostatin
- Octreotide half-life is 2 hours
- Requires TID dosing subcutaneous injection

Effective

- 95% of acromegalics see reduction of GH secretion
- 60% of patients see normalization of IGF-I

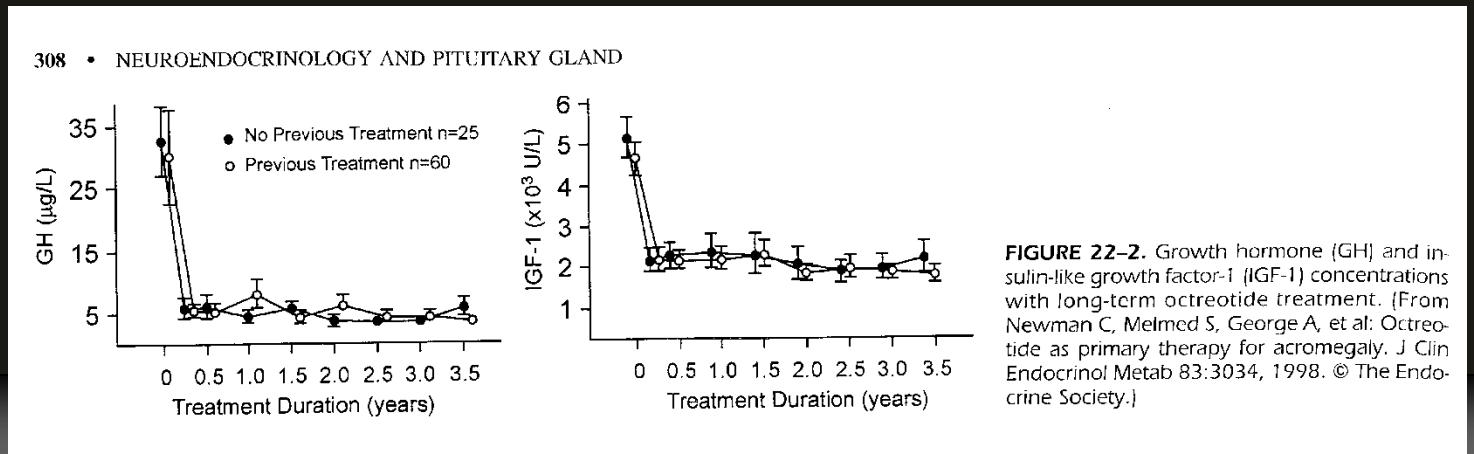


FIGURE 22–2. Growth hormone (GH) and insulin-like growth factor-1 (IGF-1) concentrations with long-term octreotide treatment. (From Newman C, Melmed S, George A, et al: Octreotide as primary therapy for acromegaly. J Clin Endocrinol Metab 83:3034, 1998. © The Endocrine Society.)

Melmed, 1998

Gigantism and Acromegaly
Treatment

Adverse Reactions to Octreotide

Cholesterol gallstones (25%)

Bradycardia (25%)

→ Usually Subclinical

GI distress → Usually NOT Subclinical

Melmed, 1998

Gigantism and Acromegaly

Treatment

octreotide

Sandostatin LAR® Depot

Once-a-Month Dosing

or

Somatuline Depot

Lanreotide

Slow Release Formulation Given I.M.

Sustainable levels for a four week period

Control in 70% of patients (who are sensitive to octreotide)

Shrinks tumor mass

Giustina, 2000

http://www.acromegalyinfo.com/prof_home/prof_home.html

Anna Swan and Martin Bates

"The Nova Scotia Giantess and the Kentucky Giant"

