The Endocrine System

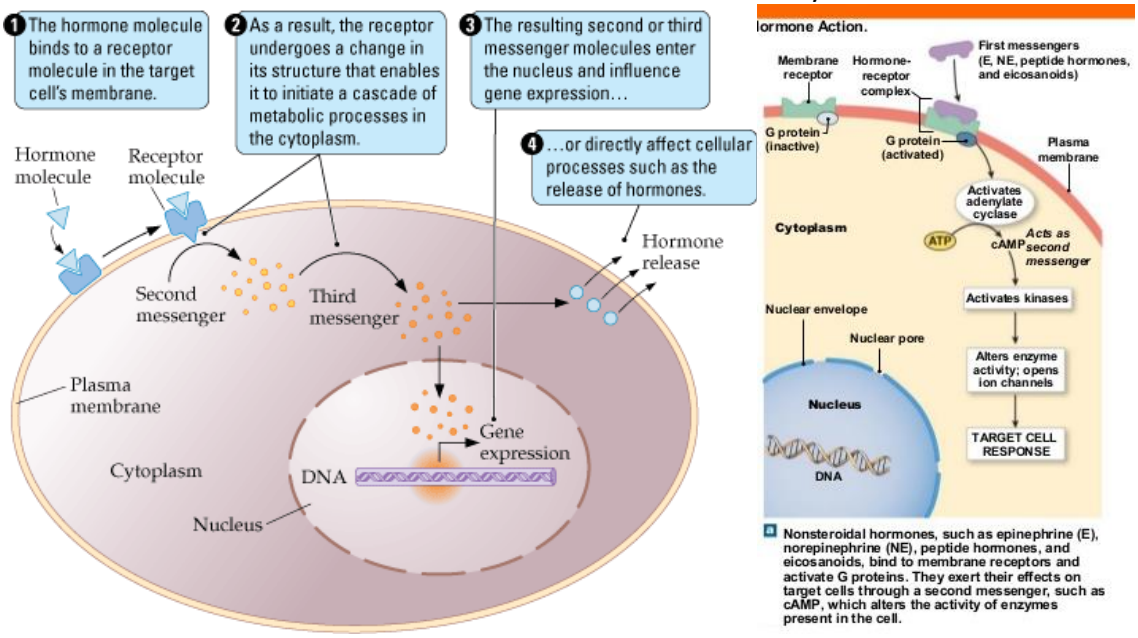
**Mechanism of Hormone Action*

Organs in the endocrine system are named **glands** which secrete **hormones** (signaling molecules that are secreted directly into the bloodstream)

Classification of Hormones by Chemical Structure

Peptide Hormones

- Made up of amino acids and have a range of sizes from small to large.
    - Are derived from larger polypeptides. Smaller unit is cleaved off during post-translation.
        - Golgi Apparatus further modifies these peptide chains to activate the hormone and direct it to correct location of the cell in order to be released by exocytosis.
    - Peptides are charged so they cannot pass through the plasma membrane, so they must bind to extracellular receptors.
        - Peptide is the **first messenger** since it binds to the receptor and triggers a second signal known as the **second messenger**
            - Common secondary messengers are **cAMP**,**IP3 & Calcium**
    - **Signaling Cascade**: The connection between the hormone at the surface of the cell and the effect brought on by the second messengers
        - **Amplification**: there is a possibility that there can be an increase in intensity of the signal at each step.
            - Receptors may activate multiple enzymes or one hormone may bind to multiple receptor sites.
    - Effects are usually rapid but short-lived since they use secondary messengers. So it is easy to turn them on and off.
        - Can also be carried in bloodstream since they are water soluble



Steroid Hormones

- Derived from cholesterol and produced mainly in the gonads and adrenal cortex.
    - Can easily cross the cell membrane since they are non-polar.
        - Receptors are usually inside the cell cytoplasm or nucleus.
- Once bound to a receptor, the hormone-receptor complex undergoes conformational changes, which allow the receptor to bind directly to the DNA in order to control the rate of gene transcription.
    - Dimerization: is the conformational change that is the pairing of two receptor-hormone complexes.
- Effects are longer but slower since the steroid hormones act directly on the DNA to cause changes in the amount of mRNA and protein present.
- Must be carried by proteins the bloodstream since they are not water soluble.
    - Usually the hormone must dissociate from the protein in order to become active.

