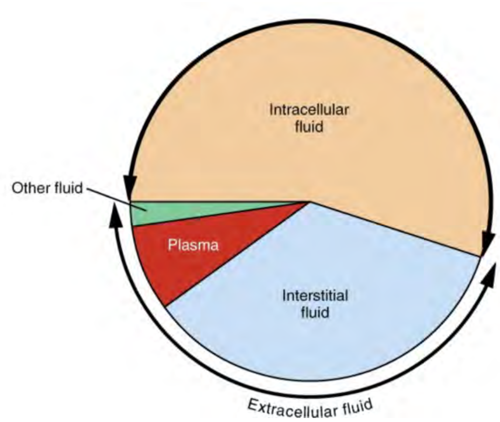
Chapter 1: Intro to Human Physiology and Principles of Homeostasis

1. **Physiology-** the science that deals with the functions of the living organism and its parts, and the physical and chemical factors and processes involved.
    a. The science of understanding how living organisms work
    b. Aim for a balance of organismic and reductionist perspectives
2. Cells are the basic unit of life
    a. Human organism is made up of 100 trillion cells
    b. Needs of a typical cell:
        i. source of nutrients
        ii. source of oxygen
        iii. elimination of wastes
        iv. maintenance of water and ions
    c. cells live in a fluid environment- extracellular fluid or internal environment
    d. all cells have 2 sets of functions (1) their essential cellular process and (2) a function specialized for the overall maintenance of the internal environment
    e. These 200 cell types fit into 4 categories: **muscle**, **neural**, **epithelial**, and **connective**
    f. The different systems involved in meeting the needs of a cell:
        i. respiratory system
        ii. digestive system
        iii. urinary system
        iv. circulatory system
        v. Integumentary system
        vi. immune system
        vii. nervous system
        viii. endocrine system
        ix. musculoskeletal system
        x. reproductive system
    g. 2/3 of this water is inside cells, the **intracellular fluid**. Of the 1/3 that is outside cells (**extracellular fluid**), about 80% is interstitial fluid, the rest being in the fluid phase of blood (**blood plasma**). These different fluids have different composition, and are kept compartmentalized.



3. homeostasis: the maintenance of constant conditions in the internal environment
    a. "constant"- for example, many physiological parameters vary across the day-night cycle, body temperature is higher during the day than at night. Homeostasis is the context of consistency for optimal function under a given set of conditions.
4. Physiological control strategies: 2 main ones- (1) negative feedback and (2) feedforward
    a. In negative feedback system, a parameter is monitored and if it changes some mechanism is activated to restore the parameter to its previous value.
    b. In feedforward system, the change in a parameter that would normally ensue from some event is compensated for before it occurs; i.e., the change is anticipated and prevented.
5. Themes:
    a. Balance: inputs and outputs are matched
    b. Integration: homeostasis requires the integrates actions of many body systems
    c. Intercellular communication: integration always requires communication, and in this case the communication is among cells of the body
    d. Movement of molecules across membranes: basis for much of physiology
    e. Compartmentalization: different compartments in the body have different compositions and mechanisms to keep substances compartmentalized
    f. Homeostasis and lack of homeostasis: the body continually tries to respond to these perturbations and compensate to remain in the homeostatic state. In the event that the compensation fails and the body fails to maintain the homeostatic state, that results in illness or disease.

Chapter 2: Membranes and the Movement of Molecules

1. Diffusion- the net movement of molecules of a specific substance from an area of higher concentration to an area of lower concentration, given enough time, the molecules will equally distribute in the space.
    a. At equilibrium, there is no net movement of molecules from one side to the other but molecules are still moving.
    b. flux one way is equal to the flux the other way
        i. influx (f_i)= $f_i – f_0$ or $F=A(C_0-C_i)$
            1. C_0 and C_i are the concentrations of the substance on either side.
    c. Diffusion has the following properties:
        i. Net movement of molecules down a concentration gradient
        ii. No energy (other than the concentration gradient itself) is required; diffusion is passive
    d. Factors that influence diffusion:
        i. Temperature: higher the temp, the more rapidly diffusion occurs
        ii. Mass of the molecule: the small the molecule the faster it moves
        iii. Surface area: the larger the surface area across which diffusion occurs, the more rapidly it occurs
        iv. The medium: diffusion occurs more rapidly in gas than liquid due to the density of molecules and therefore frequency of collisions
        v. The rate of diffusion is proportional to the surface area and the difference in concentrations
        vi. Speed: diffusion times increase in proportion to the square of the distance
2. Diffusion through membranes
    a. Membrane is a lipid bilayer
        i. Impermeant to charged or polar molecules (membrane serves as a barrier to diffusion)
        ii. Many organic molecules that the cell needs (glucose and amino acids) are polar enough to preclude diffusion through a lipid bilayer membrane
            1. Permeability=0
        iii. Small lipophilic molecules (oxygen) pass freely through the membrane as if it weren't there
            1. Permeability= infinity

iv. Bilayer contains protein. Typically 20-40% of the membrane is protein. They span the entire membrane and form pores or channels through which small molecules can pass
    1. Properties of membrane channels:
        a. channels are made of a protein or group of proteins
        b. channels are selective for specific ions or group of ions and this is based on charge and size
        c. movement of molecules through channels is by diffusion
        d. channel proteins are frequently regulated proteins that can, in response to appropriate stimuli, change their conformation thereby switching from closed to open states or visa versa.
            i. Regulated by the presence of certain chemicals - ligand gated (or chemically-gated) channel
            ii. regulated to stretch of the membrane - stretch or mechanosensitive channel
            iii. regulated by the electrical charge across the membrane - voltage gated channels