Swan 7 feet 5.5 inches

\+

Bates 7 feet 2.5 inches…

Married = 14 feet 8 inches

2 babies, both died near birth:
Giant Baby…

23 ¾ lbs, 30 inches long

http://bullseyedesigns.com/sideshow

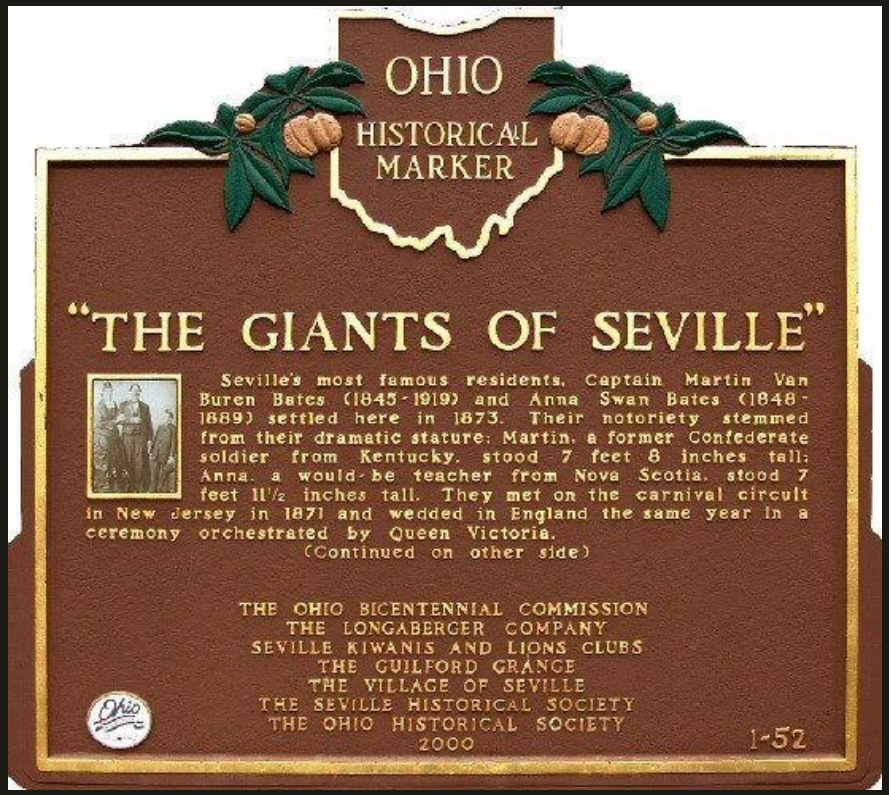
Martin Bates

1837-1919

Anna Swan

1846-1888

Martin Bates



Luckpostcards www.delcampe.net

Gigantism and Acromegaly
Treatment

- **Growth Hormone Receptor Blocker**
  - Pegvisomant (Somavert®)
  - Subcutaneous injection daily
  - Effectively reduces IGF-1
  - No effect on tumor mass
  - Similar cost of Sandostatin LAR
  - Can be added to Sandostatin tx or lanreotide