Amino Acid-Derivative Hormones

- Less common than other two hormones, but involve important hormones such as epinephrine, norepinephrine, triiodothyronine and throxine.
    - Are derived from one or two amino acids with additional modifications.
- Catecholamine (Epinephrine and Norepinephrine) bind to G-protein receptors. So they are fast and short lived.
- Thyroid Hormones bind intracellularly so they have lasting but slower effects. More involved with regulation of metabolic rate

Classification of Hormones by Target Tissue

- Direct Hormones: secreted and then act directly on a target tissue
- Tropic Hormones: Require an intermediary to act (think about GnRH causing LH causing testosterone to be produced)
    - Usually originate from the brain and anterior pituitary gland.

Endocrine Organs and Hormones

Hypothalamus

This is the bridge between the nervous and endocrine systems. This controls the entire organism by regulating the pituitary gland through tropic hormones.

- Located on the forebrain. Above the pituitary gland and below the thalamus

Hypothalamus controls pituitary through paracrine release of hormones into a portal system and receives input from a wide variety of sources.

- Regulated by **negative feedback**, which occurs when a hormone later in its pathway inhibits hormones earlier in its pathway. This restricts overproduction of substance.

Interactions with the Anterior Pituitary

Hypothalamus secretes compounds into the **hypophyseal portal system**, which is a blood vessel system that directly connects the hypothalamus to the anterior pituitary.

- Hormones released go directly to anterior pituitary and cannot be found in the bloodstream
- Hypophysis: is an alternative term for the pituitary.

- Releases tropic hormones into the portal that travel down the pituitary stalk and bind to receptors.
    - Gonadotropin-releasing Hormone (GnRH) → FSH and LH
    - Growth Hormone Releasing Hormone (GHRH) → Growth Hormone (GH)
    - Thyroid-releasing Hormone (TRH) → Thyroid Stimulating Hormone (TSH)
    - Corticotropin-releasing factor(CRF) → adrenocorticotropic hormone (ACTH)
    - Prolactin-Inhibiting factor (PIF/dopamine) causes a decree in prolactin secretion
        - Absence of PIF that allows prolactin to be released
- Each tropic hormone then causes the release of another hormone from an endocrine gland that has negative feedback effects.
- **Axes** are three organ systems which work on a negative feedback loop.
    - Hypothalamic-pituitary-adrenal axes works by releasing CRF from hypothalamus, which promotes the release of ACTH in the anterior pituitary, which then causes the adrenal cortex to increase the level of cortisol in the blood. The increased level of blood cortisol is sensed in both the anterior pituitary and the hypothalamus and the release of CRF and ACTH is inhibited.

Interactions with the Posterior Pituitary

- Does not receive tropic hormones, instead hypothalamus sends axons down the pituitary stalk.
    - **Oxytocin:** stimulates uterine contractions during labor and milk letdown for lactation
    - **Antidiuretic Hormone:** increases reabsorption of water in the collecting duct of the kidneys.

Anterior Pituitary

"Flat Peg"

Synthesizes and secretes seven different products. Four tropic hormones and three direct.

- Tropic Hormones: FSH and LH stimulated by GnRH. ACTH is stimulated by CRF. TSH is stimulated by TRH.
- Direct Hormones
    - **Prolactin**: stimulates production of milk in mammary glands. Release of dopamine decreases the production of this. Need a drop in estrogen, progesterone and dopamine levels to allow lactation to begin.
        - Nipple stimulation results in an increased oxytocin release and prohibits the release of dopamine
    - **Endorphins:** decrease the perception of pain.
    - **Growth Hormone (GH):** promotes the growth of bone and muscle. This prevents glucose uptake in certain tissues that are not growing and stimulates the production of fatty acids as a means of providing enough glucose for muscles and bones to grow.
        - Gigantism is an excess release of GH during childhood.
        - Acromegaly is when there is excess GH release in adults. Affects smaller bones since epiphyseal plates are sealed.

Posterior Pituitary

Contains the nerve terminals of neurons with their cell bodies in the hypothalamus. Stores and releases two hormones: ADH and oxytocin, hypothalamus synthesizes these two.

- ADH is secreted in response to low blood volume or increased osmolarity.
    - Increases the permeability of the collecting ducts in the kidney.
- Oxytocin is secreted during childbirth and allows for the coordinated contraction of the uterine smooth muscle.
    - May also be stimulated by suckling or may be involved in bonding behavior.
    - Runs on a **positive feedback loop**. Release of oxytocin causes muscle contractions which in turn stimulate further release of oxytocin.

Thyroid

- Controlled by TSH and is located on the front surface of the trachea.
- Two main functions are: setting the basal metabolic rate and maintaining calcium homeostasis.