3. Transport through membranes
    a. Transporter- membrane protein whose job it is to bind to glucose molecules in the extracellular fluid and transfer them across the membrane into the cell. (mediated transport).
        i. 3 factors affect the rate of mediated transport:
            1. Relative affinity (how much versus how high an affinity)- how tightly the molecule and transporter interact with each other.
            2. How many transporters
            3. How fast the transporter works
        ii. Types of mediated transport:
            1. Facilitated diffusion: solely driven by the diffusion gradient. Facilitated diffusion can result only in the net movement of the solute down its concentration gradient toward equilibrium.
            2. Active transport: utilizes energy derived from cellular metabolism to drive the transport process. Allows molecules to be moved

from up a concentration gradient from a lower to a higher concentration (pump molecules against the gradient).

a. Primary active transport- hydrolysis od ATP is involved directly
b. Secondary active transport- driven by an ion concentration gradient that was set up by a primary active transport process

b. Primary active transport- 4 key active transporters
    i. **Na^+,K^+-ATPase** (commonly called the sodium-potassium pump- high intracellular K+ concentration and low intracellular Na+ concentration. For every ATP used, 3 Na+ ions are transported out of the cell and 2 K+ ions are transported into the cell.
    ii. **H^+ (or proton) transporter-** located in plasma to pump H+ out and is also present in various organelle membranes where it pumps H+ into the organelle.
    iii. When we talk about acid secretion in the stomach, we mean the transport of H+ provided, in this case, by the **H^+K^+-ATPase**.
    iv. **Ca^{+2}-ATPase** or calcium pump: responsible for the transport of Ca++ across membranes.

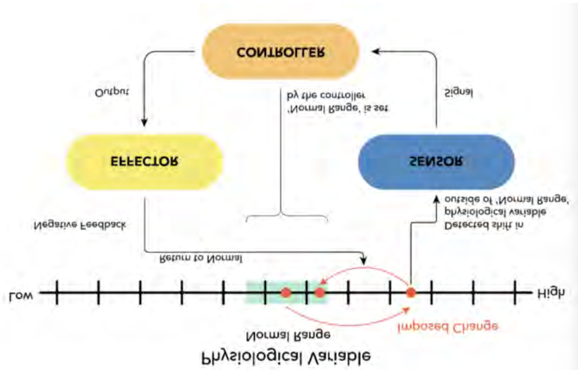
c. Secondary Active transport- Most secondary active transporters are driven by the Na+ gradient established by the Na+,K+-ATPase.
    i. Co-transport- solute being transported alone with the ion driving the secondary active transport
    ii. Counter transport- the transported solute is transported in the opposite direction
d. Vesicular transport- some substances are transported into or out pf ells by vesicles
    i. Exocytosis- vesicular membrane fuses with the cell membrane, the contents of that vesicle would be released into the extracellular fluid
    ii. Endocytosis- cell membrane engulfs extracellular substances, and then that section of plasma membrane pinches off into the cell

4. Movement of water- despite its polar nature, water readily diffuses through biological membranes. Auaporins are water channels in the membranes.
    a. The process of water moving down its concentration gradient is osmosis.
    b. We typically talk about solutes not water, but as the solute concentration goes up, the water concentration (by definition) goes down.
    c. Osmolarity; 1 osmole is equal to 1 mole of solute. Osmolarity is the number of moles of solute per liter
        i. The higher the osmolality, the lower the water concentration

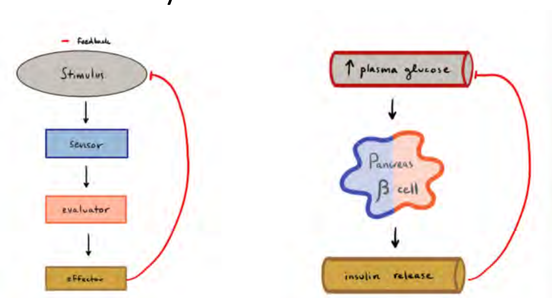
        ii. If the osmolality of one solution is equal to that of another, then they are said to be isosmotic.
        iii. If the second solution has a higher osmolality it is said to be hyperosmotic
        iv. Lower- hypoosmotic
        v. A normal solution is approximately 290 milliosmolar
    d. Tonicity and Osmotic pressure
        i. Osmotic pressure is the pressure that must be applied to counteract the osmotic flow of water.
        ii. Tonicity- expression of relative osmotic pressure between 2 solutions.
            1. Word stems for Latin meaning to stretch.
5. Epithelial transport- movement of molecules across sheets of cells that line various compartments of the body
    a. Channelopathies- in cystic fibrosis there is a malfunction of channelopathies-
        i. Loss of its function results in reduced chloride transport across certain epithelial cell linings, including the lungs. Reduced Cl- transport reduces the osmotic movement of water as well, and this results in a thickening of the mucus secreted in the airways causing a variety of respiratory problems.

