Chapter 11 Outline

- Endocrine Glands and Hormones
- Mechanisms of Hormone Action
- Pituitary Gland
- Adrenal Glands
- Thyroid and Parathyroid Hormones
- Pancreas and Other Endocrine Glands
- Autocrine and Paracrine Regulation
Endocrine Glands

- Are ductless and secrete hormones into bloodstream.
- Hormones travel to target cells that contain receptor proteins for it.
- Neurohormones are secreted into blood by specialized neurons.
- Hormones affect metabolism of targets.

Chemical Classification of Hormones

- **Amine** hormones are derived from tyrosine or tryptophan.
  - Include NE, Epi, thyroxine, melatonin.
- **Peptide hormones**
  - Polypeptide and protein hormones are chains of amino acids.
    - Include ADH, GH, insulin, oxytocin, glucagon, ACTH, PTH.
  - Glycoproteins include LH, FSH, TSH.
- **Steroids** are lipids derived from cholesterol.
  - Include testosterone, estrogen, progesterone, aldosterone, and cortisol.
Hormonal Actions and Interactions

Common Aspects of Neural and Endocrine Regulation

- Both NS and endocrine system use chemicals to communicate
- Difference between NTs and hormones is transport in blood and more diversity of effects in hormone targets
- Some chemicals are used as hormones and NTs
- Targets for both NTs and hormones must have specific receptor proteins
- Must be a way to rapidly inactivate both

Hormone Interactions

- Synergistic hormones:
  - They work together to produce an effect (complementary)
  - Produce a larger effect together than individual hormone (additive)
- Permissive effect if a hormone enhances responsiveness of a target organ to 2nd hormone
- Antagonistic: 1 hormone inhibits effect of another hormone.
Hormone Levels and Tissue Responses

- Normal tissue responses are produced only when hormones are in **physiological range**
- High (pharmacological) doses can cause a number of side effects
  - Probably by binding to receptors of different but closely related other hormones

- **Priming effect (upregulation)** occurs when a hormone induces more of its own receptors in target cells
- Results in greater response in target cell
- **Desensitization (downregulation)** occurs after long exposure to high levels of hormone
  - Subsequent exposure to this hormone produces a lesser response
- Most peptide hormones have **pulsatile secretion** which prevents downregulation
Mechanisms of Hormone Action

- Target cell receptors show specificity, high affinity, and low capacity for a hormone.
- Lipophilic hormones have receptors in target's cytoplasm and/or nucleus because can diffuse thru plasma membrane.
  - Their target is the nucleus where they affect transcription.
  - Called genomic action and takes at least 30 mins.
- Hydrophilic hormones have receptors on surface of target cell.
  - These act through 2nd messengers; effects are quick.
  - Some steroids also act on cell surface receptors.
  - Called nongenomic action.

Hormone Effects on Gene Activity

Hormones That Bind to Nuclear Receptor Proteins

- Lipid hormones travel in blood attached to carrier proteins.
  - They dissociate from carriers to pass thru plasma membrane of target.
  - Receptors are called nuclear hormone receptors.
Nuclear Hormone Receptors
- Serve as transcription factors when bound to hormone ligands
- Activate transcription
- Constitute a "superfamily" composed of steroid family and thyroid hormone family (which includes vitamin D and retinoic acid)

Nuclear Hormone Receptors
- Have ligand (hormone)-binding and DNA-binding domains
- Binds hormone and translocates to nucleus
- Binds to hormone-response element (HRE) on DNA located adjacent to target gene

Mechanisms of Steroid Hormones
- HRE consists of 2 half-sites
- 2 ligand-bound receptors have to bind to each HRE (dimerization)
  - This stimulates transcription of target gene
Mechanism of Thyroid Hormone Action

- Thyroid secretes 90% T₄ (thyroxine) and 10% T₃
- 99.96% of T₄ in blood is bound to carrier protein (thyroid binding globulin - TBG)
- Only free thyroxine and T₃ can enter cells
- Protein bound thyroxine serves as a reservoir
- T₄ converted to T₃ inside target cell
- T₃ binds to receptor protein located in nucleus

The receptor for T₃:

- T₃ and receptor bind to 1 half-site
- Other half-site binds retinoic acid
- Two partners form heterodimer that activates HRE
- Stimulates transcription of target gene
Hormones That Use 2nd Messengers

- Water soluble hormones use cell surface receptors because cannot pass through plasma membrane
- Actions are mediated by 2nd messengers
- Hormone is extracellular signal; 2nd messenger carries signal from receptor to inside of cell

Adenylate Cyclase-cAMP

- cAMP mediates effects of many polypeptide and glycoprotein hormones
- Hormone binds to receptor causing dissociation of a G-protein subunit