Triiodothyronine (T_3) & Thyroxine (T_4)

- Both are produced by the iodination of the amino acid tyrosine in the **follicular cells** of the thyroid.
- Are capable of resetting metabolic rate by making energy production more or less efficient and by altering the utilization of glucose and fatty acids.
    - An increase in T_3 & T_4 lead to an increased respiration rate, which leads to higher amounts of protein and fatty acid turnover.
- Hypothyroidism can result from a deficiency in iron or an inflammation of the thyroid.
    - Characterized by lethargy, decreased body temp, and slowed respiratory/heart rate.
    - Deficiency will result in mental retardation and development delay (**cretinism**)
- Hyperthyroidism may result from a tumor or thyroid over stimulation.

Calcitonin

- Follicular cells produce thyroid hormones and **C-cells** (parafollicular cells) produce calcitonin.
- Acts to decrease calcium levels
    - Increases calcium excretion at kidneys
    - Decreases calcium absorption at gut
    - Increases storage of calcium in the bones

Parathyroid Glands

Small structures that sit on the posterior surface of the thyroid. Produce **Parathyroid Hormone** (PTH).

- PTH is antagonistic to calcitonin, does the exact opposite of calcitonin and increases calcium levels
- Also affects phosphorus homeostasis (absorption at gut and excretion at kidneys)
- Has a significant effect increase in blood calcium levels, little effect on phosphate.
- Also activated **Vitamin D** since it is required for absorption of calcium and phosphate.

Adrenal Cortex

Adrenal Glands are located on top of the kidney. Consists of a cortex and a medulla. **Adrenal Cortex** secretes **corticosteroids**: glucocorticoids, mineralocorticoids, and cortical sex hormones.

- Glucocorticoids: Steroid hormones that regulate glucose levels and can affect protein metabolism
    - Two most common are **cortisol and cortisone**. Raise blood glucose by increasing gluconeogenesis and decreasing protein synthesis.
        - Can also decrease inflammation and immune responses.
        - Cortisol is known as a stress hormone since it provided glucose as a source of fuel to the body in precarious situations
    - Release is under the control of the ACTH.
- Mineralocorticoids: Used in salt and water homeostasis and has the most significant effect on kidneys.
    - **Aldosterone** is the most noteworthy and it acts by increasing sodium reabsorption in the distal convoluted tubule and collecting duct of the nephrons.
        - Water follows sodium into the bloodstream and increases the blood volume.
        - Also decreases the reabsorption of potassium and hydrogen ions
        - Does not affect osmolarity like ADH does.
    - Is under the control of the **renin-angiotensin-aldosterone** system.
        - Decreased blood pressure causes the **juxtaglomerular cells** of the kidneys to secrete **renin**
        - Renin cleaves **angiotensinogen** to active **angiotensin I.**
        - Angiotensin I is then converted to **angiotensin II** by **ACE**
        - **Angiotensin II** stimulates adrenal glands to secrete aldosterone.
- Cortical Sex Hormones: Androgens and Estrogens
    - Males already secrete large amount of androgens from the testes so they are not as susceptible to disorders as females are.

Adrenal Medulla

Inside the adrenal cortex and is a derivative of the nervous system. Is responsible for the production of **epinephrine and norepinephrine**. These belong to a **catecholamine** class.

- Hormones released are associated with fight or flight response
- Have the ability to directly inject hormones into the circulatory system
- Epinephrine increases breakdown of glycogen to glucose in both the liver and muscles, and will increase the basal metabolic rate.
- Both will increase the heart rate, dilate the bronchi, and alter blood floow to supply the necessary systems.
- Catecholamines are for fast responses to stress while cortisol is for more long term response to stress. However, cortisol increases secretion of catcholamines.

Pancreas

Small groups of hormone-producing cells are called the **islets of Langerhans**. These contain three distinct types of cells: **Alpha (**secrete glucagon)**, Beta** (secrete insulin) **& Delta Cells** (secrete somatostatin)**.**

Glucagon

Secreted during times of fasting, and it meant to increase the level of glucose production.

