Endocrine System I and II
Pituitary/Neuroendocrine/Thyroid/Parathyroid

Gwen V. Childs, Lecturer
Where is the pituitary located?

Depression at base of skull “sella turcica”
Or “Turkish Saddle”

Connected to brain by a Stalk

Pituia means mucous
Objectives:

1. Describe/Define the major anatomical regions of the hypophysis and the embryological origin of each. (Slides 2—5, 9, 10, 28-30)
2. Describe the blood supply to the hypophysis and its significance. (Slides 6-8)
3. Correlate the structure and function of each of the major cell types in the adenohypophysis, including their target organ(s) and major regulatory hormone(s). (Slides 10-23)
4. Describe what would happen to each of the anterior lobe cell types if the stalk were sectioned. (Class discussion)
5. Define the origin, structure, and function of the cells and axons in the neurohypophysis. (Slides 24-27)
What two regions give rise to the pituitary gland?

Downgrowth from Diencephalon = Neurohypophysis

Upgrowth from roof of mouth = Adenohypophysis; forms Rathke’s pouch. Left = shows two regions Adenohypophyseal cells proliferate and fill in the region.
Regions of Adenohypophysis
- Pars distalis (also called anterior lobe)
- Pars tuberalis
- Pars intermedia

ADH and Oxytocin are produced by both nuclei

Regions of Neurohypophysis
- Median eminence
- Infundibular stalk
- Pars nervosa (also called posterior lobe)
Blood supply to the pars distalis

1. Superior hypophyseal A. branch from the Internal Carotid A. + Post Comm Br from C of W

2. Breaks up into capillary loops in the stalk/median eminence region.

3. Capillaries send long portal veins to connect with fenestrated pars distalis capillaries, empty into hypophyseal veins

Blood supply to the pars nervosa

4. Separate from that of pars distalis. Inferior hypophyseal arteries branch from Internal carotids. Immediately break up into capillaries in pars nervosa
Neurons secrete hormone into stalk capillaries

- Capillaries provide increased surface area for lots of nerve fiber endings
- Then, portal veins provide a direct conduit or route to the anterior lobe cells.
- Releasing or inhibiting hormones are not diluted by entire blood stream.
- Don’t have to travel very far.
Target organ produces hormone that may feedback via bloodstream to brain or pituitary.

Portal veins transport the hormones to the capillaries of the pars distalis.

Negative feedback blocks the synthesis and secretion of pituitary and hypothalamic hormones. Tells the pituitary to stop stimulating the organ.

Positive feedback enhances the synthesis and secretion of pituitary and hypothalamic hormones.
Pars nervosa is fibrous
Pars distalis is more cellular
Pars intermedia: nests of cells in the pars nervosa
Major Cell types in the Adenohypophysis

**Acidophils**
- Somatotropes
  - Growth hormone (GH)
- Lactotropes
  - Prolactin
- Corticotropes
  - Adrenocorticotropic (ACTH)
  - Beta-endorphin

**Basophils**
- Gonadotropes
  - Adrenocorticotropic (ACTH)
  - Beta-endorphin
- Thyrotropes
  - Thyroid Stimulating Hormone (TSH)
  - Luteinizing hormone (LH) & Follicle stimulating hormone (FSH)

**Chromophobes**
(degranulation)
Acidophils: Red; Basophils: Blue/purple; Chromophobes: Colorless
Tricks to identification of anterior lobe cells:

- Cellular pars distalis contains cells that vary in “color”. Staining more reddish, or blue-purple.
- Red Cells = acidophils; cytoplasm will match the color of nearby red blood cells.
- Blue or purple cells = basophils. Cytoplasm matches the color of the nucleus.
- Colorless = called Chromophobes; may be degranulated acidophils or basophils.
B=Basophil, A=Acidophil, V=blood vessel, rbc=red blood cells
Focus on Acidophils

• Growth Hormone cells:
  • Produce *Growth hormone or somatotropin*.
  • Involved in growth of long bones; muscle anabolism; lipolysis.
  • Stimulation: GH releasing hormone (GHRH) from hypothalamus
  • Inhibition: somatostatin from hypothalamus

• Prolactin cells or lactotropes:
  • Produce *prolactin*.
  • Involved in the growth and development of the mammary gland
  • Inhibition (chronic) by dopamine from hypothalamus
  • Stimulation: thyrotropin releasing hormone from hypothalamus

Acidophils are red or orange cells
Somatotrope

GH=protein hormone
You would expect important components of protein translating machinery:

- Rough endoplasmic reticulum
- Prominent Nucleolus
- Golgi Complex
- Secretory granules (300-350 nm)
- Exocytosis profiles

Regulated by growth hormone releasing hormone (GHRH) (stimulatory) and somatostatin (inhibitory) from neurons in hypothalamus
Gigantism:
Too much GH before closure of the epiphyseal plate. One cause might be Anterior Pituitary GH secreting tumor.

