Hormones are chemical signals.

- The endocrine system consists of:
  - Endocrine cells which are hormone-secreting cells and
  - Endocrine glands which are hormone-secreting organs. They secrete hormones into the bloodstream.
- Specific target cells respond to specific hormones.
3.D.1.a. List the types of signals involved in communication and where they come from.

3.D.1.b. Describe the types of signal transduction pathways that are under strong selective pressure.
1. The endocrine system and the nervous system are structurally, chemically, and functionally related

- **Neurosecretory cells** secrete hormones into the blood.
- Chemicals such as epinephrine serve as both hormones of the endocrine system and signals in the nervous system.
- Feedback regulation is a feature of both the endocrine and nervous systems.
Negative feedback regulates many endocrine and nervous mechanisms, often with antagonistic hormones.
Two ways these work: big molecules, mostly proteins, latch onto a receptor on the plasma membrane of the target cell.
3.D.1.d. Using an example from below, explain how in multicellular organisms, signal transduction pathways coordinate the activities within individual cells that support the function of the organism as a whole.

1. Epinephrine stimulation of glycogen breakdown in mammals

2. Temperature determination of sex in some vertebrate organisms

3. DNA repair mechanisms
1. In response to a signal, a cell may regulate activities in the cytoplasm or transcription in the nucleus

- Ultimately, a signal-transduction pathway leads to the regulation of one or more cellular activities.
  - This may be a change in an ion channel or a change in cell metabolism.
  - For example, epinephrine helps regulate cellular energy metabolism by activating enzymes that catalyze the breakdown of glycogen. Watch here…

Different signal-transduction pathways in different cells lead to different responses to the same signal. What’s different?

(a) Contraction of a skeletal muscle cell

(b) Relaxation of a heart muscle cell

(c) Secretion by an endocrine cell

Fig. 45.4
Signal-transduction pathways allow for small amounts of a hormone to have a large effect. This is called amplification.
3.D.3.a.2. Using an example from below, explain how a receptor protein recognizes signal molecules, causing the receptor protein’s shape to change, which initiates transduction of the signal.

1. G-protein linked receptors
2. Ligand-gated ion channels
3. Receptor tyrosine kinases (insulin receptors are these)

The “signal”, or message, of the molecule is “transduced”, or passed on by a series of relay molecules inside the target cell.

Many of the relay molecules in a signal-transduction pathway are protein kinases, enzymes that lead to a “phosphorylation cascade”.

Each phosphorylation leads to a shape change in the protein because of the interaction between the phosphate group and charged or polar amino acids.

The shape change activates the protein, leading to some further action.
A single cell may have hundreds of different protein kinases, each specific for a different substrate protein.

- Fully 1% of our genes may code for protein kinases.

Abnormal activity of protein kinases can cause abnormal cell growth and contribute to the development of cancer.

An effect of a change in a STP like this is something they may ask you to describe.
3. Steroid hormones, thyroid hormones, and some local regulators enter target cells and bind to intracellular receptors

- Examples: estrogen, progesterone, vitamin D, NO.
- Usually, the intracellular receptor activated by a hormone is a transcription factor, turning genes on.
Watch this animation of a hormone that is lipid soluble such that it enters the target cell…


- Link to mechanism of steroid hormone action
- See – this kind of hormone directly stimulates transcription – turning on a gene.
- Remember how transcription factors allow for RNA polymerase to transcribe a gene???
3.D.1.c. Using an example from below, explain how in single-celled organisms, signal transduction pathways influence how the cell responds to its environment.

1. Use of chemical messengers by microbes to communicate with other nearby cells and to regulate specific pathways in response to population density (quorum sensing)

2. Use of pheromones to trigger reproduction and developmental pathways

3. Response to external signals by bacteria that influences cell movement
The responsibility for turning off a signal-transduction pathway belongs to protein phosphatases.

- These enzymes rapidly remove phosphate groups from proteins.
- The activity of a protein regulated by phosphorylation depends on the balance of active kinase molecules and active phosphatase molecules.
- When an extracellular signal molecule is absent, active phosphatase molecules predominate, and the signaling pathway and cellular response are shut down. Remember quorum sensing? Watch 1,2.
3. Certain signal molecules and ions act as so-called second messengers

- Many signaling pathways involve small, nonprotein, water-soluble molecules or ions, called second messengers.
  - These molecules rapidly diffuse throughout the cell.
  - Two of the most important are cyclic AMP and Ca$^{2+}$.
3.D.3.b. 2. Using an example from below, explain how second messengers are often essential to the function of the cascade.

1. Ligand-gated ion channels

2. Second messengers, such as cyclic GMP, cyclic AMP calcium ions (Ca2+), and inositol triphosphate (IP3)
Here’s what cyclic AMP looks like. No need to memorize, just look.
• Many hormones and other signals trigger the formation of cAMP.