Chapter 3: Physiological Control Systems and Cell-Cell Communication
Homeostasis: “dynamic constancy”- things are constant over a long time frame but are more dynamic over a shorter time frame.

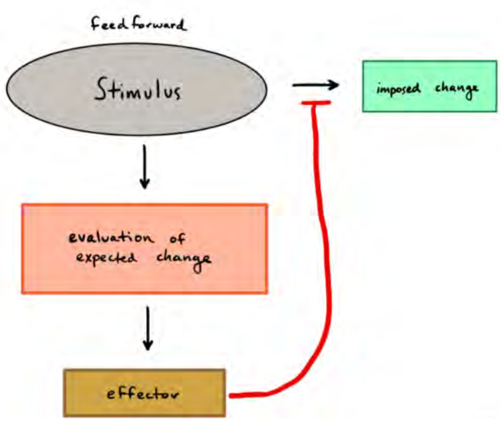
1. Negative feedback systems- works around an error signal to approximate the set point of operating point.



- The minimal necessary components of a negative feedback loop are:
  - A signal detector
  - An evaluator system
  - An effector system



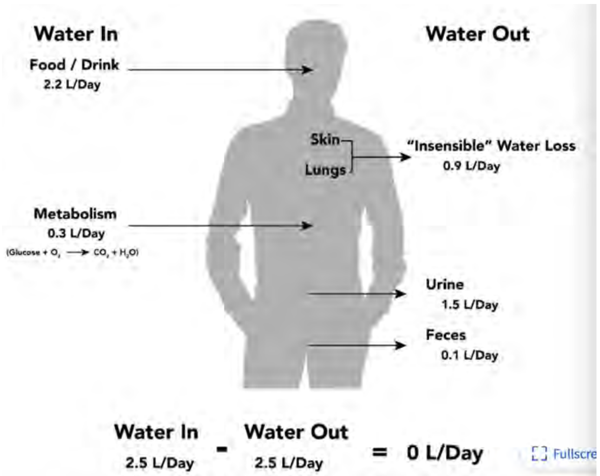
2. Feed Forward system- systems that exists to compensate for changes before they occur
   a. Example: when you stand up, gravity acts to pull blood to your feet and away from your brain, but the cardiovascular system adjusts prior to any decrease in blood flow to the brain



3. Positive feedback system- a change promotes further change in the same direction

a. Think about the process of giving birth: once it starts it keeps moving toward completion. However, as components of responses, positive feedback systems can, in some instances, contribute to physiology; an obvious example of this is the process by which blood clots, which is a non-homeostatic process (pushing clotting to completion), that contributes to reducing blood loss in response to injury.
b. Positive feedback systems are inherently non-homeostatic

4. Concept of balance- on an organismal level, input must match output



5. Intracellular communication- communication between cells occurs by one of 2 means: chemical or electrical
   a. Chemical signaling- a chemical is produced by one cell influences the processes in another cells
   b. Electrical signaling- changes in the electrical gradient across the membrane of one cell directly influences the electrical gradient across the membrane of another cell
   c. Intercellular signaling can also be classifies into three modes, direct contact, local diffusion, and long distance
6. Direct connections between cells- cells in direct contact with each other might pass signals by being directly coupled through gab junctions, where small molecules are able to pass directly between cells
   a. Cells are electrically coupled, since ionic fluxed in one cells are directly conveyed to the other.
   b. Jap junctions are made up of a type of protein called connexins
   c. Gap junctions are constructed by six connexin monomer proteins that arrange into a channel called the connexon. The full junction is formed as two connexons from adjacent cells align. Gap junctions all ions and small solutes (up to ~1 kDa) to pass between cells.
7. Direct cellular communications in interactions between proteins in the cell membranes of 2 cells
   a. Important in tissue integrity, immune function, development, etc.