Example: Mr. Robert Wadlow (Alton Giant); 6 months: 30 lbs 1 year: 62 pounds. At death (22 years): 8 ft, 11 inches, 475 lbs;

Acromegaly:
Occurs after puberty and closure of the epiphyseal plates. Excess GH causes thickening of bones in jaw and extremities (among other problems)

Use analogs of somatostatin to treat GH secreting tumors
**Lactotrope (mammotrope)**

Prominent rough ER and Golgi complex

Large secretory granules + granules that have funny shapes (dumbbell, irregular)

Regulation: Dopamine is inhibitory

Use analogs of dopamine to reduce pituitary prolactin microadenomas

If pituitary stalk is cut or damaged, these cells will proliferate and take over pituitary.
Basophils (will study regulation with target organ).

• **Gonadotropes: (see gonads)**
  - produce *luteinizing hormone (LH)*, which stimulates ovulation in the female and testosterone production in the male (ICSH=interstitial cell stimulating hormone)
  - and *follicle stimulating hormone (FSH)* which stimulates the growth of the ovarian follicles and the sperm cells.

• **Corticotropes: (see adrenal)**
  - produce *adrenocorticotropin (ACTH)* which stimulates the adrenal during the flight or fight reaction (stress). (Adrenal Zona fasciculata)
  - Also, produce *beta-endorphin* which is our body’s analgesic.

• **Thyrotropes: (see thyroid)**
  - produce *thyroid stimulating hormone (TSH)* which stimulates the thyroid gland.
  - increase body metabolism.

Basophils are purple, blue, or reddish purple.
Gonadotrope

Rough ER is displayed in filled sacs scattered throughout the cytoplasm.

Many cells have two types of granules, a large subset and a smaller subset.

Regulated by Gonadotropin releasing hormone (GnRH) from hypothalamus.
Immunostained FSH gonadotrope in human pituitary
Electron photomicrograph of human anterior pituitary cells

- Thyrotrope (Thyroid stimulating hormone)
- Somatotrope (Growth Hormone)
- Adrenocorticotropin (ACTH) cell
- Corticotrope
- Labeled for ACTH (dark granules)
- Prolactin cell (lactotrope)

Immunolabeled for ACTH
What are folliculostellate cells?

Cells with many processes that are linked by gap junctions. Often form “sacs” called follicles. May produce growth factors. Exact function unknown.

Gap junctions suggest that maybe they are a cellular communication network.

Facilitate coordinated secretion—pulses or surge.

Here the FS cells are labeled for S100 protein, a marker that also detects glial cells.
Nerve cell bodies in the paraventricular and supraoptic nuclei produce OXYTOCIN and VASOPRESSIN.

These hormones are stored in Secretory granules. Sent down axon to pars nervosa via stalk.

Oxytocin and vasopressin are released into blood stream to be distributed to the body

- Oxytocin: Contractions of uterus and mammary gland myoepithelial cells (Lactation) Direct neural stimulation.

- Vasopressin (Anti-diuretic hormone) Raises blood pressure; water and sodium conservation; Collecting ducts in kidney.
Pars Nervosa Histology

- Endothelial cell (capillary)
- Glial cell (pituicyte)
- Axons containing oxytocin or vasopressin
Axonal endings in Pars nervosa containing oxytocin or vasopressin stored in neurosecretory granules
What is the Pars Intermedia/Intermediate lobe?

- Nests of anterior lobe basophils that remain attached to the pars nervosa, in clusters or "nests".
- Look almost embedded in it at the site where the pars distalis and pars nervosa meet.
- Produce ACTH and Melanocyte stimulating hormone (MSH).
- Cause spread of melanin pigment and increases pigmentation.
What is the Pars Tuberalis?