• Follow the diagram

• Don’t sweat the details.
Many signal molecules in animals induce responses in their target cells via signal-transduction pathways that increase the cytosolic concentration of Ca\(^{2+}\).

- In animal cells, increases in Ca\(^{2+}\) may cause contraction of muscle cells, secretion of some substances, and cell division.

- In plant cells, increases in Ca\(^{2+}\) trigger responses for coping with environmental stress, including drought.
• Calcium ions may activate a signal-transduction pathway directly.

• Alternatively, Ca\(^{2+}\) binds to the protein calmodulin.
  
  • This protein is present at high levels in eukaryotes.

• When calmodulin is activated by Ca\(^{2+}\), calmodulin binds to other proteins, either activating or inactivating them.
  
  • These other proteins are often protein kinases and phosphatases - relay proteins in signaling pathways.
• Other signaling pathways do not regulate the *activity* of enzymes but the *synthesis* of enzymes or other proteins.

• Activated receptors may act as transcription factors that turn specific genes on or off in the nucleus.
Various types of cells may receive the same signal but produce very different responses.

- For example, epinephrine triggers liver or striated muscle cells to break down glycogen, but cardiac muscle cells are stimulated to contract, leading to a rapid heartbeat.

- These differences result from a basic observation:
  
  - Different kinds of cells have different collections of proteins.
  
  - Proteomics is the study of an organism’s proteins.
Review the action of the two basic types of hormones.

- Sterol (lipid) hormones *enter the cell* and do their work.  
  Watch

- Protein (peptide) hormones can’t get through the membrane, so they lock onto receptor molecules and start the action this way.

- Don’t confuse hormones with enzymes, but each does work because of the way things fit.

- Like this…
Introduction

• Tropic hormones target other endocrine glands and are important to understanding chemical coordination.

• Humans have nine endocrine glands.
3.D.2.c. Explain how signals released by one cell type can travel long distances to target cells of another cell type.


3.D.3.a.1. List the types of different chemical messengers and explain the specific one-to-one relationship with their receptors.
1. The hypothalamus and pituitary integrate many functions of the vertebrate endocrine system

- The **hypothalamus** integrates endocrine and nervous function.
  - Neurosecretory cells of the hypothalamus produce hormones.
    - **Releasing hormones** stimulate the **anterior pituitary** to secrete hormones.
    - **Inhibiting hormones** prevent the anterior pituitary from secreting hormones.
Neurosecretory cells of the hypothalamus

Portal vessels

Hypothalamic hormones

Endocrine cells of the anterior pituitary

Pituitary hormones

HORMONE

Growth hormone (GH)

Prolactin (PRL)

Follicle-stimulating hormone (FSH) and luteinizing hormone (LH)

Thyroid-stimulating hormone (TSH)

ACTH

MSH

Endorphins

TARGET

Bones

Mammary glands

Testes or ovaries

Thyroid

Adrenal cortex

Melanocytes

Pain receptors in the brain

(b) The anterior pituitary
• The **posterior pituitary** stores and secretes hormones produced by the hypothalamus.

• Know these diagrams of the hypothalamus and pituitary.
2. The pineal gland is involved in biorhythms

- The **pineal gland** is a small mass of tissue near the center of the mammalian brain.
  - The pineal gland secretes the hormone **melatonin**, an amine.
    - Involved in biological rhythms associated with reproduction.
    - Secretion regulated by light/dark cycles.
3. Thyroid hormones function in development, bioenergetics, and homeostasis

- The thyroid gland of mammals consists of two lobes located on the ventral surface of the trachea.
  - Triiodothyronine (T₃) and thyroxine (T₄): amines.
  - Stimulates and maintain metabolic processes.
  - Secretion regulated by TSH hormones from anterior pituitary.
Watch this animation of thyroxine action…


- Link to Mechanism of Thyroxine Action
• Hyperthyroidism is the excessive secretion of thyroid hormones, exhibited by high body temperature, profuse sweating, weight loss, irritability, high blood pressure.

• An insufficient amount of thyroid hormones is known as hypothyroidism.
  • Infants: cretinism (mental retardation).
  • Adults: weight gain, lethargy, cold intolerance.
  • Goiter: often associated with iodine deficiency.
5. Endocrine tissues of the pancreas secrete insulin and glucagon, antagonistic hormones that regulate blood glucose.

- The pancreas has both endocrine (secreted into bloodstream) and exocrine (secreted into a duct) functions.
  - Exocrine function: secretion of bicarbonate ions and digestive enzymes.
  - Endocrine function: insulin and glucagon secreted by islets of Langerhans.
• **Insulin**: a protein secreted by **beta cells**.

