C16.2 Endocrine

- Pituitary Gland
- Hypothalamic-hypophyseal Tract
- Hypophyseal Portal System
The Pituitary Gland and Hypothalamus

- Pituitary gland (hypophysis) has two major lobes
  - Posterior pituitary (lobe)
    - Neural tissue
  - Anterior pituitary (lobe) (adenohypophysis)
    - Glandular tissue
Histology of Pituitary Gland

(a) Anterior pituitary
- Chromophobe
- Basophil
- Acidophil

(b) Posterior pituitary
- Unmyelinated nerve fibers
- Glial cells (pituicytes)
Pituitary-hypothalamic Relationships

• Posterior pituitary (lobe)
  – Downgrowth of hypothalamic neural tissue
  – Neural connection to hypothalamus (hypothalamic-hypophyseal tract)
  – Nuclei of hypothalamus synthesize neurohormones oxytocin and antidiuretic hormone (ADH)
  – Neurohormones are transported to and stored in posterior pituitary
The hypothalamus controls release of hormones from the pituitary gland in two different ways (1 of 2).

1. Hypothalamic neurons synthesize oxytocin or antidiuretic hormone (ADH).

2. Oxytocin and ADH are transported down the axons of the hypothalamic-hypophyseal tract to the posterior pituitary.

3. Oxytocin and ADH are stored in axon terminals in the posterior pituitary.

4. When hypothalamic neurons fire, action potentials arriving at the axon terminals cause oxytocin or ADH to be released into the blood.
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Anterior Lobe: Pituitary-hypothalamic Relationships

• Vascular connection to hypothalamus

  – Hypophyseal portal system
    • Primary capillary plexus
    • Hypophyseal portal veins
    • Secondary capillary plexus
    • Carries **releasing and inhibiting hormones** to anterior pituitary to regulate hormone secretion
The hypothalamus controls release of hormones from the pituitary gland in two different ways (2 of 2).

2 Hypothalamic hormones travel through portal veins to the anterior pituitary where they stimulate or inhibit release of hormones made in the anterior pituitary.

3 In response to releasing hormones, the anterior pituitary secretes hormones into the secondary capillary plexus. This in turn empties into the general circulation.

A portal system is two capillary plexuses (beds) connected by veins.

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Posterior Pituitary and Hypothalamic Hormones

• Oxytocin and ADH

  – Each composed of nine amino acids

  – Almost identical – differ in two amino acids
Oxytocin

- Strong stimulant of uterine contraction
- Released during childbirth
- Hormonal trigger for milk ejection
- Acts as neurotransmitter in brain
ADH (Vasopressin)

- Inhibits or prevents urine formation
- Regulates water balance
- Targets kidney tubules → reabsorb more water
- Release also triggered by pain, low blood pressure, and drugs
- Inhibited by alcohol, diuretics
- High concentrations → vasoconstriction
ADH

• **Diabetes insipidus**
  – ADH deficiency due to hypothalamus or posterior pituitary damage
  – Must keep well-hydrated

• **Syndrome of inappropriate ADH secretion (SIADH)**
  – Retention of fluid, headache, disorientation
  – Fluid restriction; blood sodium level monitoring
Anterior Pituitary Hormones

- Growth hormone (GH)
- Thyroid-stimulating hormone (TSH) or thyrotropin
- Adrenocorticotropic hormone (ACTH)
- Follicle-stimulating hormone (FSH)
- Luteinizing hormone (LH)
- Prolactin (PRL)
Anterior Pituitary Hormones

• All are proteins

• Activate cyclic AMP second-messenger systems at their targets (all except GH)

• TSH, ACTH, FSH, and LH are all tropic hormones (regulate secretory action of other endocrine glands)
Growth Hormone (GH, or Somatotropin)

- Produced by somatotropic cells
- Direct actions on metabolism
  - Increases blood levels of fatty acids; (encourages use of fatty acids for fuel); protein synthesis
  - Decreases rate of glucose uptake and metabolism – conserving glucose
  - Glycogen breakdown and glucose release to blood (anti-insulin effect)
Growth Hormone (GH, or Somatotropin)

- Indirect actions on growth

- Mediates growth via growth-promoting proteins
  - insulin-like growth factors (IGFs)

- IGFs stimulate
  - Uptake of nutrients → DNA and proteins
  - Formation of collagen and deposition of bone matrix

- Major targets - bone and skeletal muscle
Growth Hormone (GH)

- GH release chiefly regulated by hypothalamic hormones
  - Growth hormone–releasing hormone (GHRH)
    - Stimulates release
  - Growth hormone–inhibiting hormone (GHIH) (somatostatin)
    - Inhibits release

- Ghrelin (hunger hormone) also stimulates release
Homeostatic Imbalances of Growth Hormone

• Hypersecretion
  – In children results in **gigantism**
  – In adults results in **acromegaly**

• Hyposecretion
  – In children results in **pituitary dwarfism**
Growth-promoting and metabolic actions of growth hormone (GH).