- Region derived from adenohypophysis where it met the stalk.
- A Collar of cells: contains gonadotropes or thyrotropes—depending on the species.
- May contain “clock” genes and respond to stimuli from neurons that regulate circadian rhythms.
Median eminence would be attached here

Stalk includes a tract of nerve fibers running to the pars nervosa

It has a collar of anterior lobe (pars distalis) cells called the pars tuberalis
Endocrine System II
Thyroid and Parathyroid Glands

Gwen V. Childs, Lecturer

Endocrine Cells in Thyroid and Parathyroid Glands

Figure 13-6 Schematic diagram of the thyroid and parathyroid glands.
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Objectives

1. Locate and be able to identify thyroid and parathyroid glands (Slides 1, 3, 4, 14-17)
2. Describe how the thyroid follicular (Principal cells) cells are organized and how they produce and store their hormone. (Slides 3-12)
3. Correlate the structure and function of the parafollicular cells and principal cells of the parathyroid gland with respect to calcium metabolism. (Slides 13-19)
Thyroid histology

Thyroid Follicles

colloid
Thyroid histology: how would you classify these cells?
Synthesis and Storage of thyroid hormones

- Thyroid hormone is made of two amino acids, linked together. (Tyrosines)
- Iodine is attached to each.
- The iodinated amino acids are inserted in a large (660,000 MW) protein molecule called “thyroglobulin”.
- Stored OUTSIDE THE THYROID CELLS in colloid.
- Once they are outside the cell in colloid, they have to be brought back in to be secreted in the blood stream.
1. Stimulation by TSH

2. AA, Iodide uptake

3a. Synthesis of Thyroglobulin

3b. Oxidation of Iodide

4. Packaging of Thyroglobulin

5. Secretion of Thyroglobulin

6. Iodination, Storage
1. Stimulation by TSH

2. AA, Iodide uptake

3. Synthesis

3b. Oxidation Of Iodide

4. Packaging

5. Secretion & iodination

6. Iodination, Storage
TSH-stimulated thyroid cell
Functions of Thyroid hormone

- Increases metabolism throughout the body.
- We become energized, more active, heat producing
- Cold stimulates thyroid hormone release to raise body heat.
- Low thyroid: sluggish, tired, cold, speech slurred.
- In amphibians, important for metamorphosis
- Important for brain development in mammals. (in infant, low thyroid can cause mental retardation)
Portal veins provide a direct conduit or route for TRH to the anterior lobe cells.

Neurons produce Thyrotropin Releasing hormone (TRH)

Send TRH, in axons to Stalk - Median eminence region. Release TRH in capillary bed

TRH stimulates TSH cells to synthesize and secrete TSH

TSH is released through Pituitary Venous system

Regulation of Thyroid
What happens to the thyroid cells when they are stimulated?
Regulation of blood levels of calcium

- **Thyroid C cells or parafollicular cells**
  - lie outside follicles either in clusters, or singly.

- **Produce the peptide hormone, calcitonin**
  - Protein synthesizing organelles prominent.
  - Inhibits calcium resorption from bones. What cell type is involved?
  - Lowers blood calcium

- **Regulated by calcium levels. High Ca will stimulate its release.**
Parafollicular or C cells

Left: C Cells labeled immunocytochemically for calcitonin
Right: Electron micrograph of C-Cell
Parathyroid gland

- At least 4 glands in the region of the thyroid gland
- Have three cell types: adipose (Fat) cells, chief cells and oxyphil cells.
- Parathyroid hormone is a peptide that raises serum calcium; produced by Chief cells. Called PTH.
Parathyroid Gland

P = Parathyroid Chief cells
O = Oxyphil cells
C = capillary

The chief cells are the active endocrine cells.

When calcium levels drop, PTH is released by exocytosis and goes to the bone to stimulate breakdown and release of calcium, PTH also works on the kidney and intestine. See Physiology lectures for details.
Parathyroid Gland

Oxyphil cells

Chief cells

PTH is a polypeptide hormone, stored in secretion granules.

Rough endoplasmic reticulum, Golgi complex, and secretory granules
Electron microscopic view

Oxyphil Cells increase in number with age.

Filled with mitochondria; gives them acidophilic appearance

Oxyphil cell
Distinguish chief and oxyphil cells

- **Chief cells** have larger nuclei
- **Paler cytoplasm**
- **Function?**
  - Produce parathyroid hormone

- **Oxyphil cells** have central nucleus
- **Red Acidophilic cytoplasm**
- **Often in clusters**
- **Function?**
  - To help you identify the parathyroid gland