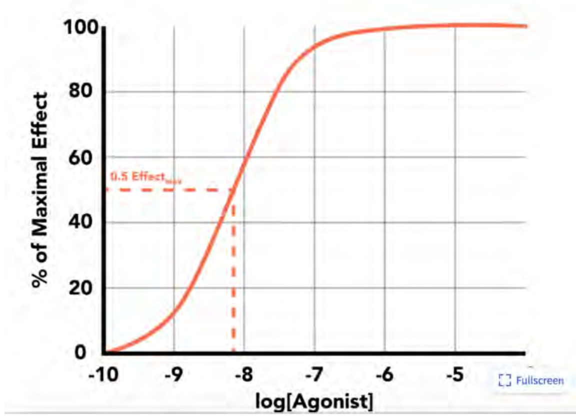
8. Chemically-mediated intercellular communication- one cell secretes a chemical that acts on another cell
    a. Paracrine signaling: chemical released into interstitial fluid to influence cells within a localized area of diffusion.
        i. autocrine is also used to refer to this type of localized communication but specifically among cells of a similar type
    b. endocrine signaling or hormonal signaling: chemical messenger distributed to the entire body by way of the blood stream
    c. neurocrine or neurotransmission: chemically-mediated transmission between neurons or neurons and their effector targets.
    d. Neuroendocrine- a neuron releases it's signaling molecule into the blood
9. Classification based on the type of tissue sending the signal
    a. Another system of classification based on the type of cell or tissue from which the signal arises
    b. The term cytokine, for example, refers to a signaling molecule released by a cell of the immune system. Cytokines released by a cell can act as a paracrine, or endocrine, or both. Most tissue types release signal molecules, so we can talk about adipokines released from adipose cells (fat) or myokines released from muscle cells
    c. Indeed, the notion that signaling molecules are used in multiple sites in multiple ways seems to be more the rule than the exception.
10. Components of chemically-mediated signaling
    a. 3 components
        i. The messenger molecule
        ii. What causes the cell to release the messenger chemical
        iii. How does the molecule get from the sending cell to the responding cell
        iv. How is the responding cell influenced by the messenger
    b. Messenger molecules
        i. Either regulated synthesis or regular release.
        ii. Some messenger molecules, for example small charged molecules or peptides, are synthesized, stored in vesicles, and released by exocytosis in response to appropriate signals. Other messenger molecules, for example prostaglandins or nitric oxide or steroid hormones are synthesized on demand and diffuse across the cell membrane out of the cell.
    c. How do these signaling molecules move among cells?
        i. Diffusion is key. For paracrine signaling, the signaling molecules will diffuse away from the release sites to impact nearby cells
        ii. Endocrine signaling would involve diffusion of the hormone into blood then into the interstitial fluid
    d. How do cells respond?
        i. Signaling molecules must interact with a receptor in order to elicit a response

1. Receptors are proteins that specifically bind to the messenger molecule and the interaction between the messenger and this protein elicits a response.

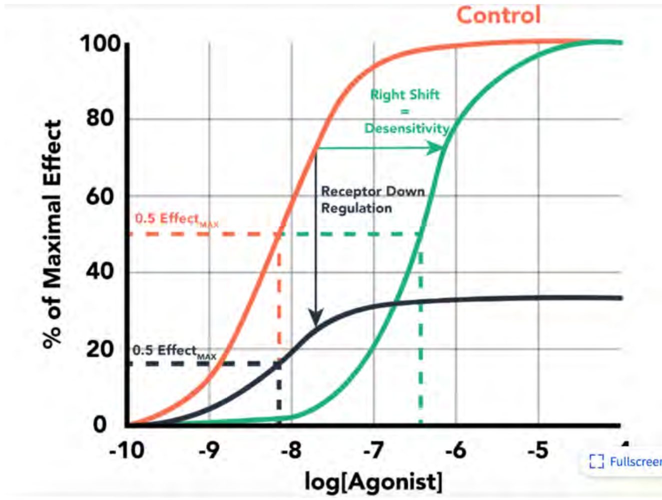
e. Nuclear receptor signaling
    i. Lipid soluble signaling molecules that can freely diffuse through lipid membranes and bind to intracellular receptors.
    ii. Slow responses
f. Membrane- bound receptors
    i. Responses mediated by the membrane bound receptors can be divided into 2 main classes: ionotropic and metabotropic
        1. Ionotropic receptors: mediated by ligand gates ion channels, where the signaling molecule binding to the receptor causes the opening (or closing) of an ion channel and the cellular response being mediates by the flow of ions through the channel.
            a. Ionotropic responses tend to be rapid in onset and offset
        2. Metabotropic receptors: receptors that are linked to enzymes inside the cell. Binding of the signaling molecule to the extracellular side of the receptor results in some change being transduced intracellularly.
            a. Signaling cascades- biochemical signaling the transduces the signaling molecule interacting with the membrane-bound receptor, as one biochemical step leads to another
            b. Signal amplification- the initial effect of one signaling molecule acting on a receptor can be amplified to a larger cellular response
            c. Second messenger- next step in transduction pathway
            d. Membrane bound metabotropic receptors can be classified into three broad categories: receptor-enzymes, integrin receptors, and g-protein coupled receptors.
                i. G-protein couple receptors- binding of an agonist the receptor will cause dissociation of g-protein complex, with various g-protein subunits binding to other membrane. Such interactions, channels resulting in them opening or closing, or can change the conformation of other structural proteins.
            e. Ca++ as a "second messenger"- Increases in cytosolic Ca^{++} can serve as an important 'second messenger' that initiates other cellular responses, and many examples of this will come up throughout the course.
        3. Receptor related terms to know:
            a. Receptor- the protein to which the signaling molecule binds to initiate a response
            b. Ligand- a molecule that binds to a receptor