- Stimulates degradation of protein and fat and conversion of glycogen to glucose.
- Is stimulated by gastrointestinal hormones such as cholecystokinin and gastrin

Insulin

- This is antagonistic to glucagon and is secreted when glucose levels are high.
- Induces muscle and liver cells to take up glucose and store it as glycogen for later use.
- Stimulates anabolic processes such as fat and protein synthesis.
- Hypoglycemia: Excess insulin will cause low glucose concentrations.
- Diabetes Mellitus (hyperglycemia): is caused by underproduction, insufficient secretion and insensitivity to insulin.
    - Diabetics often report polyuria (increases peeing) and polydipsia (increases thirst) since presence of glucose lead to excess secretion of water
    - Type I: is insulin dependent diabetes which is caused by an autoimmune destruction of the beta cells in the pancreas.
    - Type II: result of the receptor-level resistance to the effects of insulin.

Somatostatin

An inhibitor of both insulin and glucagon secretion. Is stimulated by high blood glucose and amino acid concentrations. Is also stimulated by the hypothalamus where it functions to decrease growth hormone secretion.

Gonads

- Testes secrete testosterone in response to LH and FSH. This causes sexual differentiation of the male during gestation.
- Ovaries secrete estrogen and progesterone in response to LH and FSH. Estrogen is involved in the development of the female reproductive system.

Pineal Gland

- Located deep within the brain and secretes **melatonin**. This is involved in **circadian rythms**. Are responsible for the sensation of sleepiness.

Other Organs

Specific cells and tissues in other organs are capable of endocrine signaling. Include ones that are found in the gastrointestinal tract (secretin, gastrin, and cholecystokinin.

- Kidneys produce **erythropoietin** which stimulates bone marrow to increase production of red blood cells. Secreted in response to decrease oxygen levels.
- Heart release **atrial natriuretic peptide (ANP)** which helps in regulating salt and water balance. Stimulated by overstretching of cells in the atria, functions to lower B.P.
- Thymus releases **thymosin** which is needed for proper T-cell development and differentiation. Thymus atrophies by adulthood.

Major Vertebrate Endocrine Glands and Some of Their Hormones

Gland	Hormone	Chemical Class	Representative Actions	Regulated by
Hypothalamus	Hormones released by the posterior pituitary and hormones that regulate the anterior pituitary (see below)			
Pituitary gland Posterior lobe (releases hormones made by hypothalamus)	Oxytocin	Peptide	Stimulates contraction of uterus and mammary gland cells	Nervous system
	Antidiuretic hormone (ADH)	Peptide	Promotes retention of water by kidneys	Water/salt balance
Anterior lobe	Growth hormone (GH)	Protein	Stimulates growth (especially bones) and metabolic functions	Hypothalamic hormones
	Prolactin (PRL)	Protein	Stimulates milk production	Hypothalamic hormones
	Follicle-stimulating hormone (FSH)	Protein	Stimulates production of ova and sperm	Hypothalamic hormones
	Luteinizing hormone (LH)	Protein	Stimulates ovaries and testes	Hypothalamic hormones
	Thyroid-stimulating hormone (TSH)	Protein	Stimulates thyroid gland	Thyroxine in blood; hypothalamic hormones
	Adrenocorticotropic hormone (ACTH)	Protein	Stimulates adrenal cortex to secrete glucocorticoids	Glucocorticoids; hypothalamic hormones
Pineal gland	Melatonin	Amine	Involved in rhythmic activities (daily and seasonal)	Light/dark cycles
Thyroid gland	Thyroxine (T_4) and triiodothyronine (T_3)	Amine	Stimulate and maintain metabolic processes	TSH
	Calcitonin	Peptide	Lowers blood calcium level	Calcium in blood
Parathyroid glands	Parathyroid hormone (PTH)	Peptide	Raises blood calcium level	Calcium in blood
Thymus	Thymosin	Peptide	Stimulates T-cell development	Not known
Adrenal glands Adrenal medulla	Epinephrine and norepinephrine	Amines	Increase blood glucose; increase metabolic activities; constrict certain blood vessels	Nervous system
Adrenal cortex	Glucocorticoids	Steroids	Increase blood glucose	ACTH
	Mineralocorticoids	Steroids	Promote reabsorption of Na^+ and excretion of K^+ in kidneys	K^+ (potassium) in blood
Pancreas	Insulin	Protein	Lowers blood glucose	Glucose in blood
	Glucagon	Protein	Raises blood glucose	Glucose in blood
Testes	Androgens	Steroids	Support sperm formation; development and maintenance of male secondary sex characteristics	FSH and LH
Ovaries	Estrogens	Steroids	Stimulate uterine lining growth; development and maintenance of female secondary sex characteristics	FSH and LH
	Progesterone	Steroid	Promotes uterine lining growth	FSH and LH

©Addison Wesley Longman, Inc.