• **Receptors are tyrosine kinases**

• Lowers blood glucose levels.
  
  • Stimulates all body cells (except brain cells) to take up glucose.

• Now **some detail**.

• Slows glycogenolysis.

• Inhibits gluconeogenesis.

• Secretion regulated by glucose in blood (negative feedback).
Hypoinsulinism (not enough insulin): type I diabetes mellitus. Can be autoimmune, right?

- Hereditary factors and obesity play a role in its development.

- High blood sugar levels – sugar excreted in the urine.

- Symptoms: excessive urination and excessive thirst.

- If severe: fat substitutes for glucose as major fuel source → production of acidic metabolites → life threatening lowering of blood pH.
• **Type II diabetes mellitus** (non-insulin-dependent diabetes).

  • Usually due to target cells having a decreased responsiveness to insulin. Too much sugar, usually from white rice, bread, pasta (*refined* foods).

  • Usually occurs after age 40, but lately, much younger. Complicated! Still not fully understood

  • Accounts for over 90% of diabetes cases.
More on diabetes and sugar

• Fructose is the bad guy. Only liver cells metabolize it, and with lots of it (soda, candy), they turn it to fat.

• High fructose corn syrup is only slightly worse than sucrose, putting fructose into the blood the fastest. It was invented by the Japanese for its long shelf life.

• Liver LDL’s block insulin receptors, which leads to a rise in blood sugar which leads to a rise in insulin which blocks leptin, the hormone that decreases appetite, so you get hungrier and it gets worse.

• And here’s the link to heart disease. Glycation. 2min

• Watch 10 min. Good for health info!
• **Glucagon**: a protein hormone secreted by alpha cells.

  • Raises blood glucose levels.
    
    • Stimulates glycogenolysis in the liver (as does epinephrine, remember?) and skeletal muscle.
    
    • Secretion regulated by glucose in blood (negative feedback).
    
    • Insulin (Beta cells) decreases blood glucose.
    
    • Glucagon (alpha cells) increases blood glucose.

  • And now, a video summary with our favorite puppy.
Fig. 45.10

**Homeostasis:** Blood glucose level

**Stimulus:**
- Removal of excess glucose from blood
- Low blood glucose level (e.g., after skipping a meal)

**Insulin**
- Body cells take up more glucose
- Blood glucose level declines to a set point; stimulus for insulin release diminishes
- Alpha cells of pancreas stimulated to release glucagon into the blood

**Glucagon**
- Liver breaks down glycogen and releases glucose to the blood

**Beta cells of pancreas stimulated to release insulin into the blood**
- High blood glucose level (e.g., after eating a carbohydrate-rich meal)
- Liver takes up glucose and stores it as glycogen
- Blood glucose level rises to set point; stimulus for glucagon release diminishes

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6. The adrenal medulla and adrenal cortex help the body manage stress

- The adrenal glands are located adjacent to the kidneys. Ad (next to) renal (kidneys).
  - The adrenal cortex is the outer portion. Cortex = outer.
  - The adrenal medulla is the inner portion. Medulla - inner.
• **Epinephrine** (adrenaline) and **norepinephrine** (noradrenaline). Secreted by adrenal medulla.
  
  • **Catecholamines**: amines synthesized from tyrosine.
  
  • Secretion regulated by the nervous system in response to stress.
  
  • Raises blood glucose level and blood fatty acid level.
  
  • Increase metabolic activities.
    
    • Increases heart rate and stroke volume and dilates bronchioles.
  
  • Shunts blood away from skin, digestive organs, and kidneys, and increases blood flow to heart, brain, and skeletal muscle. Makes you ready for **fight or flight**.
• **Adrenal cortex** reactions to stress:
  
  • Secretion of **corticosteroids** is regulated by the nervous system in response to stress.

• **Glucocorticoids.**
  
  • Raises blood glucose level.

  • Secretion regulated by ACTH (negative feedback).

  • Abnormally high doses are administered as medication to suppress the inflammation response.
Scary update on estrogen mimics

- Chemicals in plastics, especially bisphenol A (BPA) and phthalates, are estrogen mimics.
- They can connect with estrogen receptors due to phenolic hydroxyl groups they contain. Phenols are $C_6H_5OH$ aromatics (rings).
- This will cause earlier puberty in women as well as cancer, and abnormalities in genital development in men.
- Any type of plastic will leach out some of these particles.
- BPA can even permanently reprogram genes so that BPA in a pregnant woman that crosses the placenta will not only effect the fetus but also the development of its testes or ovaries, and therefore the pregnant woman’s grandchildren.
- Now watch this really cool video of all this stuff you just learned.