Chapter 13

The Endocrine System
End of Chapter 13

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Comparison: Nervous v. Endocrine

Nervous system
- Neurons release neurotransmitters at synapses, neuromuscular or neuroglandular junctions
- Effectors include other neurons, muscles, glands
- Rapid responses from effectors

Endocrine system
- Releases hormones into interstitial fluid → blood → general circulation
- Effectors: virtually any type of body cell so can have widespread effects on diverse aspects of metabolism
- Slower, longer-lasting responses as hormones linger in blood
Comparison: Endocrine v. Exocrine

- **Endocrine glands**
  - Secretions enter interstitial fluid and then → bloodstream
  - Stay in the body: endo-
  - Examples: all hormones such as growth hormone, insulin, adrenalin, estrogen, testosterone

- **Exocrine glands**
  - Secrete substances that enter ducts
  - Ultimately exit the body (exo-)
  - Examples: mucus, saliva and other digestive secretions, sweat, tears
Endocrine Cells that Make Hormones

- In endocrine glands
  - Pituitary, thyroid, parathyroid, adrenal, pineal
- In cells within organs that do produce hormones but also have other functions
  - Hypothalamus, thymus, pancreas, ovaries, testes, kidneys, stomach, liver, small intestine, skin, heart, adipose tissue, and placenta
Hormone Action

- Hormones are carried in blood stream
- But only certain cells can be affected by hormones
  - These target cells have 1000’s of receptors specific for a particular hormone.
  - Response determined by responding cell: different cells may respond differently to the same hormone.
  - Cell may have > 1 type of receptor, so can respond to more than one hormone
Hormone Chemistry

- Lipid-soluble
  - Steroids, such as testosterone, estrogens
  - Thyroid hormones: $T_3$ and $T_4$
  - Nitric oxide (NO)

- Water-soluble
  - Amino acid derivatives, such as epinephrine, norepinephrine
  - Peptides: antidiuretic hormone (ADH), oxytocin
  - Proteins: insulin and growth hormone

- General action depends on chemistry
Lipid-Soluble Action

- Hormone detaches from carrier in bloodstream
- Diffuses through interstitial fluid and cell membrane into cell
- Binds to receptor and activates it
- Receptor-hormone complex alters gene expression
- If new mRNA → protein synthesis
- New proteins alter cell activity
Lipid-Soluble Hormone Action

1. Lipid-soluble hormone diffuses into cell

2. Activated receptor-hormone complex alters gene expression

3. Newly formed mRNA directs synthesis of specific proteins on ribosomes
Water-Soluble Action

- Hormone (first messenger) diffuses from blood and binds to receptor in plasma membrane
- Starts reaction inside cell forming second messenger
  - Cyclic AMP is a common one
- Second messenger causes activation of several proteins (enzymes)
- Activated proteins produce physiological responses
- Second messenger is inactivated
1. Binding of hormone (first messenger) to its receptor activates G protein, which activates adenylate cyclase.

2. Activated adenylate cyclase converts ATP to cAMP.

3. cAMP serves as a second messenger to activate protein kinases.


5. Millions of phosphorylated proteins cause reactions that produce physiological responses.

6. Phosphodiesterase inactivates cAMP.

Target cell
Control of Hormone Secretions

- Release occurs in short bursts
- Regulated by
  - Signals from nervous system
    - Example: adrenal medulla release of epinephrine
  - Chemical changes in blood
    - Example: blood Ca\(^{2+}\) affects parathyroid hormone
  - Other hormones
    - Example: ACTH from pituitary stimulates release of cortisol from adrenal cortex
Hormone Regulation

*Interactions Animation*

- Introduction to Hormonal Regulation, Secretion, and Concentration

You must be connected to the internet to run this animation.
Hypothalamus and Pituitary

- Serve as major link between nervous and endocrine systems
- Hypothalamic cells synthesize
  - Many releasing and inhibiting hormones
  - Two hormones (oxytocin and ADH) that are then stored and released from the posterior pituitary
- Anterior pituitary synthesizes 7 hormones
- Regulate growth, development, metabolism and homeostasis
Pituitary