Adenylate Cyclase-cAMP

- G-protein subunit binds to and activates adenylate cyclase
- Which converts ATP into cAMP
- cAMP attaches to inhibitory subunit of protein kinase
Adenylate Cyclase-cAMP
- Inhibitory subunit dissociates, activating protein kinase
- Which phosphorylates enzymes that produce hormone’s effects
- cAMP inactivated by phosphodiesterase

Phospholipase-C-Ca²⁺
- Serves as 2nd messenger system for some hormones
- Hormone binds to surface receptor, activates G-protein, which activates phospholipase C

Phospholipase C splits a membrane phospholipid into 2nd messengers IP₃ and DAG
- IP₃ diffuses through cytoplasm to ER
- Causing Ca²⁺ channels to open

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Phospholipase-C-Ca²⁺

- Ca²⁺ diffuses into cytoplasm and binds to and activates calmodulin
- Ca²⁺-Calmodulin activates protein kinases which phosphorylate enzymes that produce hormone's effects

Epinephrine Can Act Via Two 2nd Messengers

Tyrosine Kinase 2nd Messenger System

- Is used by insulin and many growth factors to cause cellular effects
- Surface receptor is tyrosine kinase
- Consists of 2 units that form active dimer when insulin binds
Tyrosine Kinase 2nd Messenger System

- Activated tyrosine kinase phosphorylates signaling molecules that induce hormone/growth factor effects

Insulin Action

- Insulin stimulates glucose uptake by means of GLUT-4 carrier proteins
- 2nd messengers cause vesicles containing GLUT4 transporters to be inserted into plasma membrane

Endocrine Organs

- Pituitary
- Gonads (portion of chapter 20) – Produce gametes
- Adrenal gland - Stress
- Thyroid – Metabolism and Calcium Regulation
- Parathyroid – Calcium Regulation
- Pancreas – Glucose Regulation
Pituitary Gland

- Is structurally and functionally divided into anterior and posterior lobes
- Hangs below hypothalamus by infundibulum
- Anterior produces own hormones
  - Controlled by hypothalamus
- Posterior stores and releases hormones made in hypothalamus

Pituitary Gland is located beneath hypothalamus at base of forebrain.
Posterior Pituitary

- Stores and releases the hormones vasopressin (ADH) and oxytocin that are made in the hypothalamus.

Anterior Pituitary

- Secretes 6 trophic hormones that maintain size of targets:
  - High blood levels cause target to hypertrophy
  - Low blood levels cause atrophy

- Growth hormone (GH) promotes growth, protein synthesis, and movement of amino acids into cells
- Thyroid stimulating hormone (TSH) stimulates thyroid to produce and secrete T<sub>4</sub> and T<sub>3</sub>
- Adrenocorticotropic hormone (ACTH) stimulates adrenal cortex to secrete cortisol, aldosterone
- Follicle stimulating hormone (FSH) stimulates growth of ovarian follicles and sperm production
- Luteinizing hormone (LH) causes ovulation and secretion of testosterone in testes
- Prolactin (PRL) stimulates milk production by mammary glands
Anterior Pituitary

- Release of Anterior Pituitary hormones is controlled by hypothalamic
  - releasing factors
  - inhibiting factors
  - feedback from levels of target gland hormones
Anterior Pituitary

- Releasing and inhibiting hormones from hypothalamus are released from axon endings into capillary bed in median eminence.
- Carried by hypothalmo-hypophyseal portal system directly to another capillary bed in A. Pit.
- Diffuse into A. Pit. and regulate secretion of its hormones.

Feedback Control of Anterior Pituitary

- The hypothalamic-pituitary-gonad axis (control system)
- Involves short feedback loop in which retrograde flow of blood and hormones from A. Pit. to hypothalamus inhibits secretion of releasing hormone.
- Involves negative feedback of target gland hormones.
- And during menstrual cycle, estrogen stimulates “LH surge” by positive feedback.

Sex and Reproductive Hormones

- Gonads (testes and ovaries) secrete steroid hormones testosterone, estrogen, and progesterone.
- Placenta secretes estrogen, progesterone, hCG, and somatomammotropin.
The Ovarian Cycle – 3 phases

- **Follicular Phase** - first ½ of ovarian cycle
  - Follicle development
- **Ovulation** – Midpoint of ovarian cycle
  - Oocyte exits from one ovary
    - Enters the peritoneal cavity
    - Is swept into the uterine tube
- **Luteal Phase** – second ½ of ovarian cycle
  - Remaining follicle becomes a corpus luteum
    - Secretes progesterone
    - Acts to prepare for implantation of an embryo

Ovarian Cycle Summary

The Uterine Cycle

- Series of cyclic phases of the endometrium
- Phases coordinate with the ovarian cycle
- Endometrial phases directed by FSH and LH
- Phases of uterine cycle – 3 phases
  - **Menstrual phase** – days 1-5
    - Stratum functionalis is shed
  - **Proliferative phase** – days 6-14
  - **Secretory phase** – days 15-28

