Endocrine system Review

• Slow acting, far reaching effects
• Important in regulation of:
  • Water, electrolyte, energy balance
  • Growth and development
  • Reproduction & lactation
• Nervous/endocrine control overlaps tremendously
  – Hypothalamus (releasing/inhibiting hormones
  – Anterior pituitary (tropic hormones)
  – Target endocrine glands (thyroid, adrenal cortex, gonads)

What governs magnitude of hormone response?

• Secretion rate
• Excretion/degradation of hormone (1/2 life may be minutes to hours)
• Amount of binding protein in blood
• # or target cells (e.g. thyroidectomy to treat too much pituitary thyrotropin (Fig 18.12)

Response, cont.

• # of cell receptors
  – Up regulation
  – Down regulation
• "Down-stream events in hormone signal transduction
  – Type II diabetes (insulin resistance)
  – Early stages, insulin often high, but cells can’t respond

Hormones seldom act alone

• Synergism
  – Cortisol, glucagon and epinephrine all elevate blood glucose
  – Additive response greater than individual responses
• Push-pull dual control
  – Increase glucagon, decrease insulin to elevate blood glucose
• Permissive
  – Thyroid hormone necessary for growth

Cretinism: lack of iodine/thyroid hormone has developmental and growth effects

Hormone-receptor-target cell

Receptor: responsible for recognizing hormone, signal transduction

How hormones work

- Can they cross the cell membrane (lipid soluble)?
  - Steroids (e.g. testosterone, estrogens, progesterone, cortisol)
  - Thyroid hormones
- Can they NOT cross (water soluble)
  - Proteins (insulin, glucagon)
  - Amino acid chains (Anti-diuretic hormone)
  - Amino acid derivatives (epinephrine)

Lipid soluble hormones (Fig 18.3)

- “free” hormone can enter cell
- Binds to its receptor in cytoplasm or in cell nucleus
- Turns on specific genes in DNA
- New proteins (structural, enzymes)
- Response time may be minutes to hours

Water-soluble hormones need second messenger (Fig 18.4)

- One example of a common signal transduction pathway:
  - Membrane-bound receptor
  - Binding activates G-protein
  - Activate enzyme to make cyclic AMP
  - cAMP (second messenger) activates any number of other reactions in an amplifying cascade
    - Change membrane permeability
    - Activate enzymes
    - Make new protein

Diabetes mellitus (most common endocrine disorder)

- High blood sugar
- should be 80-120 mg/100ml, even after glucose ingestion

Diabetes really a heterogeneous collection of diseases

- At least 10 million people in the US
- ~10% have type I (insulin-dependent DM)
  - Destruction of beta cells in Islets in pancreas (autoimmune disease)
  - No insulin - must take insulin
- ~90% have type II (non-insulin dependent DM) “epidemic” in US
  - May have either high or low insulin, usually are “insulin resistant”
Type I DM - symptoms like starvation

- Role of Insulin/glucagon (Fig 18.19)
- Absorptive State - food in GI tract
  - High nutrients in blood, use glucose for energy, store excess as liver glycogen, lipids in fat (adipose) cells, or make proteins
- High I/G ratio promotes all the above
  - Use or store glucose, blood glucose levels drop if not eating

Post-absorptive state (several hours after eating)

- Falling blood glucose --> reverse I/G ratio
- Switch to burning fat for fuel
- Provide glucose for brain
- Make glucose from liver glycogen or from amino acids and fat breakdown products
- Most humans can fast for days while keeping blood glucose fairly constant

If there is no insulin (untreated IDDM):

- Cells can’t take up glucose and use or store it (lost in urine)
- Sugar in urine means you lose a lot of water in urine too (high volume of urine)
- Cells can’t make protein well
- Break down fat stores for energy
  - Ketoadidosis upsets acid/base balance
- LETHAL: dehydration, protein wasting, acid base imbalance, kidney failure, coma and death

Treatment of IDDM

- Insulin injections must mimic normal person (Intensive Insulin Therapy)
- Match the type and amount of insulin to the food consumed and the amount of exercise performed
- Multiple injections/day or insulin pump
- Measure blood sugar often
- Live a fairly normal life

Long-term effects of IDDM

- Regulate blood glucose on the high side (~150 ng/100ml) WHY?
- Vascular and heart disease common
- Retinopathy and blindness
- Infection rate high, gangrene and amputation
- Neuropathy, poor GI tract response to food (gastroparesis)

Type II (NIDDM)

- generally develops after ~age 50 associated with obesity in ~80% of people
- Insulin can be high, low, or normal
- multiple causes
  - beta cell unresponsive to high BG (rare)
  - target cells are “insulin-resistant”
- Strong genetic component, diet-related
- Treatment: weight loss, exercise, drugs to increase insulin secretion, exogenous insulin