- Located in depression in sphenoid bone just inferior to the brain
- Pituitary is attached to hypothalamus by stalk (infundibulum)
- Pituitary has 2 lobes: anterior and posterior
Effects of Hypothalamus on Pituitary

- Axons of hypothalamic neurons (neurosecretory cells) end near capillaries of hypothalamus
- Secrete releasing hormones or inhibiting hormones $\rightarrow$ portal veins
- These hormones regulate release of anterior pituitary hormones
Pituitary Gland Blood Supply
Seven Anterior Pituitary Hormones

1. Human growth hormone (hGH)
2. Thyroid-stimulating hormone (TSH)
3. Follicle-stimulating hormone (FSH)
4. Luteinizing hormone (LH)
5. Prolactin
6. Adrenocorticotropin hormone (ACTH)
7. Melanocyte-stimulating hormone (MSH)
1. Human Growth Hormone (hGH)

- hGH promotes synthesis of insulinlike growth factors (IGFs) = somatomedins
  - Secreted by liver, muscle, cartilage, bone cells
  - Actions of IGFs much like those of insulin

- Regulation
  - By hypothalamic hormones
    - Growth hormone-releasing hormone (GHRH)
    - Growth hormone-inhibiting Hormone (GHIH )
  - By blood glucose levels
    - Low blood glucose levels → release of GHRH
1. Human Growth Hormone (hGH)

- Actions of hGH
  - Stimulates protein synthesis
    - Maintains muscle and bone mass
    - Promotes healing of injuries, tissue repair
  - Makes “fuel” (ATP) available for growth
    - Causes fat breakdown (“baby fat”) and release of fatty acids into blood
    - Breaks down liver glycogen → releases glucose into blood
2. Thyroid-Stimulating Hormone (TSH)

- Stimulates the formation and secretion of thyroid hormones \((T_3, T_4)\) by thyroid gland
- Regulation of TSH (negative feedback)
  - Low blood levels of \(T_3, T_4\) →
  - Hypothalamus → Thyrotropin-releasing hormone (TRH) →
  - TRH stimulates release of TSH
  - TSH stimulates thyroid production of \(T_3, T_4\)
3, 4. Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH)

- **In females**
  - FSH starts follicle development →
    - Starts egg production
    - Starts estrogen production from follicle cells
  - LH stimulates formation of corpus luteum
    - Completion of egg and its ovulation
    - Secretion of progesterone + estrogen

- **In males**
  - FSH → sperm production in testes
  - LH → release of testosterone from testes
3, 4. Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH)

- Regulation (feedback mechanisms)
  - Gonadotrophin-releasing hormone (GnRH) from hypothalamus $\rightarrow$ release of FSH or LH from anterior pituitary
  - FSH $\rightarrow$ increases estrogen in females
  - LH $\rightarrow$ increases estrogen (E) and progesterone (P) in females and testosterone (T) in males
  - High levels of these ovarian or testicular hormones (E, P, and T) suppress production of GnRH
5. Prolactin (PRL)

- Initiates and maintains milk production by mammary glands
  - Ejection of milk depends on oxytocin

- Regulation
  - Prolactin inhibiting hormone (PIH) suppresses prolactin release
  - High levels of estrogens $\rightarrow$ PRH $\rightarrow$ prolactin release

- Unknown function in males
  - Hypersecretion $\rightarrow$ erectile dysfunction
6. Adrenocorticotropic Hormone (ACTH)

- Controls production and secretion of glucocorticoids from adrenal cortex

- Regulation of ACTH
  - Corticotrophin releasing hormone (CRH) from hypothalamus stimulates secretion of ACTH
  - Stress-related stimuli can also stimulate ACTH release
  - Glucocorticoids inhibit CRH and ACTH release
7. Melanocyte Stimulating Hormone (MSH)

- Small amounts in bloodstream
- Excess amounts causes skin darkening
Posterior Pituitary

- Hormones made in hypothalamus pass down axons to posterior pituitary
  - Nerve impulses there cause release of hormones

