Chapter 18: The Endocrine System

Chemical Messengers

1. Neural
2. Endocrine
3. Neuroendocrine
4. Paracrine
5. Autocrine

Endocrine System

--Endocrine and nervous systems work together
--Endocrine vs. Nervous Systems

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nervous</th>
<th>Endocrine</th>
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</thead>
<tbody>
<tr>
<td>Mediator molecules</td>
<td>NT released locally in response to nerve impulses</td>
<td>Hormones delivered to tissues throughout the body by the blood</td>
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<tr>
<td>Site of mediator action</td>
<td>Close to site of release (at synapse); binds to receptors in postsynaptic membrane</td>
<td>Far from site of release (usually); binds to receptors on/in target cells</td>
</tr>
<tr>
<td>Response to:</td>
<td>External stimuli</td>
<td>Internal stimuli</td>
</tr>
<tr>
<td>Types of target cells</td>
<td>Muscle (sm, sk, car), gland cells, other neurons, some cells release hormones into blood</td>
<td>Virtually all body cells</td>
</tr>
<tr>
<td>Time to onset of action</td>
<td>Within milliseconds</td>
<td>Seconds to hours to days</td>
</tr>
<tr>
<td>Duration of action</td>
<td>Briefer</td>
<td>Longer</td>
</tr>
</tbody>
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Regulation of Hormone Secretion

1. Neuronal
   * stress or exercise
   * release of epinephrine and norepinephrine

2. Hormonal
   * TRH stimulates release of TSH
   * TSH stimulates release of T\(_3\) and T\(_4\)
   * Negative feedback and to target tissues

3. Other substances (metabolites, etc.)
Types of Hormones

--Circulating
*Endocrine hormones: act on distant targets, travel in blood
  a. secreted into the blood by specialized cells; travels some distance to
     target tissues; influences specific activities

--Local Hormones
*Paracrine hormones: act on neighboring cells
  a. produced by a wide variety of tissues and secreted into tissue
     spaces; usually has a localized effect on other tissues
*Autocrine hormones: act on same cell that secreted them
  a. secreted by cells in a local area and influences the activity of the
     same cell type from which it was secreted

--Neurohormone
*”NT” released into the blood
*produced by neurons and functions like hormones

--Neurotransmitter
*produced by neurons and secreted into extracellular spaces by presynaptic
  nerve terminals; travels short distances; influences postsynaptic cells

--Pheromone
*secreted into the environment, modifies physiology and behavior of other
  individuals

Control of Secretion Rate

--most hormones are not secreted at a constant rate
--Patterns of regulation
  a. involves action of substance other than hormone on an endocrine gland
  b. involves neural control of endocrine gland
  c. involves control of secretory activity of one endocrine gland by hormone or
     neurohormone secreted by another endocrine gland

--Factors that Influences the Half-Life of Hormones
  a. Means by which the half-life is SHORTENED:
    *Excretion: hormones are excreted by the kidney into the urine or
     excreted by the liver into bile
    *Metabolism: hormones are enzymatically degraded in the blood,
     liver, kidney, lungs, or target tissues
    *Active Transport: some hormones are actively transported into cells
       and are used again as either hormones or NT substances
    *Cojugation: substances such as sulfate or glucuronic acid groups are
       attached to hormones primarily in the liver, normally making
       them less active as hormones and increasing the rate at which they are
       excreted in the urine or bile
b. Means by which the half-life is LENGTHENED:
* some hormones are protected from rapid excretion or metabolism by binding reversibly with plasma proteins
* some hormones are protected by their structure. The carbohydrate components of the glycoprotein hormones protect them from proteolytic enzymes in the circulatory system

--Negative Feedback Systems
* decrease in blood levels of thyroid hormones
* receptors in hypothalamus and thyroid
* cells activated to secrete more TSH or more T₃ or T₄
* blood levels increase

--Positive Feedback
* Oxytocin stimulates uterine contractions
* Uterine contractions stimulate oxytocin release

Transport and Distribution

--Hormones dissolve in blood plasma and are transported in free form or bound to plasma proteins
--As concentration of free hormone molecules increase, more hormones molecules diffuse from capillaries into interstitial spaces to bind to target cells
--level of carriers can affect response to hormone

--Hormonal Targets
* Generalists: some hormones affect almost all cells in body
* Specialists: some only affect specific tissues/cells

Types of Hormones

--Water soluble
a. Amine, peptide, and glyco/protein hormones: modified AA or AA put together, serotonin, melatonin, histamine, epinephrine, some glycoproteins
b. Eicosanoids: derived from arachidonic acid (fatty acid); prostaglandins or leukotrienes