c. Agonist-antagonist- an agonist is a ligand for a receptor that initiates a response. An antagonist is a ligand for a receptor that prevents an agonist for eliciting a response.
d. Specificity- refers to how selective a receptor is in terms of how specific it is for a certain ligand
e. Saturation- refers to all of the binding sites being bound to a ligand
f. Affinity- how tightly the ligan and receptor bind to each other
g. Competition- refers to how different ligands may interact in binding to a binding site
h. **up-regulation, down-regulation, supersensitivity** - refer to changes in responses of cells to signaling molecules. Up and down regulation refer to increasing or decreasing the number of receptors and therefore the maximal response that can be generated by an agonist. Supersensitivity refers to an increase in agonist affinity, such that lower concentrations of an agonist elicit a greater response.

ii. Concentration- response curve- Note that as the concentration of the agonist increases, the effect (you can also picture this as percent of the receptors that are bound to agonist) increases, but it can only increase to 100%, the point at which receptors are saturated with agonist. We can describe the affinity of the receptor for the agonist as the concentration of agonist that causes a half-maximal response (or 50% of the receptors being bound).



1. However, don't picture concentration-response curve for an agonist in a given system as a constant. Rather, things might change. One type of change is the number of receptors expressed on the membrane. For example, if the number of receptors were to decrease, the maximal response would also decrease, but the EC50 would not change. The is reflected by the curve in black in Figure 3.14B below, representing receptor down-regulation.



g. What determines if a cell responds to a messenger?
    i. Whether or not it had a receptor and whether the messenger is present in sufficient concentration to influence a sufficient number of receptors to elicit a response
h. What determines what the response will be?
    i. changes in the permeability, transport properties, or electrical state of the cell membrane
    ii. changes in the cell's metabolism; changing enzyme activities or which enzymes the cell makes
    iii. changes in the cell's secretory activity
    iv. changes in the cell's contractile activity (muscle)
i. cell signaling in the context of physiological control systems
    i. The baroreceptor reflex (a negative feedback reflex maintaining a normal arterial blood pressure: example of increased blood pressure slowing the heart. There are sensory cells responding to stretch on the walls of the major arteries. The nerve cells signal other nerve cells in the brain which in turn signal other nerve cells that signal the heart and blood vessels.

Overview of the Endocrine System

1. Endocrine system- one of the two major systems of intercellular communications (nervous system is the other) acting to regulate and integrate organ systems.
    a. Comprised of endocrine glands and the hormones they secrete. It would not work without blood, that is how messenger molecules are distributed to their target tissues or target cells.
    b. There must me target tissues with receptors for these hormones.
2. What sets it apart from other forms of signaling?
    a. Circulation in blood
    b. Some of the same molecules are used as neural signals and endocrine signals
    c. Neural is more rapid precise responses, endocrine is slower, suited for regulation of internal environment
3. 6 major classes of processes regulated by the endocrine system
    a. Regulation of metabolism, water, ions
    b. Response to stress
    c. Smooth, sequential growth and development
    d. Reproduction
    e. Maintenance of blood cells
    f. Integration with the autonomic nervous system in control of physiological systems
4. Hormones

Gland/Tissue	Hormone(s)	Target(s)	Action(s)	Chemical class
Adipose tissue	Leptin, others	Brain, others	Regulation of feeding, metabolism	peptide
Adrenal cortex	Aldosterone	Kidneys, others	Na^+ and K^+ homeostasis	steroid
	Cortisol	Many tissues	Glucose utilization, stress response	steroid
Adrenal medulla	Epinephrine/ norepinephrine	many	Many; "fight or flight response"	catecholamine
Gonads (ovaries, testes)	Ovaries: estrogens, progesterone	many	Female sexual characteristics, others	steroid
	Testes: testosterone	many	Male sexual characteristics, others	steroid
Heart	Atrial natriuretic hormone	Kidneys, blood vessels	Excretion of Na^+ and water	peptide
hypothalamus	Many; see section in text on hypothalamus-pituitary	Anterior pituitary	Stimulate or inhibit the release of anterior pituitary hormones	Peptides (with one exception)
Kidneys	Erythropoietin	Bone marrow	Regulation of red blood cell production	peptide
	Renin (generating Angiotensin II)	Adrenal cortex, blood vessels, kidneys	Control of aldosterone secretion, constriction of blood vessels, Na^+ and K^+ handling by kidneys	Protein, generating peptide
Pancreas	Insulin, glucagon, others	many	Glucose metabolism; metabolism of other nutrients	peptide
Parathyroid gland	Parathyroid hormone	Kidneys, bone	Ca^{++} homeostasis	peptide
Pineal gland	Melatonin	Brain, others	Circadian rhythms	Serotonin derivative
Pituitary, anterior	Many (see text)	Other endocrine tissues	Control of many hormones, other	peptide
Pituitary, posterior	Antidiuretic hormone	Kidneys (also blood vessels)	Control of water excretion, blood volume, blood pressure	peptide
	Oxytocin	Uterus, breast, others	Parturition, lactation, other	peptide
Stomach, small intestine	Several (see text)	GI tract and associated tissues	Control of digestion	peptide
Thyroid	Thyroid hormones (T3, T4)	Many	Metabolism	Unusual tyrosine derivative
	Calcitonin	bone	Ca^{++} and phosphate homeostasis	peptide

