The neuroendocrine growth hormone clock and body mass

Are we programmed to grow to a certain size, to stop growing and to decay?
What is growth?

• Growth is the process through which the nutrient energy is assimilated into structural components of the body.
How many kinds growth are there?

• **Statural or incremental growth**
  – addition to the whole body mass
  – increases in height

• **Reparative growth**
  – maintenance of lean body mass
  – repairs of damage

• **Hypertrophic growth**
  – selective increase in the mass of organs
    subjected to increased functional demands
Statural or incremental growth

- What controls it?
- Genetic program (prenatal phase)
  - growth factors
  - nutrient abundance
- Neuroendocrine clock (postnatal phase)
  - prepubertal growth spurt
Statural or incremental growth

- How does human growth (———) compare to other mammals (———)?
Statural or incremental growth in humans

- early rapid growth
- slower growth during childhood
- growth acceleration around puberty
- cessation of growth
What programs the rate of statural growth?

- During prenatal and early postnatal growth
  - genetic program
  - nutrient abundance
Nutrient abundance and early statural growth

- Early development depends on abundance of energy
- If energy inadequate, growth is stunted
- Reversibility (catch-up) depends on timing of deprivation
Does exercise affect early statural growth?

- **Exercise represents energy drain**
- **Maternal exercise affects infant size**
  - body fat
  - no impact on skeletal growth
- **Young animals forced to exercise**
  - reduced fat-pad development
  - some growth stunting
- **Juvenile athletes in weight-sensitive sports are often underweight**
Is growth stunting by energy deprivation reversible?

- Depends on timing of deprivation
- The earlier the deprivation, the less it is correctable
- The later the deprivation, the greater is the catch-up growth
Development of capacity for catch-up growth

- With earliest energy deprivation little catch-up growth
- Energy deprivation at a later age is made up (through faster or catch-up growth)
Does exercise induce growth?

- Onset of puberty depends on
  - execution of some minimal amount of growth
  - attainment of some minimal body size
  - accumulation of some minimal amount of body fat
How is postnatal statural growth programmed?

• Through brain control of several growth hormones
  – growth hormone
  – insulin-like growth factor
  – thyroid hormones
  – sex hormones
    • estrogen
    • testosterone
What controls growth hormone secretion?

- The brain
  - hypothalamus
  - limbic forebrain
- GH releasing hormone
- Somatostatin
- Ultradian pulses
What determines GH pulses?

- **genes**
  - inheritance of tall or short stature due to GH

- **early nutrition**
  - epigenetic programming due to environment
What does GH secretion look like in adult humans?

- **Ultradian pulses**
  - caused by GHRF and SRIF
The role of growth hormone in growth

• GH action direct
  – cell differentiation
  – receptors for growth factors

• GH action indirect
  – expression of growth factors (IGF-I, EGF, HGF etc)
  – growth factors induce growth
Growth in length

- Endochondral growth from cartilage model
- Epiphysis and diaphysis calcify
- Growth persists in epiphyseal growth zone
- Closure at puberty
  - estrogen
More about growth-promoting action of GH

- Statural growth depends on GH pulsatility
- Growth is stimulated when high GH peaks are followed by low GH troughs
- In males this pattern is more clearly expressed than in females (genetic programming)
Does the pattern of secretion matter?

- Pulses stimulate growth of muscle and bone
- 3 and 9 GH pulses/day induced greater growth than 1 pulse/day
Pattern of GH secretion affects statural growth

- Pulses stimulate growth of muscle and bone
- Continuous GH does not
- Pulses also induce lipolysis
What stops or extends statural growth?

• Statural growth is extended if growth rate is slowed
  – underfed adolescents grow longer until they attain a “critical body mass”

• It is stopped after a “critical body mass” is attained
What stops or extends statural growth?

- Statural growth is stopped by a brain mechanism that inhibits secretion of hormones of growth.
- This inhibitory mechanism can be damaged and will reinstate rapid growth.
- Tissues must remain competent to grow.
What stops statural growth?

- **Initiation of puberty**
  - depends on “critical body mass”

- **Sex hormones (estrogen)** close the epiphyseal growth zone in humans
Exercise-induced weight gain is due to whole-body growth

- Skeletal elongation
Exercise-induced weight gain is due to whole-body growth

- Axial bone growth
- Appendicular bone growth
- Growth of the skull
- Growth acceleration by exercise starts when spontaneous growth slows
Can exercise induce whole-body growth?

- Running in adult hamster stimulates GH pulses
  - stimulates growth
- Abundant nutrition is necessary for growth expression
What causes acceleration of growth in exercising hamsters?

- Doubling of:
  - GH pulses
  - GH amplitudes
Can exercise stimulate statural growth in humans?

• Endurance exercise can act as energy drain and stunt instead of accelerating growth
• Endurance exercise can stimulate pulsatile GH secretion
Can exercise increase GH pulsatility in humans?

- 32-y old women
  - variable training intensity
- Increased GH pulse amplitude and daily secretion at high intensity

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Can exercise increase GH pulsatility in humans?

- Post-menopausal women
  - variable training intensity
- Increased GH pulse frequency and amplitude at high intensity
What regulates reparative growth?

• The same mechanism as in statural growth with anabolic hormone secretion turned down
• Adequate nutrition
• Adequate stimulation of hormones of growth
What regulates reparative growth?

- Nutritional control
What regulates reparative growth?

- Adequate stimulation of hormones of growth
- Exercise
  - intensity
  - type
- Specific nutrients
What controls hypertrophic growth?

- Mechanical loading of musculo-skeletal system
- Low dependence on nutrition
- Low dependence on hormones of growth
What is hypertrophic growth?

• Expression of genes for structural proteins and growth factors within the stimulated tissue
• Usually measured as increased mRNA production
GH is not necessary for hypertrophic growth (body building)

- Hypox rats
- Food-restricted rats both exhibit
  - muscle hypertrophy
  - increased expression of IFG-I genes
Does GH administration increase hypertrophic growth?

- GH abuse in athletics
- No selective increase in muscle mass
- No increase in muscle strength
- Increase in lean body mass as a whole
- Water retention
- Insulin resistance
Do other hormones during high-resistance exercise facilitate hypertrophy?

- Cortisol secretion?
- Androgen secretion?
- IGF-I secretion?
What is the function of exercise-induced GH surges?

- Metabolic?
- Reparative?
  - muscle
  - bone
  - conn.tissue
Dual effects of exercise on growth/GH secretion

- **Reparative or whole-body growth**
  - GH-dependent
  - diet dependent

- **Hypetrophic growth**
  - GH-independent
  - diet independent
Is growth programmed or is it determined by the environment?

- Can we alter period, pattern or duration of statural growth?
- Can we alter magnitude of reparative growth (and by consequence the rate of aging)?
- Does hypertrophic growth make a difference with respect to aging and longevity?