Gigantism and Acromegaly

Treatment

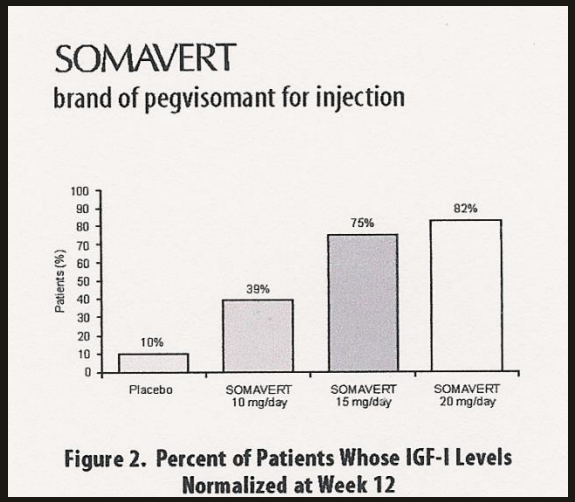


Figure 2. Percent of Patients Whose IGF-I Levels Normalized at Week 12

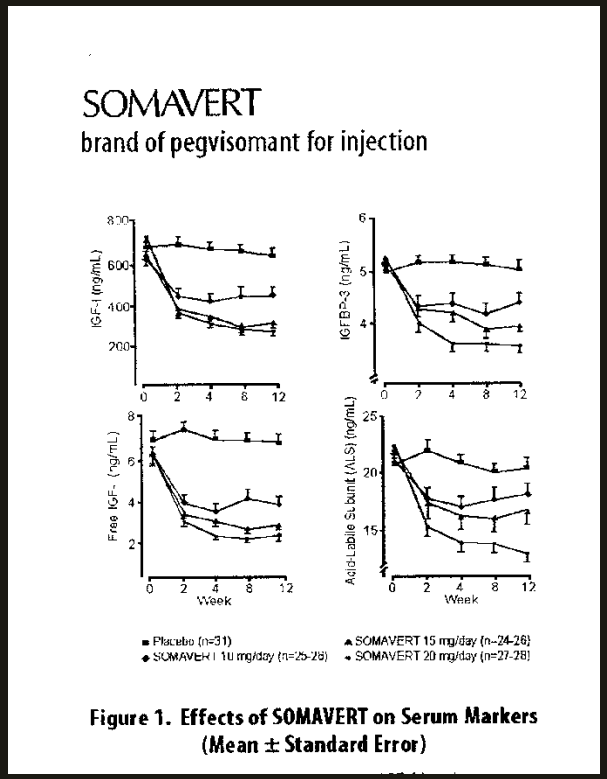


Figure 1. Effects of SOMAVERT on Serum Markers (Mean ± Standard Error)

Growth Hormone Receptor Blocker

Gigantism and Acromegaly
Treatment

Dopamine Agonists

- Pergolide, bromocriptine, cabergoline
- Inhibit secretion of GH in those with mammosomatotrophic tumor
- Poor efficacy
  - IGF-I levels normalize in only 10% of patients
- Many side effects

Melmed, 1998

Gigantism and Acromegaly
Treatment

Radiotherapy

- Delayed benefit (years)
- Only 50% controlled at 10 yr mark
- Potential for HP axis dysfunction
- Preliminary results of trials involving stereotactic radiosurgery are promising

Melmed, 1998
Giustina, 2000

Gigantism and Acromegaly

Treatment Follow-up

Labs at 6-12 weeks S/P treatment

GH : < 1 ng/ml

IGF-I : normalized

Assess other pituitary function

MRI

Visual Field exam

Giustina, 2000

Gigantism and Acromegaly
Treatment Follow-up

- Lifelong surveillance
  - Recurrence
  - Colonic polyps/cancer
  - Cardiovascular disease
    - Beta-blockers and ACE inhibitors/ARBs
  - Arthropathy

Guiness Book of Records 2008
World's Tallest Living Man

- **Fast Facts**
- Full name: **Leonid Ivanovych Stadnyk**
- Born: 1971 - 2014
- Resides: Podoliantsi, Ukraine
- Height: 8' 5.5"
- Occupation: Farmer

Refused to be remeasured in 2009,
so lost coveted title to:
Sultan Kosen of Turkey;
only 8'3' tall

Sultan Kosen of Turkey; 8’3’ tall

7. Which of the following statements regarding the tallest man that ever lived is FALSE?

A. His recorded height was 8’ 11’ tall
B. He worked in the same profession as Al Bundy (“Married with Children”)
C. He was born in Alton, Indiana
D. He wore size 37 ½ shoes
E. He died of septicemia

Robert Wadlow (1918- 1940)

"The Alton Giant"

The Tallest Man in History

Normal size (8.5 lbs) at birth

Age 5	5' 4"
Age 9	6' 2" (discovered by *Time*)
Age 10	6' 5" (210 lbs)
Age 11	6' 7" (dx with pituitary gigantism)
Age 14	7' 5" (301 lbs, tallest Boy Scout)
Age 16	7' 10" (plagued by leg injuries)
Age 18	8' 3" (attempted to attend college)
Age 19	8' 5" (joined Ringling Brothers)
Age 22	**8' 11.1" (439 lbs) prior to death**

Robert Wadlow
"The Alton Giant"

- Born in Alton, Illinois in 1918
- Diagnosed with pituitary abnormality at age 11 (surgery was deemed too dangerous)
- Earned income as a pitchman for a shoe company
- Had dreams of becoming a lawyer, but unable to function in college
- Joined Ringling Bros side show, but refused to have his height augmented
- Developed lower extremity cellulitis and died of sepsis in 1940

Robert Wadlow
“The Alton Giant”

In 1936
With siblings

Robert Wadlow

"The Alton Giant"

8 Feet 11.1" Tall

490 pounds

Summary

These growth disorders are rare but debilitating

While dwarfism and gigantism are clinically obvious, acromegaly may be more subtle

Identification of growth hormone excess early is amenable to treatment

Screen with IGF-1

Appropriate therapy can reverse morbidity and mortality

Association of skin tags, colon polyps and risk of colon cancer

References

Drimmer, F. Very special people. New York, Amjon Publishers, Inc. 1973.

