ENDOCRINE SYSTEM

Lecturer: Dr. Bruce Fenderson

READINGS

Educational Goals

- Understand structure - function relationships in the endocrine system.
- Investigate the microscopic anatomy of the pituitary gland.
- Understand the hypothalamo-hypophyseal system (vascular network and sites of hormone production, storage, and release).
- Investigate the microscopic anatomy of the adrenal cortex and medulla.
- Investigate the microscopic anatomy of the endocrine pancreas.
- Investigate the microscopic anatomy of the thyroid gland.
- Relate morphological variations in the thyroid epithelium to changes in function.
- Investigate the microscopic anatomy of the parathyroid glands.

Key Words

- Adrenal glands (cortex and medulla)
- Beta (β) cells (insulin-producing cells of endocrine pancreas)
- Chief cells (parathyroid - parathyroid hormone)
- Follicular cells (thyroid - thyroglobulin)
- Hypophysis (pituitary, anterior and posterior)
- Hypothalamic releasing hormones
- Hypothalamo-hypophyseal neuroendocrine system
- Islets of Langerhans
- Oxyphil cells (parathyroid)
- Parafollicular cells (thyroid - calcitonin)
- Pars distalis (anterior pituitary)
- Pars nervosa (posterior pituitary)
- Pituicyte
- Spongyocyte
- Zona glomerulosa, fasiculata, reticularis
Introduction to the Endocrine System

**Hormones** are potent chemical signaling substances (messengers) that are produced by secretory cells and released into the circulatory system. The hormone is subsequently delivered via the circulation to target cells with appropriate cellular receptors. The secretory cells and target cells may lie in close proximity to one another, or they may be scattered widely throughout the body. Based on distance, mechanisms of chemical signaling are often described as: endocrine, paracrine or autocrine. Secretory cells of the endocrine system are in most cases linked to the hypothalamo-hypophyseal (neuroendocrine) system via feedback loops. The endocrine glands that we will explore in class this week include:

- Pituitary
- Adrenals
- Islets of Langerhans
- Thyroid
- Parathyroids

### Pituitary Gland (Hypophysis)

- Lies in a cavity of the sphenoid bone (sella turcica).
- Normal weight 0.5 gm.
- Develops embryologically from oral ectoderm (Rathke’s pouch) and floor of diencephalon (see Figure below).

### Derivatives of Oral Ectoderm = Adenohypophysis = Anterior Pituitary

- Pars distalis (anterior pituitary)
- Pars tuberalis (surrounds neural stalk)
- Pars intermedia (vestigial)

### Derivatives of Diencephalon = Neurohypophysis = Posterior Pituitary

- Neural stalk (infundibulum) includes stem and median eminence
- Pars nervosa (posterior pituitary)
Vascular Supply & Innervation of the Pituitary

Superior and inferior hypophysial arteries are branches of the internal carotid arteries. A primary capillary plexus in the median eminence (derived from superior hypophysial arteries) serves to absorb and deliver inhibiting/releasing hormones to the pars distalis.

Long portal veins leave the primary capillary plexus and descend down the pituitary stalk to the pars distalis of the anterior pituitary. Long portal veins ultimately give rise to a secondary capillary plexus within the anterior pituitary.

Owing to this hypothalamo-hypophyseal portal circulation, cells of the pars distalis receive releasing and inhibitory factors synthesized by neurons of hypothalamic nuclei that are stored within the median eminence. Hormones synthesized in the pars distalis enter the general circulation via the secondary capillary plexus (see Figure below).

An additional capillary plexus within the pars nervosa (posterior pituitary) carries products of supraoptic and paraventricular nuclei to the general circulation (see below).
Hypothalamo-Hypophyseal Neuroendocrine System

There are 3 sites for production of these polypeptide, neuroendocrine hormones:

(1) Peptides synthesized by secretory neurons in the supraoptic and paraventricular nuclei are transported along axons to the neurohypophysis (posterior pituitary).
(2) Peptides (releasing hormones) synthesized by neurons in the hypothalamus (dorsal-medial, ventral-medial and infundibular nuclei) are released in the median eminence and transported to the anterior pituitary via a capillary portal system.
(3) Polypeptide hormones synthesized by cells of the pars distalis (anterior pituitary).

