Anatomy, Physiology & Homeostasis

- Anatomy: study of form
- Physiology: study of function
  - In essence, human physiology is the study of how the body perceives and achieves homeostasis

Homeostasis

- The regulation of the body’s fluid environment within a specific range of values, or around a set point
Fluid Environment

- Human body is ~70% water, by weight
- Human cells are ~70% water, by volume
- Homeostasis involves regulating this water, and this is physiology

Negative Feedback

- Homeostasis is generally achieved using negative feedback mechanisms
- “Deviation from a set point is resisted”
  - If the variable is too high, we act to lower it
  - If the variable is too low, we act to raise it
Negative Feedback

- Negative feedback loops require
  - Receptor (to sense stimulus)
  - Control center (to compare stimulus to set point)
  - Effector (to change the value of the stimulus variable)

Negative Feedback – Example

- Baroreflex: primary determinant of blood pressure
- Identify?
  - Receptors
  - Control center
  - Effector
Positive Feedback Loops

- If variable is increasing, the body acts to increase it more
- Requires a mechanism to break the loop

Positive Feedback Loops

- Uterine labor
  - Receptor: stretch receptors in cervix
  - Control center: hypothalamus and posterior pituitary gland (secretes oxytocin=OT)
  - Effectors: muscular wall of uterus (lots of oxytocin receptors)
  - Mechanism to break loop: after birth, stretch receptors no longer stimulated
Positive Feedback Loops

- Breast feeding
  - Receptor: mechanoreceptors in nipple
  - Control center: hypothalamus and posterior pituitary gland (secretes oxytocin)
  - Effectors: myoepithelial cells surrounding milk sacs
  - Mechanism to break loop: mechanoreceptor stimulation ceases

Regulation of Blood Gases

- Blood gases of interest: oxygen, carbon dioxide
- How do we regulate these?
Regulation of Blood Gases

- Most important equation in this course!

\[ \text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{HCO}_3^- + \text{H}^+ \]

- \( \text{pH} = -\log[\text{H}^+] \)
- Range: 0-14
- pH 7=pure water (neutral)
- Log scale, so a pH change of 1, reflects a 10-fold change in hydrogen ions (acidity)
- As hydrogen ions increase, pH goes down
• $H^+$ = an acid
• Definition of acid: anything that gives up $H^+$ in water
• Strong acids (HCl) dissociate into separate ions ($H^+$ and $Cl^-$) more readily in water
• Where are acids produced? And how?
Regulation of Blood Gases

- $\text{HCO}_3^-$ = a base (bicarbonate ion)
- Bases can collect extra $\text{H}^+$ to increase pH
- Can use the equation to alter pH, and to produce hydrogen and bicarbonate ions
- Where is bicarbonate produced?

Regulation of Blood Gases – $\text{CO}_2$

- $\text{CO}_2$ levels in blood drive breathing rate and depth
- Small changes in $\text{CO}_2$ levels result in rapid responses of changes in breathing
- Body uses breathing to eliminate extra $\text{CO}_2$ and to restore acid-base balance
Regulation of Blood Gases – CO₂

- The respiratory center increases ventilation when blood pH decreases.
- Decreased ventilation increases blood CO₂, which results in an increase in blood pH and hydrogen.
- Follow the red arrows when blood pH decreases.
- Follow the green arrows when blood pH increases.
- Increased ventilation decreases blood CO₂, which results in an increase in blood pH and oxygen.
- Follow the blue arrows when blood pH increases.

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Regulation of Blood Gases – O₂

- Although oxygen intake is a necessary part of respiration, O₂ levels don’t drive respiration the same way CO₂ levels do
- Human body is relatively unresponsive to O₂ changes until O₂ levels are seriously compromised

Regulation of Acid-Base Balance

- CO₂ + H₂O ⇌ HCO₃⁻ + H⁺
- Regulating CO₂ is regulating pH
- Eliminating CO₂ drives equation to the left, reducing free hydrogen ions, and raising pH
Regulation of Acid-Base Balance

Regulation of Nutrients

- Macronutrients = sugars, fats, proteins
- Glucose regulation is regulated by insulin and glucagon negative feedback loop
  - As blood sugar increases, the body acts to decrease it (insulin)
  - As blood sugar decreases, the body acts to increase it (glucagon)
Regulation of Glucose

- Pancreas directly evaluates blood sugar levels, when glucose levels are too high, the beta cells in the pancreas secrete insulin (hormone)
- Insulin binds to insulin receptors (on virtually all body cells)
- Insulin receptors tell cell to increase activity and number of glucose carriers, resulting in increased uptake of glucose into cells
- Result: blood glucose drops

Regulation of Glucose

- When glucose levels are too low, the alpha cells in the pancreas secrete glucagon (another hormone)
- Glucagon travels to areas of stored carbohydrates
- Glucagon activates an enzyme that stimulates glycogenolysis (chains of mostly glucose molecules)
- Result: blood glucose increases
Regulation of Glucose
Regulation of Glucose

- Blood sugar levels are constantly increasing and decreasing
  - Without meal, insulin secreted every ~20 min
  - Meals result in a large blood sugar increase, and thus a large increase in insulin secretion, followed by a hypoglycemic rebound
- For what part of the body is blood sugar regulation most important?

Regulation of Fats (Lipids)

- Most common storage lipid=triglyceride [TG] (glycerol molecule + 3 fatty acid [FA] chains)
- Lots of energy is stored in each FA/TG
- TG is unwieldy, so when the body needs to access energy, it breaks off the FA chains
Regulation of Fats (Lipids)

- The rate that the body converts TG into free FA chains using adipose lipase = the rate that FA becomes available for use
- What causes us to break TG into FA?