- Two hormones released
  - Oxytocin causes
    - Smooth muscle contraction of uterus during childbirth
    - Causes “letdown” of milk from glands to ducts
    - Some sexual pleasure during sexual activity
Posterior Pituitary

- Antidiuretic Hormone (ADH) = vasopressin
  - Causes kidneys to retain more water
  - Causes vasoconstriction $\rightarrow$ increases blood pressure
  - Dehydration, pain, stress $\rightarrow$ increase ADH secretion
Posterior Pituitary

Hypothalamus

Pituitary gland

Cell bodies of neurosecretory cells

HYPOTHALAMUS

Optic chiasm

Infundibulum

Axons of neurosecretory tract

Axon terminal

POSTERIOR PITUITARY

ANTERIOR PITUITARY

Capillaries of posterior pituitary

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High blood osmotic pressure stimulates hypothalamic osmoreceptors. Osmoreceptors activate the neurosecretory cells that synthesize and release ADH. Nerve impulses liberate ADH from axon terminals in the posterior pituitary into the bloodstream. Target tissues: Kidneys retain more water, which decreases urine output; Sudoriferous (sweat) glands decrease water loss by perspiration from the skin; Arterioles constrict, which increases blood pressure. Low blood osmotic pressure inhibits hypothalamic osmoreceptors. Inhibition of osmoreceptors reduces or stops ADH secretion.
Thyroid Gland

- **Location**: inferior to larynx: two lobes

- **Structure and function**
  - Follicular cells produce hormones and store them in follicles
    - Thyroxin ($T_4$)
    - Triiodothyronine ($T_3$)
  - Parafollicular cells (C-cells) produce
    - Calcitonin (CT)
Thyroid Gland

- Hyoid bone
- Larynx
- Internal jugular vein
- LEFT LOBE OF THYROID GLAND
- Common carotid artery
- Trachea
- Sternum

Anterior view of thyroid gland
Thyroid Gland

Parafollicular cell

Follicular cell

Thyroid follicle

Stored thyroid hormones

Thyroid follicles

LM 500x
Thyroid Hormones: Actions

- $T_4$ (thyroxine) and $T_3$ increase basal metabolic rate, protein synthesis, and growth
  - Blood level is controlled by TRH and TSH
  - Increase in the body’s demand for ATP can also raise blood levels

- Calcitonin inhibits osteoclasts
  - Inhibits osteoclasts. Effects:
    - Strengthens bones
    - Decreases blood $Ca^{2+}$
  - Feedback control based on $Ca^{2+}$ blood levels
Thyroid Hormone Regulation

1. Low blood levels of T₃ and T₄ or low metabolic rate stimulate release of
   Hypothalamus

2. TRH, carried by hypophyseal portal veins to anterior pituitary, stimulates release of TSH by thyrotrophs

3. TSH released into blood stimulates thyroid follicular cells

4. T₃ and T₄ released into blood by follicular cells

5. Elevated T₃ inhibits release of TRH and TSH (negative feedback)

Actions of Thyroid Hormones:

- Increase basal metabolic rate
- Stimulate synthesis of Na⁺/K⁺ ATPase
- Increase body temperature (calorigenic effect)
- Stimulate protein synthesis
- Increase the use of glucose and fatty acids for ATP production
- Stimulate lipolysis
- Enhance some actions of catecholamines
- Regulate development and growth of nervous tissue and bones
Parathyroid Glands

- Small round masses in posterior of thyroid gland
- Release parathyroid hormone (PTH)
  - Increases blood Ca\(^{2+}\) in 3 ways
    - Increases number and activity of osteoclasts that break down bone
    - Slows loss of Ca\(^{2+}\) and Mg\(^{2+}\) in urine
    - Promotes production of calcitriol (vitamin D) \(\rightarrow\) increases rate of Ca\(^{2+}\), Mg\(^{2+}\) and HPO\(_4\)\(^{2-}\) absorption in GI tract \(\rightarrow\) increase blood blood Ca\(^{2+}\)
  - Decreases blood HPO42- by decreasing loss of HPO\(_4\)\(^{2-}\) in urine
Parathyroid Glands

Parathyroid glands (behind thyroid gland)

Trachea

LEFT SUPERIOR PARATHYROID GLAND

Esophagus

LEFT INFERIOR PARATHYROID GLAND

Thyroid gland

RIGHT SUPERIOR PARATHYROID GLAND

RIGHT INFERIOR PARATHYROID GLAND

Trachea

Posterior view
High level of $\text{Ca}^{2+}$ in blood stimulates thyroid gland parafollicular cells to release more CT.