5. Chemical nature of hormones:
    a. Hormones fall into 3 general chemical structures
        i. Peptides/ proteins
        ii. Steroids
        iii. Amines
        iv. A couple outliers (thyroid hormones, melatonin)
    b. Peptide hormones
        i. Peptide and protein hormones are commonly encoded with additional sequences as signal peptides with other proteins that aid in vesicle storage.
        ii. Peptide hormones are made by normal protein synthesis machinery and then cleaved into smaller peptide hormones while they are stored in vesicles
        iii. Secreted by exocytosis
        iv. Act on membrane-bound receptors, the vast majority of which are G-protein coupled receptors
    c. Steroid hormones
        i. All steroid hormones have a basic steroid structure and are all synthesized from cholesterol
            1. 4 ring structure
            2. Small alterations on the side chains produce huge differences in function because they are recognized by different receptors
        ii. Steroid hormones can be classified in 3 groups:
            1. Mineralocorticoids- the main one in humans is aldosterone. It is critical in the regulation of "minerals"- Na^+ and K^+ ions. Released by cells in adrenal cortex
            2. Glucocorticoids- main one in humans is cortisol. Involved in regulation of glucose metabolism in cells. Released by cells in the adrenal cortex but cells are different from the aldosterone-releasing cells
            3. Sex steroids- testosterone and estrogens
    d. Catecholamines
        i. Dopamine, norepinephrine, epinephrine are 3 signaling molecules that share the general catecholamine structure
        ii. Synthesized enzymatically from the amino acid tyrosine.
        iii. Some cells have only the enzymes needed to make dopamine, whereas other cells convert dopamine to norepinephrine and yet other cells convert norepinephrine to epinephrine.
        iv. Catecholamines are stored in vesicles and secreted by exocytosis in response to appropriate stimuli.
        v. Catecholamine hormones, all act via membrane-bound receptors (as might be expected from the charged nature of the compounds) and these are all G-protein coupled receptors.
    e. Thyroid hormones

        i. Thyroxine, also called T4, and triiodothyronine, also called T3, are the primary hormones of the thyroid gland and are involved in regulating basal metabolism.
        ii. Thyroglobulin (TG) is produced by normal protein synthesis mechanisms in the thyroid follicle cells. It is then secreted along with iodine that is taken up by thyroid cells (via secondary active transport), into the follicle lumen of the thyroid gland.
        iii. Thyroid hormones act on intracellular receptors and the action of these hormones is mediated through gene transcription.
    f. Melatonin
        i. Melatonin, the hormone of the pineal gland, is synthesized enzymatically from the amino acid tryptophan
        ii. Melatonin is involved in the regulation of circadian processes
    g. Release is differently regulated for these different chemical classes of hormones
        i. Thyroid hormones: cleavage from colloid
        ii. Catecholamines (and melatonin): exocytosis from vesicles
        iii. Peptides: exocytosis from vesicles
        iv. Steroids: secreted as synthesized
            1. Still, however, it is that the hormone gets secreted by the cell, it diffuses away from the cell, down its concentration gradient, into blood. Once in the bloodstream, it circulates throughout the body, diffusing out of blood into tissue, down its concentration gradient.
6. Hormone action on cells
        i. thyroid hormones and steroids have intracellular receptors and act on genome (though steroid hormones can also have 'non-classical' rapid actions via membrane receptors).
        ii. Catecholamines and proteins have surface receptors, coupled to cell processes. These are typically (though not always) G-protein coupled receptors.
    b. What can hormones acting on these receptors do to cells?
        i. alter the activity of certain enzymes
        ii. alter the membrane permeability or transport of specific molecules
        iii. alter the proteins which the cell expresses; action at the genes
7. what determines the blood level of hormone (and thus the concentration reaching the tissue?
    a. Since hormones circulate in the blood, all cells in the body are exposed to essentially similar concentrations
    b. Whether or not it has a receptor and whether the messenger is present in sufficient concentration to influence a sufficient number of receptors to elicit a response.
    c. Secretion rate influenced the level of the hormone.
    d. The signals that influence secretion rate
        i. Changes in the concentration of ECF ions (sodium, potassium, hydrogen)

ii. Changes in the concentration of ECF organics (glucose)
iii. Neurotransmitter
iv. Other hormone
v. Stretch?

e. Control of hormone secretion by negative feedback
   i. The control of secretion of many hormones is by simple negative feedback regulation. In many instances, there is also feedforward control. In some cases, positive feedback is involved (e.g., in the case of parturition).