Regulation of Fats (Lipids)

- Factors that increase TG breakdown to FA
  - Low insulin levels (and therefore low glucose)
  - Epinephrine/norepinephrine (increase with stress and/or exercise)
  - Growth hormone
  - Thyroid hormone
Appetite Regulation

• Hunger center
  – Hypothalamus (hunger/satiety centers)
  – Major regulator of appetite in most animals
• What else influences our hunger? what we eat? how much we eat?

Appetite Regulation

• Leptin
  – Released from from adipose cells when they are full, reducing appetite
  – As adipose cells shrink (because TGs are being converted to FA and used), the leptin release decreases, stimulating appetite
  – Many obese people are leptin-resistant, but have high levels of leptin (receptor deficit)

Guess which mouse doesn't make leptin?
Regulation of Ion Concentration

• Cells use ion concentrations as a major mechanism of directing cell activity
• Sodium (Na\(^+\)) and potassium (K\(^+\)) ions are balanced by kidney (covered in more detail in A&P I)
• All cells, but especially neurons, work because of appropriate ion amounts inside and outside cell

Regulation of Ion Concentration

• Na\(^+\) levels higher outside the cell
• K\(^+\) levels higher inside the cell, but intracellular environment has a net negative charge
Regulation of Ion Concentration

- Muscle cell – example
  - When stimulated, Na⁺ channels open, allowing Na⁺ to rush in, the cell becomes positively charged and the voltage change results in muscle contraction
  - To reset the internal negative charge, K⁺ flows out of the cell through channels
  - What happens if there is a high [K⁺] outside the cell?

Regulation of Ion Concentration

- Muscle cell – example
  - Excessive [K⁺] concentrations in the extracellular fluid (ECF) result in cell's inability to reset and contract again
  - K⁺ levels evaluated by receptors on the adrenal cortex
  - Response: aldosterone secretion by adrenal glands
Regulation of Ion Concentration

Water exists in three compartments:
- Intracellular
- Interstitial (extracellular fluid=ECF)
- Blood

Regulation of Blood Volume
Regulation of Blood Volume

- What is the “normal” amount of blood?
- Where does fluid come from/go to?

- What are blood flow destination priorities?
  - BRAIN (nearly constant)
  - Heart (varies – why?)
  - Either (depending on demands)
    - Muscles and skin
    - Guts, kidneys, liver, etc.
Regulation of Low Blood Volume

- Decreased blood volume
  - Receptor: osmoreceptors sense high osmolarity (solute [salt] concentration) in ECF
  - Control center: hypothalamus
  - Effectors:
    - Thirst center neurons create thirst
    - Antidiuretic hormone (ADH) secreting cells of posterior pituitary act on kidney to conserve water in urine
Regulation of Blood Volume

• Increased blood volume
  – Receptor: stretch receptor in atrium
  – Atrial myocytes secrete ANF (atrial natriuretic factor or peptide)
  – Effectors: in response to ANF, kidneys excrete more Na⁺ and water follows, resulting in decreased blood volume
Regulation of Water Temperature

- Directed by autonomic nervous system (sympathetic vs. parasympathetic)
- Too warm? Direct blood to skin (dilating skin arterioles) while restricting blood to the guts and viscera [sympathetic]
- Too cold? Shunt blood to body core, constricting the vessels to the skin [parasympathetic]
Cancer

- Deviation from homeostasis: disruption in the number of and behavior of cells
- Overall lifetime risk of cancer diagnosis in US (ACS):
  - 50% for men
  - 33% for women
- Overall lifetime risk of cancer death in US (NCI):
  - 23% for men
  - 20% for women

Cancer

- In homeostasis, the growth rate of cells equals the death rate (even replacement)
- Cancer: abnormal net growth rate of tissue and abnormal behavior of cells
  - Cells stop dying off and/or reproduce too quickly
  - Cells stop differentiating and acquire ability to metastasize
  - All these changes accumulate to malignant cancer
Characteristics of Cancer Cells

- Lose contact inhibition
- Live longer than most cells
- Undifferentiated
- High metabolic rate
- All of these characteristics are the result of accumulated mutations
Cancer & Genetics

- All cancers are “genetic”
  - Cancer (abnormal and uncontrolled cell growth) is due to a series of mutations in DNA
- Not all cancer is “hereditary”
  - Most genetic mutations that lead to cancer are acquired over a person's lifetime
  - Roughly 5% of cancer death is attributable to inherited genetic mutations that predispose a person to a particular type of cancer

Cancer Progression

- Cancer is usually the result of the accumulation of multiple mutations, and the progression of disease process
- Finding cancer early (benign) or before much metastasis results in better outcome
Cancer Progression

- Prevention easier, more effective, and less expensive than treatment
  - Primary prevention (prevent cancer from occurring)
  - Secondary prevention (early diagnosis and treatment)
  - Tools for prevention? Screening/early detection?
• Carcinogens cause mutations
• Cancer typically multifactorial:
  – genetic predisposition
  – toxic chemicals
  – infection (HPV, H. pylori)
  – physical factors (trauma, radiation)

Attributable Causes of Cancer Death

Mechanisms of carcinogenesis

- Turning on dormant oncogene
- Conversion of proto-oncogene to oncogene
- Turning off tumor suppressor gene (TSG)