**Feedback**
- Inhibits GHRH release
- Stimulates GHIH release
- Inhibits GH synthesis and release

**Hypothalamus** secretes growth hormone–releasing hormone (GHRH), and GHIH (somatostatin)

**Anterior pituitary**
- Inhibits GHRH release
- Stimulates GHIH release
- Inhibits GH synthesis and release

**Growth hormone (GH)**

**Indirect actions (growth-promoting)**

**Liver and other tissues**
- Produce Insulin-like growth factors (IGFs)

**Insulin-like growth factors (IGFs)**
- Effects
  - **Skeletal**
    - Increased cartilage formation and skeletal growth
  - **Extraskeletal**
    - Increased protein synthesis, and cell growth and proliferation
  - **Fat metabolism**
    - Increased fat breakdown and release
  - **Carbohydrate metabolism**
    - Increased blood glucose and other anti-insulin effects

**Direct actions (metabolic, anti-insulin)**

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Disorders of pituitary growth hormone.
Thyroid-stimulating Hormone (Thyrotropin)

- Produced by thyrotropic cells of anterior pituitary
- Stimulates normal development and secretory activity of thyroid
- Release triggered by thyrotropin-releasing hormone from hypothalamus
- Inhibited by rising blood levels of thyroid hormones that act on pituitary and hypothalamus (negative feedback homeostatic mechanism)
Control of Pituitary: Feedback from Target Organs

- **negative feedback** - increased target organ hormone levels inhibits release of hormones

- **positive feedback** - stretching of uterus increases OT release, causes contractions, causing more stretching of uterus, etc. until delivery
Note:

Negative Feedback Mechanism
Regulation of thyroid hormone secretion.

- Hypothalamus
  - TRH
  - Anterior pituitary
    - TSH
    - Thyroid gland
      - Thyroid hormones
  - Target cells
    - Stimulates
    - Inhibits
Adrenocorticotropic Hormone (Corticotropin)

- Secreted by corticotropic cells of anterior pituitary
- Stimulates adrenal cortex to release corticosteroids
Adrenocorticotropic Hormone (Corticotropin)

• Regulation of ACTH release
  – Triggered by hypothalamic corticotropin-releasing hormone (CRH) in daily rhythm
  – Internal and external factors such as fever, hypoglycemia, and stressors can alter release of CRH
Gonadotropins

- Follicle-stimulating hormone (FSH)
- Luteinizing hormone (LH)

- Secreted by gonadotrophs of anterior pituitary

- FSH stimulates gamete (egg or sperm)
- ------ production (estrogen – women / androgen binding protein by Sertoli Cells also called Nurse Cells)

- LH promotes production of gonadal hormones
- ------ women – progesterone // men - testosterone

- Absent from the blood in prepubertal boys and girls
Gonadotropins

• Regulation of gonadotropin release
  – Triggered by gonadotropin-releasing hormone (GnRH) during and after puberty
  – Suppressed by gonadal hormones (feedback)
After ovulation corpus luteum produces progesterone and inhibin.

Inhibin’s negative feedback on anterior pituitary stops FSH secretion so another follicle does not mature.

LH secretion continues.

LH stimulates CL to produce progesterone which maintains endometrium.
1. GnRH from hypothalamus stimulates the anterior pituitary to secrete FSH and LH.

2. FSH stimulates sustentacular cells to secrete androgen-binding protein (ABP).

3. LH stimulates interstitial cells to secrete testosterone (androgen).

4. In the presence of ABP, testosterone stimulates spermatogenesis.

5. Testosterone also stimulates the libido and the development of secondary sex organs and characteristics.

6. Testosterone has negative feedback effects that reduce GnRH secretion and pituitary sensitivity to GnRH.

7. Sustentacular cells also secrete inhibin, which selectively inhibits FSH secretion and thus reduces sperm production without reducing testosterone secretion.

Key
- Green arrows: Stimulation
- Red arrows: Inhibition
Prolactin (PRL)

- Secreted by prolactin cells of anterior pituitary
- Stimulates milk production
- Role in males not well understood
Prolactin (PRL)

- Regulation of PRL release
  - Primarily controlled by prolactin-inhibiting hormone (PIH) (dopamine)

- Blood levels rise toward end of pregnancy

- Suckling stimulates PRL release and promotes continued milk production

- Hypersecretion causes inappropriate lactation, lack of menses, infertility in females, and impotence in males