Eugster, E. Commentary. Gigantism. The Journal of Clinical Endocrinology and Metabolism. Vol. 84, No. 12. 1999. Pgs. 4379-4384.

Giustina, A. et al. Criteria for Cure of Acromegaly: A Consensus Statement. The Journal of Clinical Endocrinology and Metabolism. 2000. Vol. 85, No. 2. Pgs. 526-529.

Hull, K. and Harvey, S. Growth Hormone Resistance: Clinical States and Animal Models. Journal of Endocrinology. 1999. 163. Pgs 165-167 (article ends on pg. 172).

Jenkins, P. Clinical Perspective. Acromegaly and Cancer: A Problem. The Journal of Clinical Endocrinology and Metabolism. 2001. Vol. 86. Vol 7. Pgs. 2935-2941

Laron, Z. The Essential Role of IGF-I: Lessons from the Long-Term Study and Treatment of Children and Adults with Laron Syndrome. The Journal of Endocrinology and Metabolism. 1999. Vol. 84, No. 12. Pgs. 4397-4404.

References

Maugens and Coates, Diagnosis and Treatment of Acromegaly. American Family Physician. July, 1995. Pgs. 208-211 (article starts on pg 207 and ends on 213).

Melmed,S. et al. Current Treatment Guidelines for Acromegaly. Journal of Clinical Endocrinology and Metabolism. 1998. Vol 83, No. 8. Pgs. 2646-2652.

NPR's All Things Considered, The Jewish Giant, 1999

Sotos. Overgrowth. Section II Hormonal Causes. Clinical Pediatrics. 1996. Pgs. 579-584 (article ends at pg 590).

Web sites…

References

http://arbl.cvmbs.colostate.edu/hbooks/pathphys/endocrine/hypopit/gh.html
http://hsc.virginia.edu/medicine/basic-ci/pharm/dab_…
lab/docs/course/pdf/slides.pdf
http://us.imdb.com/Name?Petursson,+Johann
members.tripod.co.uk/Bryvoski/ Bryvoski-net/Gallery/andre.jp
www.acromegalyinfo.com/prof_home/prof_home.html
www.altonweb.com/history/wadlow
www.amazon.com
www.angelfire.com/al/andrethegiant/bio.html
www.ashleighhotel.co.uk/chang.html
www.bullseyedesigns.com/sideshow/people/big_little
www.coloncancer.org/KF_01.jpg
www.denverbroncos.com/fanfare/ sesamest/davis3.html
www.driesen.com/pituitary_gland.htm
www.buffaloneuro.com/pittumo/ ENDOPI.HTM
www.enteract.com/~rosa/ prostatedrawing.html
www.fotw.ca/flags/is.html (Iceland Flag)

References

www.geocities.com/Hollywood/Makeup/6353/andre.htm
www.ghresearchsociety.org
www.globalmark.com/sandy/diff02.jpg
www.guinnessworldrecords.com
www.islandia.is/~juljul/ johann/johann_uk.htm
www.kumc.edu/.../medicine/pathology/ ed/ch_21/c21_s27.html
www.mc.vanderbilt.edu/peds/pidl/endocr/index.htm
www.movieweb.com/movie/mygiant
www.msnbc.com/news/602102.asp
www.orura.com/cards/p35.jpg
www.puroresu.com/wrestlers/andre/
www.roadsideamerica.com
www.talkinghistory.org/isay.html
www.tallwomen.org/tallest/
www.thebni.com/index.asp?catid=au&pg=au_giant
www.twinstuff.com/twinfact1.htm
www.umanitoba.ca/dnalab/med/pit2.gif
www.usc.edu/.../projects/comm544/ library/images/528bg.jpg