Chapter 12: Growth Hormones

Lecture 14

Growth: increase in size

1) hypertrophic: cells enlarge
2) hyperplastic: cells increase #s
3) extracellular matrix: production of intercellular substance

Growth Hormone (GH)

- source: anterior pituitary
- polypeptide: 191 aa \( C_{990}H_{1532}N_{262}O_{300}S_7 \)
- growth & cell reproduction: availability of materials
- binds to cell receptors
  - ↑ height & growth of all organs except brain
  - Ca\(^{++}\) retention
  - strengthens & ↑ bone mineralization
  - ↑ muscle mass: ↑ new muscle cells ↑ protein synthesis
  - ↑ lipolysis: ↓ adipose tissue (body fat)
Somatomedins

GH: growth of epiphyseal regions of long bones $\rightarrow$ incorporation of sulfur
Indirect effects on bone through sulfation factor

Somatomedin hypothesis:
under control of GH somatomedins promote incorporation of sulfate into cartilage

Somatomedins
plasma: insulin-like growth factors I & II (IGF – I & IGF – II)
source: liver

Peptides: similar to proinsulin
affinity to insulin receptors

↑↑ insulin $\rightarrow$ binds to IGF receptors
insulin $>$ IGF $\rightarrow$ metabolic effects
IGF $>$ insulin $\rightarrow$ cell proliferation
Structure of IGF-1

Black aa indicate identical positions as human insulin

Human Insulin

Structure of insulin & IGF receptors

Structurally related heterotetrameric glycoproteins
- two α subunits & two β subunits
- α subunits entirely extracellular with cysteine-rich domains
- β subunits transmembrane joined by disulfide bonds with tyrosine kinase domains
- 85% aa similarity in tyrosine kinase domains
Pathophysiology

Congenital hyposecretion → dwarfism

Children
hypersecretion → gigantism
growth failure & short stature

Adult
↓ strength
↓ energy
↓ bone mass
↑ cardiovascular risk

Adult: benign tumor of pituitary gland → adenoma
hypersecretion: diagnosis middle age adults → acromegaly
1) abnormal growth of hands & feet
2) facial bone growth
   protrusion of brow & jaw
   nasal growth of hands & feet
   teeth space out
3) arthritis
   overgrowth of bone & cartilage
4) carpal tunnel syndrome
   tissue thickens
5) body organ enlargement (heart)
Other acromegaly symptoms

6) joint aches
7) thick, coarse, oily skin
8) skin tags (benign skin growth)
9) enlarged lips, nose & tongue
10) deepening of voice: enlarged sinuses & vocal cords
11) sleep apnea—breaks in breathing during sleep due to obstruction of airway
12) excessive sweating and skin odor
13) fatigue & weakness
14) headaches
15) impaired vision
16) abnormalities of menstrual cycle & sometimes breast discharge in women
17) erectile dysfunction in men
18) decreased libido
GH receptor deficiency inbred Ecuadorian family

#8: 16 years old
#9: 21 years old
#10: 6.5 years old