8. Hormone transport in blood
   a. Water- soluble hormones are often transported through the body dissolved in plasma.
   b. In contrast, some lipid-soluble hormones (e.g., steroids) and thyroxine are transported through blood loosely bound to transport or carrier proteins.
   c. Inly free hormones are able to diffuse out of the blood stream and interact on target cells
   d. The free pool is in equilibrium with the bound pool, and so as blood flows through tissues, and the some of the hormone in the free pool diffuses out of the blood, hormone in the bound pool dissociates from the protein it is bound to. This effectively slows the rate at which hormone diffuses out of blood and limits the concentration gradient driving diffusion.
9. Hormone clearance from blood
   a. Hormone levels in blood decline as a result of metabolism and excretion.
   b. Some hormones stay around in the blood much longer than others and therefore have a longer duration of action following secretion.
      i. Half-life- the length of time it takes for the hormone level to decrease by half
   c. Binding of hormones to carrier proteins tends to slow the clearance of the hormone (same as it slows the diffusion from the blood)
   d. Most hormones are inactivated by metabolism but some are activated:
      i. converting an inactive precursor to active hormone, as in the case of angiotensin II production in blood
10. Pituitary gland- master controller of the endocrine system

	Hormone	Major action
Posterior Pituitary		
	Antidiuretic hormone (ADH) (also called vasopressin)	Acts on kidneys to cause water reabsorption; constriction of blood vessels
	Oxytocin	Acts on uterus to promote parturition and on breasts to promote lactation, other?
Anterior Pituitary		
	Adrenocorticotropic hormone (ACTH)	Acts on adrenal cortex to stimulate cortisol secretion
	Thyroid stimulating hormone (TSH)	Acts on thyroid to stimulate thyroid hormone secretion
	Growth Hormone (GH)	Promotes growth, many tissues
	Gonadotropins, LH and FSH	Acts on gonads to promote sex steroid secretion
	Prolactin	Acts on breasts to promote lactation. Other?

a. Anatomy of the pituitary and hypothalamus
    i. The pituitary lies underneath the brain, embedded in the sphenoid bone

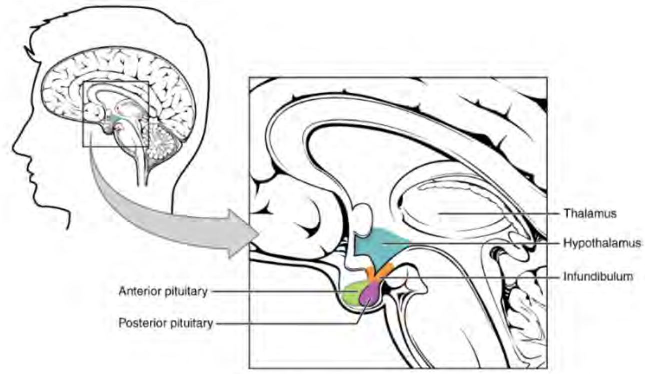


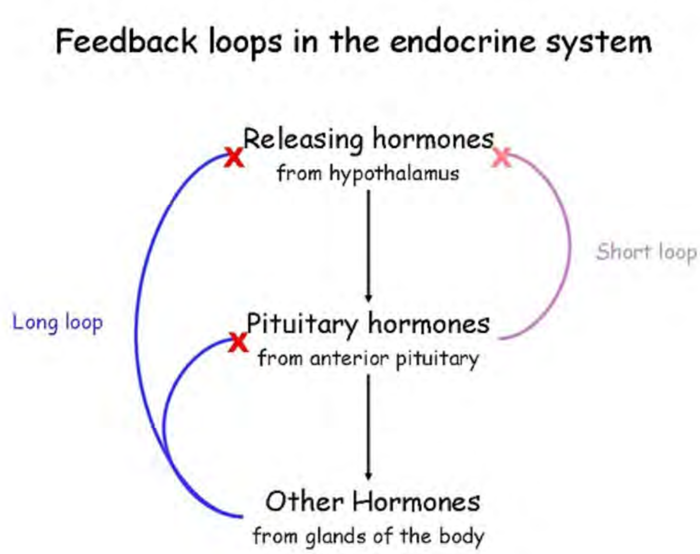
Figure 4.8. Pituitary gland

b. The pituitary is really two distinct structures residing next to each other. The anterior pituitary gland (in front) and the posterior pituitary (behind).
c. The hypothalamus, a region of the brain that lies just ventral to thalamus in the diencephalon, contains many regions (nuclei) that are distinct both anatomically and functionally
d. The hypothalamic nuclei that are most important in the context of the posterior pituitary are the paraventricular and supraoptic nuclei. The hypothalamic nuclei that are most important in the context of the anterior pituitary gland are the paraventricular nucleus (though different cells that are involved with the posterior pituitary) as well as the arcuate nucleus and preoptic nucleus, plus the median eminence.
e. neurons in the paraventricular and supraoptic nuclei send projections (axons) through the pituitary stalk to terminate in the posterior pituitary. The two posterior pituitary hormones, antidiuretic hormone (ADH, also called vasopressin) and oxytocin, are synthesized by distinct cells in the paraventricular and supraoptic nuclei. These protein hormones are then transported in the axons to the posterior pituitary, where they are stored until released.
f. In contrast, the hypothalamus is connected to the anterior pituitary gland by an unusual portal circulation. In a portal circulation, two capillary beds are connected in series, such that blood from one tissue flows directly to a second tissue.