Low level of $\text{Ca}^{2+}$ in blood stimulates parathyroid gland chief cells to release more PTH.

Calcitonin inhibits osteoclasts, thus decreasing blood $\text{Ca}^{2+}$ level.

Parathyroid hormone (PTH) promotes release of $\text{Ca}^{2+}$ from bone extracellular matrix into blood and slows loss of $\text{Ca}^{2+}$ in urine, thus increasing blood $\text{Ca}^{2+}$ level.

Calcitriol stimulates increased absorption of $\text{Ca}^{2+}$ from foods, which increases blood $\text{Ca}^{2+}$ level.

PTH also stimulates the kidneys to release calcitriol.
Pancreas

- Flattened organ in curve of duodenum
- Mostly an exocrine organ that secretes digestive enzymes
- Endocrine cells in pancreatic islets (of Langerhans)
- Several cell types
  - Alpha cells $\rightarrow$ glucagon
  - Beta cells $\rightarrow$ insulin
Pancreas
Pancreas

Pancreatic islet and surrounding acini

Blood capillary
Exocrine cells
Alpha cell (secretes glucagon)
Beta cell (secretes insulin)
Pancreas

Pancreatic islet and surrounding acini

Exocrine cells
Beta cell
Alpha cell

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**Actions of Insulin and Glucagon**

- **Low blood glucose stimulates glucagon release**
  - Glucagon stimulates liver to release glucose → increased blood glucose
- **High glucose levels stimulate insulin release**
  - Insulin increases glucose transport into skeletal muscle and adipose cells → decreased blood glucose
  - Insulin promotes amino acid uptake, protein synthesis, and lipid storage
- **ANS also modulates hormone release**
Glucagon acts on hepatocytes (liver cells) to:
- convert glycogen into glucose (glycogenolysis)
- form glucose from lactic acid and certain amino acids (gluconeogenesis)

Glucose released by hepatocytes raises blood glucose level to normal

If blood glucose continues to rise, hyperglycemia inhibits release of glucagon

High blood glucose (hyperglycemia) stimulates beta cells to secrete

Insulin acts on various body cells to:
- accelerate facilitated diffusion of glucose into cells
- speed conversion of glucose into glycogen (glycogenesis)
- increase uptake of amino acids and increase protein synthesis
- speed synthesis of fatty acids (lipogenesis)
- slow glycogenolysis
- slow gluconeogenesis

Blood glucose level falls

If blood glucose continues to fall, hypoglycemia inhibits release of insulin
Adrenal Glands

- Location: on top of kidneys
- Two separate gland structures
  - Adrenal cortex: 3 zones make steroids
    - Outer zone → mineralocorticoids (aldosterone)
    - Middle zone → glucocorticoids (cortisol)
    - Inner Zone → androgens (testosterone)
  - Adrenal medulla: produces epinephrine (adrenalin) and norepinephrine
Adrenal Glands

Section through left adrenal gland

Capsule
Adrenal cortex
Adrenal medulla

Capsule
Adrenal cortex:
Zona glomerulosa secretes mineralocorticoids, mainly aldosterone

Zona fasciculata secretes glucocorticoids, mainly cortisol

Zona reticularis secretes androgens

Adrenal medulla chromaffin cells secrete epinephrine and norepinephrine (NE)

Subdivisions of the adrenal gland

LM 50x
Mineralocorticoids

- **Aldosterone is the major form**
- **Action**
  - Stimulates Na$^+$ and H$_2$O reabsorption from urine to blood
  - Stimulates excretion of K$^+$ into urine
- **Part of renin-angiotensin-aldosterone pathway**
  - Decreased BP $\rightarrow$ release of renin from kidney
  - Renin causes angiotensinogen $\rightarrow$ angiotensin I
  - In lungs angiotensin converting enzyme (ACE) causes angiotensin I $\rightarrow$ angiotensin II
  - Angiotensin II stimulates aldosterone release
Mineralocorticoids