--Actions of Water Soluble
a. cannot diffuse through plasma membrane
b. hormone receptors are integral membrane proteins that act as 1st messenger
c. receptor protein activates G-protein in membrane
d. G-protein activates adenylate cyclase to convert ATP to cAMP (2nd messenger that activate kinases) in the cytosol
e. cAMP activates kinases in the cytosol to speed up/slow down physiological
responses
f. phosphodiesterase inactivates cAMP quickly
g. cell response is turned off unless new hormone molecules arrive
**response is faster for water soluble hormones**

--Lipid soluble
a. Steroids: lipids derived from cholesterol on smooth ER, different functional
groups attached to core of structure provides uniqueness
b. Thyroid hormones: tyrosine ring plus attached iodines
c. Nitric oxide is gas

--Actions of Lipid Soluble Hormones
a. hormone diffuses through phospholipid bilayer and into cell
b. binds to receptor turning on/off specific genes (intracellular)
c. new mRNA is formed and directs synthesis of new proteins
d. new protein alters cell’s activity

Chemical Structure of Hormones

--Proteins
--Peptides
--Amino acid Derivatives
--Lipids and Steroids

Hormone Receptors

--Hormones only affect target cells with specific proteins called receptors
--Hormones bind via ligand or chemical signals (binding site, receptor site, specificity)
--Types of Hormone Receptors
a. On Cell Surface (Membrane-bound) \(\rightarrow\) binds to water-soluble or
large-
molecular-weight hormones
*proteins or glycoproteins that have polypeptide chains folded to
cross cell several times
*results of ligand binding changes permeability of plasma membrane,
alters activity of G proteins, alters activity of intracellular
enzymes
b. Intracellular (in cytosol or nucleus) \(\rightarrow\) bind to lipid-soluble hormones
*are proteins in cytoplasm or nucleus (only thyroid hormone)
*hormones bind with intracellular (cytosolic or nuclear) receptor,
receptor-hormone complex activates genes, which in turn are
transcribed to mRNA and translated into proteins
(enzymes) that produce response of target cell to hormone
*slow acting because time is required to synthesize mRNA and protein
*longer lasting effect
*processes limited by breakdown of receptor-hormone complex
--Role of Hormone Receptors
*constantly being synthesized and broken down
*a range of 2,000-100,000 receptors/target cell
*Down Regulation
→ excess hormone, produces a decrease in number of receptors
   (undergo endocytosis and are degraded)
→ decreases sensitivity of target cell to hormone
*Up Regulations
→ deficiency of hormone produces an increase in the number of receptors
→ increases sensitivity of target cell to hormone
*Desensitization: the signaling cascade becomes exhausted – 4 ways
  a. Sequestration
  b. Degradation
  c. Inactivation
  d. Downstream signaling inactivation
--Blocking Hormone Receptors
*synthetic hormones that block receptors for naturally occurring hormones:
   RU486 (mifepristone) binds to the receptors of progesterone preventing it
   from maintaining the uterus in a pregnant woman
*Hormone is prevented from interacting with its receptors and cannot perform its normal functions
--Second Messengers
*Some hormones exert their influence by increasing the synthesis of cAMP (ADH, TSH, ACTH, glucagon, epi)
*Some exert their influence by decreasing the level of cAMP (growth hormone inhibiting hormone)
*Other substances (in addition to cAMP) can act as 2ndary messengers (calcium ions, cGMP)
*Same hormone may use different 2ndary messengers in different target cells
--IP_3 and DAD 2ndary messenger system
*the cell membrane phospholipid second messenger system by which some hormones exert their control of cell function

**Hormonal Interactions**

--Permissive effect
*a second hormone strengthens the effects of the first (thyroid strengthens epi’s effect upon lipolysis)

--Synergistic effect
*two hormones acting together for greater effect (estrogen and LH are both needed for oocyte production)

--Antagonistic effect
*two hormones with opposite effects (insulin promotes glycogen formation and glucagon stimulates glycogen breakdown)

**Cholera Toxin and G Proteins**

--Toxin is deadly b/c it produces massive watery diarrhea and person dies from dehydration
--Toxin of cholera bacteria causes G-protein to lock in the activated state in intestinal epithelium
--Cyclic AMP causes intestinal cells to actively transport chloride (Na⁺ and water follow) into the lumen
--Person dies unless ions and fluids are replaced and receive antibiotic treatment