Figure 25.18c, d
Menstrual and Ovarian Cycles

Higher Brain Function and Anterior Pituitary Secretion
- Hypothalamus receives input from higher brain centers that can affect Anterior Pituitary secretion
- e.g. emotional states and psychological stress can affect circadian rhythms, menstrual cycle, and adrenal hormones

Posterior Pituitary
- Stores and releases 2 hormones produced in hypothalamus:
  - **Antidiuretic hormone** (ADH/vasopressin)
    - Promotes H₂O conservation by kidneys
  - **Oxytocin**
    - Stimulates contractions of uterus during parturition
    - Stimulates contractions of mammary gland alveoli for milk-ejection reflex
Hypothalamic Control of Posterior Pituitary

- Supraoptic nuclei of hypothalamus produce ADH
- Paraventricular nuclei produce oxytocin
- Both transported along hypothalamo-hypophyseal tract to posterior pituitary
- Release controlled in hypothalamus by neuroendocrine reflexes

Adrenal Gland

- Sit on top of kidneys
- Each consists of outer cortex and inner medulla
- Which arise differently during development
Adrenal Glands

- Medulla synthesizes and secretes 80% Epinephrine and 20% Norepinephrine
- Controlled by sympathetic division of ANS
- Cortex is controlled by ACTH and secretes:
  - Cortisol which inhibits glucose utilization and stimulates gluconeogenesis
  - Aldosterone which stimulate kidneys to reabsorb Na⁺ and secrete K⁺
  - And some supplementary sex steroids

Adrenal Medulla

- Hormonal effects of Epinephrine last 10X longer than Norepinephrine
- Innervated by preganglionic Sympathetic fibers
- Activated during "fight or flight" response
  - Causes:
    - Increased respiratory rate
    - Increased HR and cardiac output
    - General vasoconstriction which increases venous return
    - Glycogenolysis and lipolysis

Stress and the Adrenal Gland

- Stress induces a non-specific response called general adaptation syndrome (GAS)
- Causes ACTH and cortisol release
Stress and the Adrenal Gland

- Chronic stress can induce high levels of cortisol that cause a number of negative effects:
  - atrophy of hippocampus (involved in memory)
  - reduced sensitivity of tissues to insulin (insulin resistance)
  - inhibition of vagus nerve activity
  - suppression of growth hormone, thyroid hormone, and gonadotropins

Thyroid Gland

- Is located just below the larynx
- Secretes T₄ and T₃ which set Base Metabolic Rate (BMR) and are needed for growth, development
- A scan of the thyroid 24 hrs. after intake of radioactive iodine (b)
Thyroid Gland

- Consists of microscopic **thyroid follicles**
- Outer layer is **follicle cells** that synthesize T₄
- Interior filled with **colloid**, a protein-rich fluid

Production of Thyroid Hormones

- Iodide (I⁻) in blood is actively transported into follicles and secreted into colloid
- Where it is oxidized to iodine (I₂) and attached to tyrosines of **thyroglobulin**
- A large storage molecule for T₄ and T₃
- TSH stimulates hydrolysis of T₄ and T₃ from thyroglobulin and then secretion
**Diseases of the Thyroid - Goiter**

- In absence of sufficient dietary iodide, $T_4$ and $T_3$ cannot be made and levels are low.
- Low $T_4$ and $T_3$ don’t provide negative feedback and TSH levels go up.
- Because TSH is a trophic hormone, thyroid gland grows.
- Resulting in a goiter.

**Hypothyroid** - People with inadequate $T_4$ and $T_3$ levels.
- Have low BMR, weight gain, lethargy, cold intolerance.

**Hyperthyroid** – People with increased $T_4$ and $T_3$ levels.
- Characterized by weight loss, heat intolerance, irritability, high BMR, exophthalmos.

**Goiter** – Enlargement of thyroid gland due to iodine deficiency.

**Grave’s disease**
- Autoimmune disease where antibodies act like TSH and stimulate thyroid gland to grow and oversecrete.
Parathyroid Glands

- Are 4 glands embedded in lateral lobes of posterior side of thyroid gland
- Secrete Parathyroid hormone (PTH)
- Most important hormone for control of blood Ca^{2+} levels

Parathyroid Hormone

- Release stimulated by decreased blood Ca^{2+}
- Acts on bones, kidney, and intestines to increase blood Ca^{2+} levels

Islets of Langerhans
Islets of Langerhans

- Are scattered clusters of endocrine cells in pancreas
- Contain alpha and beta cells

Islets of Langerhans

- Alpha cells secrete glucagon in response to low blood glucose
  - Stimulates glycogenolysis and lipolysis
  - Increases blood glucose

Islets of Langerhans

- Beta cells secrete insulin in response to high blood glucose
  - Promotes entry of glucose into cells
  - And conversion of glucose into glycogen and fat
  - Decreases blood glucose