Microscopic Anatomy of the Adenohypophysis (Anterior Pituitary)

Pars Distalis
➢ Cords of glandular cells surrounded by capillaries
➢ Chromophobes and Chromophils (Acidophils & Basophils)
➢ Hormones include: somatotrophin (GH), prolactin, FSH, LH, MSH, TSH, ACTH

Pars Intermedia
➢ Rudimentary region in humans
➢ Weakly basophilic cells

Pars Tuberalis
➢ Cells arranged in cords along blood vessels - surrounds the neural stalk
➢ Most of these cells secrete FSH or LH

Microscopic Anatomy of the Neurohypophysis (Posterior Pituitary)

Neurons of the supraoptic and paraventricular nuclei produce hormones that are stored and liberated from the posterior pituitary. Axons of neurons within these nuclei extend down through the median eminence into the posterior pituitary (pars nervosa). Hormones synthesized by neurons of these nuclei are transported along axons and occupy storage granules (Herring bodies) within the pars nervosa. The stored hormones, typically bound to a carrier protein - neurophysin, are released into adjacent capillaries as a result of neuronal stimulation from other regions in the brain.

Cells of the Neurohypophysis (Axons and Pituicytes)

➢ Axons of hypothalamic neurons (from supraoptic and paraventricular nuclei)
➢ 25% of volume of neurohypophysis = pituicytes (highly branched glial cells)
➢ Herring bodies = aggregates of neurosecretory granules in dilated axon terminals
Hormones of the Neurohypophysis (Posterior Pituitary)

- Oxytocin
- Vasopressin (arginine vasopressin / antidiuretic hormone)
- Binding protein for each = neurophysin
- Released from storage via neuronal impulses from the hypothalamus
- Clinical correlation: diabetes insipidus (patient has polyuria due to antidiuretic hormone deficiency)

**Adrenal (Suprarenal) Glands**

Paired organs near the superior poles of the kidneys. They are embedded in adipose tissue. Their weight and size varies with age and physiology. Closer examination reveals 2 concentric layers: an outer (yellow) cortex and a central (red-brown) medulla (see Figure below).

The adrenal glands are derived during development from 2 sources: coelomic epithelium and neural crest.

The metabolic activity of the adrenal cortex is regulated by ACTH from the anterior pituitary, whereas the metabolic and secretory activity of the adrenal medulla is controlled by preganglionic sympathetic nerve fibers. Adrenal cortical hormones regulate metabolism (corticosteroids), maintain normal electrolyte balance (aldosterone), and influence reproductive organs (generation of weak androgens). Hormonal targets for epinephrine and norepinephrine include: glandular epithelial cells, cardiac muscle, and smooth muscle of blood vessels & viscera.
Vascular Supply to the Adrenal Glands

The adrenals are highly vascular organs. Blood vessels enter at various points around the gland. Capillaries eventually drain through a common suprarenal vein. The arteries can be divided into three groups:

- Capsular arteries provide an extensive subcapsular network
- Cortical arteries irrigate the cortex
- Medullary arteries pass through the cortex directly to the medulla

Cortical and medullary arterioles originate as branches of capsular arteries. Together, they supply the parenchyma of the gland. The medullary capillary bed receives blood from two sources: cortical veins and medullary arterioles. Capillaries of the cortical and medullary arterials form a single suprarenal vein.

Lymphatic vessels are only associated only with capsule and connective tissue around the large blood vessels. Lymphatics are not associated with parenchymal elements.

Microscopic Anatomy of the Adrenal Cortex

Cells of the adrenal cortex have the typical ultrastructure of steroid-secreting cells (foam cells with lipid droplets). Cords of glandular tissue are grouped along capillaries. There are 3 concentric zones with different physiological functions (salt/sugar/sex):

| Zona Glomerulosa (salt - aldosterone) |
| Zona Fasiculata (sugar - cortisol) |
| Zona Reticularis (sex hormones) |

Zona Glomerulosa
- Thin outer zone adjacent to the capsule
- Small columnar or pyramidal cells arranged in clusters
- Continuous with cords of cells in subjacent region

Zona Fasiculata
- Large polyhedral cells arranged in parallel columns with lipid droplets
- Columns of these spongyocytes are separated by cortical sinusoids

Zona Reticularis
- Innermost layer of cortex
- Lipofuchsin granules present

Developmental Considerations: Fetal (Provisional) Cortex
- Large by midgestation - produces precursors to placental estrogen (helps mother)
- Regresses postnatally
- Zones of adult cortex develop during first 3 postnatal years
Summary of Adrenal Cortical Hormones

**Aldosterone**
- Mineralocorticoid that helps regulate systemic blood pressure
- Primary site of synthesis is zona glomerulosa

**Cortisol (hydrocortisone)**
- Glucocorticoid helps regulate metabolism
- Primary site of synthesis is zona fasiculata

**Androgens**
- Small amounts produced by cells of zona reticularis
- Minute amounts also produced by cells of zona fasiculata
- Weak androgens (e.g., androstenedione)

Adrenal Medulla: Microscopic Anatomy

Like the cortex, the adrenal medulla is composed of polyhedral cells in cords with a surrounding network of capillaries.