Dehydration, Na⁺ deficiency, or hemorrhage

Decrease in blood volume and blood pressure

Kidney

Renin

Angiotensin I

ACE

Angiotensin II

Adrenal cortex

Aldosterone

In kidneys, more Na⁺ and water return to blood and more K⁺ eliminated in urine

Increase in blood volume and blood pressure

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Glucocorticoid (Cortisol) Actions

- Increases rate of protein breakdown
- Stimulates liver formation of glucose
- Breaks down triglycerides in adipose
- Anti-inflammatory effects
  - Inhibit white blood cells
- Depresses immune system
- Regulated by negative feedback: CRH and ACTH
Androgens

- Small amount secreted from adrenal cortex in both females and males
  - At puberty, in both genders, androgens
    - Stimulate axillary and pubic hair growth
    - Contribute to adolescent growth spurt
  - In females, androgens
    - Contribute to libido
    - Are converted to estrogens by other body tissues
Adrenal Medulla

- Inner portion of adrenal glands
- Part of sympathetic nervous system
  - Consists of sympathetic postganglionic cells
  - Stimulated by preganglionic sympathetic neurons
  - Releases epinephrine and norepinephrine
  - Actions mimic sympathetic nerves in stress
    - Increases heart rate and blood pressure
    - Increases blood glucose, dilates airways
Gonads: Ovaries and Testes

- Produce gametes: sperm and oocytes
- Produce hormones
  - Testosterone in males
  - Estrogen and progesterone in females
  - Inhibin that inhibits FSH release
  - Relaxin during pregnancy: facilitates birth
- Regulated by
  - GnRH from hypothalamus
  - FSH + LH from anterior pituitary
Pineal Gland

- Small gland attached to roof of third ventricle of brain
- Produces melatonin
- Sets body’s biological clock
  - More released in darkness, less in sunlight
Other Hormones

- Thymus: thymosin
- GI tract
  - Gastrin
  - Glucose-dependent insulinotrophic peptide (GIP)
  - Secretin
  - Cholecystokinin (CCK)
- Kidney: erythropoietin (EPO)
- Heart: atrial natriuretic peptide (ANP)
Other Hormones

- Adipose tissue: leptin
- Placenta: human chorionic gonadotropin (hCG)
- Prostaglandins (PG) and leukotrienes (LT)
- Derived from fatty acids
- Act locally in most tissues and released from most body cells
Other Hormones

- LTs stimulate white blood cells and mediate inflammation
- PGs affect many visceral functions, modulate inflammation, promote fever, and intensify pain
Stress Responses

- Response to stressors
- When successful leads to extra physiological capacity and long term adaptation
- Three stages
  1. Initial “fight-or-flight” response
     - Nerve mediated response-sympathetic
     - Aldosterone: to raise blood pressure
  2. Resistance (slower) → → →
  3. Exhaustion (may occur eventually)
Stress Responses

- Slower and longer than initial response
- Hypothalamus $\rightarrow$ increased CRH, GHRH, TRH
  - CRH $\rightarrow$ ACTH $\rightarrow$ cortisol $\rightarrow$ mobilizes metabolites (amino acids, glucose and fat)
  - GHRH $\rightarrow$ hGH $\rightarrow$ mobilizes fats and glucose for energy and promote tissue growth and repair
  - TRH $\rightarrow$ TSH $\rightarrow$ thyroid hormones $\rightarrow$ increased metabolic capacity
Aging

- Some decrease in function with aging
  - Loss of negative feedback sensitivity so decline in circulating thyroid hormones
  - PTH levels rise → loss of bone mass
  - Less glucocorticoid production
  - Slower release of insulin
  - Thymus declines after puberty
  - Ovarian response to gonadotropins stops
  - Slow decline in testosterone production