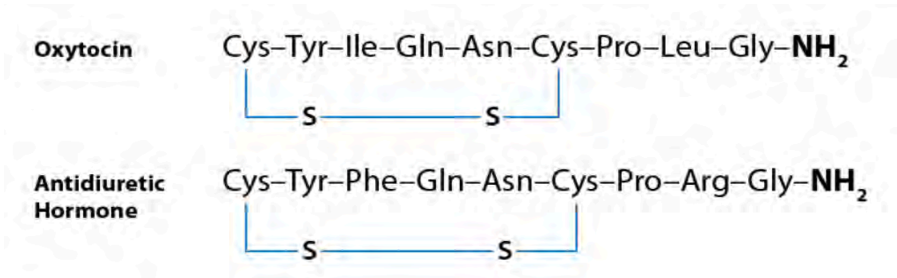
11. Hypothalamic hormones either stimulate (**releasing hormones**) or inhibit (**release inhibiting hormones**) the secretion of anterior pituitary hormones.

Hypothalamic Hormone	Production	Effect/Anterior Pituitary
Thyrotropin-releasing hormone (TRH)	Parvocellular cells - paraventricular nucleus	TSH and prolactin release
Corticotropin-releasing hormone (CRH)	Parvocellular cells - paraventricular nucleus	ACTH release
Growth hormone - releasing hormone (GHRH)	Neuroendocrine cells of the arcuate nucleus	GH release
Gonadotropin-releasing hormone (GnRH)	Neuroendocrine cells of the preoptic area	FSH and LH release
Prolactin-inhibitory hormone (PIH or dopamine)	Neuroendocrine cells of the arcuate nucleus	Prolactin inhibition
Growth hormone - inhibitory hormone (GIRH, Somatostatin)	Neuroendocrine cells of the periventricular nucleus	GH and TSH inhibition

a. **growth hormone-releasing hormone** (GHRH), **growth hormone-inhibitory**
b. In the absence of any input from the hypothalamic releasing and release-inhibiting hormones, the anterior pituitary cells will not release their hormone, with the exception of prolactin releasing cells, which will release large amounts of prolactin. This indicates that for most anterior pituitary hormones the hypothalamic control is largely stimulatory, whereas for prolactin it is largely inhibitory.



12. Functions of the pituitary hormones
    a. Posterior pituitary hormones
        i. Each neuron will only produce one of the 2 hormones and store it in vesicles that are transported in the axons to the nerve terminals in the posterior pituitary.
        ii. At the level of the posterior pituitary they are released in response to appropriate stimuli and enter circulation.



iii. Antidiuretic hormone (ADH or vasopressin)- main action is on the kidney to regulate water retention/excretion. In higher concentrations it also acts to constrict blood vessels and thereby increase blood pressure

iv. Oxytocin- 2 key actions: milk ejection in lactating females and uterine contraction during the birthing process. It is now thought to mediate some aspects of positive social behavior and pair-bonding with mates. Some evidence its involved in Na+ homeostasis.

b. Anterior pituitary hormones

i. Thyroid stimulating hormone (TSH)- acts on the thyroid gland to promote the secretion of the thyroid hormone's thyroxine

ii. Adrenocorticotropic hormone (ACTH)- acts on the adrenal cortex to promote the secretion of cortisol. This steroid hormone has a variety of actions throughout the body. ACTH and cortisol levels increase in response to stressful stimuli and this contributes to the mobilization and use of energy stores during stress.

iii. Growth Hormone (GH)- acts on a variety of tissues to promote growth and development. One of the major targets of growth hormone is the liver, where growth hormone acts to promote the section of insulin-like growth factor I (IGF-I), which mediates many of the growth-promoting actions of growth hormone.

iv. Follicle stimulating hormone (FSH) and luteinizing hormone (LH)- referred to as the gonadotropins, act on the male and female gonads to stimulate the production and secretion of the sex steroids.

v. Prolactin- The primary action ascribed to prolactin is the promotion of lactation in women. However, it is likely that prolactin has many other actions, and roles in growth, development, immune function, and sodium homeostasis have all been suggested.

1. Prolactin stands out from other anterior pituitary hormones in two key ways. First, its primary action is not via stimulation of production of another hormone. Second, its primary control by the hypothalamus is inhibitory. Indeed, in the absence of hypothalamic control (e.g., disruption of the pituitary stalk) there is massive secretion of prolactin while none of the other anterior pituitary hormones are secreted.

13. Endocrine pathophysiology

a. As with most endocrine diseases of loss of function this could result from the hormone not being there or the hormone being present but not eliciting the appropriate response (i.e., loss of receptor or downstream receptor signaling). In the case of diabetes mellitus, this is the distinction between type 1 and type 2.