Cells of the medulla are considered to be modified postganglionic neurons of the sympathetic nervous system. These neural crest derived cells are referred to as chromaffin cells.

Summary of Adrenal Medullary Hormones

- Catecholamines (epinephrine and norepinephrine)
- These similar hormones are synthesized by 2 different populations of cells
- Stored in membrane-bound, electron-dense, secretory granules
Islets of Langerhans are multi-hormonal micro-organs located in the pancreas. They are approximately 100-200 μm in diameter. Each islet includes several hundred cells. They are embedded within pancreatic exocrine tissue. There are approximately 1 million islets per pancreas.

**Islets: Microscopic Anatomy**

- Spherical configuration of islets
- Composed of rounded/polygonal cells
- Fenestrated capillary network
- Separated from exocrine tissue by reticular fibers
- 10% of cells innervated by autonomic nerve fibers

**Islet Cell Types** *(immunocytochemical methods are used to identify types)*

- Quantities not uniform within or between islets
- A cells (20%) - synthesize glucagon
- **B cells (70%)** – synthesize insulin
- D cells (<5%) --synthesize somatostatin
- F cells (rare) - pancreatic polypeptide
The thyroid gland is located anterior to the larynx. It originates during development from endoderm of the primitive gut. It synthesizes thyroid hormones (T3 and T4) that are important for growth, differentiation, and control of metabolic rate (e.g., oxygen consumption).

The gland is composed of **20-30 million follicles**, that are lined by a simple epithelium. The central cavity stores extracellular hormone precursor (thyroglobulin) in a gelatinous matrix called **colloid**. Thyroid follicles contain a 3-month store of thyroid hormone.

**Thyroid Gland: Microscopic Anatomy**

- Loose connective tissue capsule with septae
- Highly vascular organ
- Fenestrated capillaries (functional significance)
- Follicles (spherical shape; simple epithelium with variable morphology)
  - squamous to low columnar
  - follicular diameter is variable (depends on functional state)
- Colloid (thyroglobulin stains with PAS due to high sugar content)
Effect of Thyroid-Stimulating Hormone (TSH) on the Thyroid

- Stimulates thyroid hormone synthesis
- Increases height of follicular epithelium
- Decreases quantity of colloid as well as follicle diameter

Functional Aspects of Follicular Morphology

**Larger diameter**
- distended with colloid
- cuboidal to squamous epithelium
- in hypoactive thyroid the most common epithelium is squamous

**Smaller diameter**
- less colloid
- simple columnar epithelium
- associated with higher metabolic activity (hyperactive thyroid)
- clear vacuoles in the colloid next to the follicular epithelium (scalloping of the colloid) indicates rapid uptake of thyroglobulin (hyperfunction)

Parafollicular or C-Cells: Microscopic Anatomy

- Clear cells may form part of follicular epithelium, or….
- May exist as isolated clusters between follicles
- Larger and less intensely stained compared to follicular cells
- Arise from infiltrating neural crest cells

Parafollicular or C-Cells: Endocrine Function

- Synthesize and secrete the hormone - calcitonin
- Calcitonin decreases blood calcium levels by inhibiting bone resorption
- Secretion of calcitonin stimulated by increased levels of blood calcium (hypercalcemia)

Clinical Correlations

- Nodular goiter (common and benign)
- Graves hyperthyroidism (an autoimmune disease)
- Hashimoto thyroiditis (associated with hypothyroidism)
- Benign and malignant neoplasms (adenoma vs carcinoma)
### Parathyroid Glands

There are typically 4 parathyroid glands, located behind the thyroid gland at each upper and lower pole (see Figure below). They are usually found within the capsule that covers the lobes of the thyroid; however, they may be found embedded in the thyroid parenchyma. The glands are derived during development from the 3rd and 4th pharyngeal pouches. Ectopic glands are found in the mediastinum, beside the thymus. Each gland contains a connective tissue capsule with endocrine cells arranged in cords. The two types of parathyroid parenchymal cells are **chief cells** and **oxyphil cells**. Chief cells secrete parathyroid hormone in response to hypocalcemia.

#### Parathyroid Glands: Microscopic Anatomy

- Parenchymal component includes **chief cells** and **oxyphil cells**
- Chief cells are smaller and produce parathyroid hormone
- Oxyphil cells are larger polygonal cells, smaller population, of unknown function
- Stromal component includes connective tissue capsule and septae
- **With increasing age, adipose tissue comes to replace the secretory cells**

#### Summary of Parathyroid Hormone Function

- Increases blood calcium levels (acts on osteoclasts)
- Reduces blood phosphate levels (acts on kidneys)
- Promotes increased calcium absorption from the gut
NOTES: