Chapter 17
Endocrine System

- Overview
- Hypothalamus and pituitary gland
- Other endocrine glands
- Hormones and their actions
- Stress and adaptation
- Eicosanoids and paracrine signaling
- Endocrine disorders

Overview of Cell Communications

- Necessary for integration of cell activities
- Mechanisms

Components of Endocrine System

- Hormone
- Target cells
- Endocrine system

Endocrine Organs

- Major organs of endocrine system

Endocrine vs. Exocrine Glands

- Exocrine glands
- Endocrine glands
- Endocrine system

Differences in Nervous and Endocrine Systems

- Means of communication
- Speed and persistence of response
- Adaptation to long-term stimuli
- Area of effect
Communication by the Nervous & Endocrine Systems

Similarities in Nervous and Endocrine Systems
- Several chemicals function as both hormones and neurotransmitters
- Some hormones secreted by neuroendocrine cells (neurons)
- Both systems with overlapping effects on same target cells
- Systems regulate each other

Hypothalamus

Pituitary Gland (Hypophysis)

Embryonic Development of Pituitary

Pituitary Gland Anatomy and Hormones of the Neurohypophysis
Gonadotropin-releasing hormone controls FSH + LH release
Thyrotropin-releasing hormone
Corticotropin-releasing hormone
Prolactin-releasing hormone
Prolactin-inhibiting hormone
GH-releasing hormone
Somatostatin

Hypothalamo-Hypophyseal Portal System

- Hormones secreted by hypothalamus, travel in portal system to anterior pituitary
- Hormones can also be secreted by anterior pituitary (under control of hypothalamic releasers and inhibitors)

Anterior Pituitary Hormones

- Principle hormones and target organs shown
- Axis - refers to way endocrine glands interact

Pituitary Hormones - Pars Intermedia

- Absent from adult human although present in fetus
- Reminant cells
  - produce POMC (pro-opiomelanocortin) which is processed into ACTH and endorphins
- Produces MSH in animals influencing pigmentation of skin, hair or feathers
  - not apparently present/functioning in humans

Pituitary Hormones - Posterior Lobe

Pituitary Hormone Actions:
Anterior Lobe Hormones

- FSH (secreted by gonadotrope cells)
- LH (secreted by gonadotrope cells)
- TSH (secreted by thyrotropes)
### Pituitary Hormone Actions:
#### Anterior Lobe Hormones
- ACTH or corticotropin (secreted by corticotropes)
- PRL (secreted by lactotropes)
- GH or somatotropin – see next 2 slides

### Growth Hormone
- Secreted by somatotropes of anterior pituitary
- Promotes tissue growth
- Functions of GH-IGF

### Growth Hormone and Aging
- Childhood and adolescence
- Adulthood
- Levels of GH

### Pituitary Hormone Actions:
#### Posterior Lobe Hormones
- ADH
  - targets kidneys to ↑ water retention, reduce urine
  - also functions as neurotransmitter
- Oxytocin
  - labor contractions, lactation
  - possible role sperm transport, emotional bonding

### Control of Pituitary:
#### Hypothalamic and Cerebral Control
- Anterior lobe control - releasing hormones and inhibiting hormones of hypothalamus
- Posterior lobe control - neuroendocrine reflexes

### Control of Pituitary:
#### Feedback from Target Organs
- Negative feedback
- Positive feedback
Pineal Gland
• Peak secretion 1-5 yr. olds, by puberty 75% lower
• Produces serotonin by day, converts it to melatonin at night
• May regulate timing of puberty in humans
• Melatonin ↑ in SAD + PMS, ↓ by phototherapy
  – depression, sleepiness, irritability and carbohydrate craving

Thyroid Gland Anatomy
• Largest endocrine gland with high rate of blood flow
• Anterior and lateral sides of trachea
• 2 large lobes connected by isthmus

Histology of the Thyroid Gland

Parathyroid Glands
• PTH release
  – ↑ blood Ca²⁺ levels
  – promotes synthesis of calcitriol
    • ↑ absorption of Ca²⁺
    • ↓ urinary excretion
    • ↑ bone resorption

Adrenal Gland

Thymus
• Location: mediastinum, superior to heart
• Involution after puberty
• Secretes hormones that regulate development and later activation of T-lymphocytes
  – thymopoietin and thymosins

Larynx
Thyroid gland
Trachea
Thymus
Lung
Adrenal Medulla
- Sympathetic ganglion innervated by sympathetic preganglionic fibers
- Hormonal effect is longer lasting
- Stress causes medullary cells to stimulate cortex

Adrenal Cortex
- Layers -- (outer) zona glomerulosa, (middle) zona fasciculata, (inner) zona reticularis
- Corticosteroids

Pancreas
- Retroperitoneal, inferior and dorsal to stomach

Pancreatic Hormones
- 1-2 Million pancreatic islets producing hormones
- 98% of organ produces digestive enzymes (exocrine)
- Insulin (from β cells)

Pancreatic Hormones 2
- Glucagon (from α cells)
- Somatostatin from delta (δ) cells
- Hyperglycemic hormones raise blood glucose
- Hypoglycemic hormones lower blood glucose

Histology of Ovary
- Follicles = egg surrounded by granulosa cells
Histology of Testis

Seminiferous tubules produce sperm.

Endocrine Functions of Other Organs

• Heart –
  – atrial natriuretic peptide released with an increase in BP
  – ↓ blood volume + ↓ BP by ↑ Na⁺ and H₂O loss by kidneys
• Skin
  – keratinocytes help produce D₃, first step in synthesis of calcitriol
• Liver
  – converts vitamin D₃ to calcidiol
  – source of IGF-I that works with GH
  – secretes about 15% of erythropoietin
  – secretes angiotensinogen (a prohormone)
    • precursor of angiotensin II, a vasoconstrictor

Endocrine Functions of Other Organs

• Kidneys
  – converts calcidiol to calcitriol (active form of vitamin D)
    • ↑ absorption by intestine and inhibits loss in the urine
    • more Ca²⁺ available for bone deposition
  – produces 85% of erythropoietin –
    • stimulates bone marrow to produce RBC’s
  – convert angiotensinogen to angiotensin I
• Stomach and small intestines (10 enteric hormones)
  – coordinate digestive motility and secretion
• Placenta
  – secretes estrogen, progesterone and others
    • regulate pregnancy, stimulate development of fetus and mammary glands

Hormone Chemistry

• Steroids
  – derived from cholesterol
    • sex steroids, corticosteroids
• Peptides and glycoproteins
  – OT, ADH; all releasing and inhibiting hormones of hypothalamus; most of anterior pituitary hormones
• Monoamines (biogenic amines)
  – derived from amino acids
    • catecholamines (norepinephrine, epinephrine, dopamine) and thyroid hormones

Hormone Synthesis: Steroid Hormones

Hormone Synthesis: Peptides

• Cellular steps
• Insulin formation
Hormone Synthesis: Monoamines

Thyroid Hormone Synthesis

Thyroid Hormone Synthesis

Hormone Transport

• Monoamines and peptides are hydrophilic so mix easily with blood plasma
• Steroids and thyroid hormone are hydrophobic and must bind to transport proteins for transport

• Transport proteins in blood plasma

Hormone Receptors

Hormone Mode of Action

• Hydrophobic hormones (steroids and thyroid hormone) penetrate plasma membrane – enter nucleus
• Hydrophilic hormones (monoamines and peptides) can not pass through membrane so must bind to cell-surface receptors
**Thyroid Hormone Effects**

**Hydrophilic Hormones: Mode of Action**

**cAMP as Second Messenger**

1. Hormone binding activates G protein
2. Activates adenylate cyclase
3. Produces cAMP
4. Activates kinases
5. Activates enzymes
6. Metabolic reactions: synthesis, secretion, change membrane potentials

Peptides and catecholamines bind to receptors in cell membrane

**Hydrophilic Hormones: Mode of Action**

Other 2nd & 3rd Messengers

Hormones may use different second messengers in different tissues.

**Enzyme Amplification**

**Modulation of Target Cell Sensitivity**

Hormones may use different second messengers in different tissues.
Hormone Interactions

Stress and Adaptation

Alarm Reaction

Stage of Resistance

Stage of Exhaustion

Paracrine Secretions

- Chemical messengers that diffuse short distances and stimulate nearby cells
  - unlike neurotransmitters not produced in neurons
  - unlike hormones not transported in blood
- Examples and their functions
  - histamine from mast cells in connective tissue causes relaxation of blood vessel smooth muscle
  - nitric oxide from endothelium of blood vessels causes vasodilation
  - somatostatin from gamma cells inhibits secretion of alpha and beta cells in pancreas
  - catecholamines diffuse from adrenal medulla to cortex
Eicosanoids: a Paracrine Secretion

- Derived from arachidonic acid (fatty acid)
- Hormone releases arachidonic acid from plasma membrane and 2 enzymes convert it into eicosanoids

Eicosanoid Synthesis

Endocrine Disorders

- Variations in hormone concentration and target cell sensitivity have noticeable effects on the body
- Hyposcretion – inadequate hormone release
  - tumor or lesion destroys gland
- Hypersecretion – excessive hormone release
  - tumors or autoimmune disorder

Pituitary Disorders

- Hypersecretion of growth hormones
  - acromegaly
  - thickening of the bones and soft tissues
  - problems in childhood or adolescence
  - gigantism if oversecretion
  - dwarfism if hyposecretion

Thyroid Gland Disorders

- Congenital hypothyroidism (↓ TH)
  - infant suffers abnormal bone development, thickened facial features, low temperature, lethargy, brain damage
- Myxedema (adult hypothyroidism, ↓ TH)
  - low metabolic rate, sluggishness, sleepiness, weight gain, constipation, dry skin and hair, cold sensitivity, ↑ blood pressure and tissue swelling
- Endemic goiter (goiter = enlarged thyroid gland)
  - dietary iodine deficiency, no TH, no - feedback, ↑ TSH
- Toxic goiter (Graves disease)
  - antibodies mimic TSH, ↑TH, exophthalmos

Endemic Goiter
Parathyroid Disorders

- Hypoparathyroid
  - surgical excision during thyroid surgery
  - fatal tetany 3-4 days
- Hyperparathyroid = excess PTH secretion
  - tumor in gland
  - causes soft, fragile and deformed bones
  - ↑ blood Ca^{2+}
  - renal calculi

Adrenal Disorders

- Cushing syndrome is excess cortical secretion
  - causes hyperglycemia, hypertension, weakness, edema
  - muscle and bone loss occurs with protein catabolism
  - buffalo hump & moon face = fat deposition between shoulders or in face
- Adrenogenital syndrome (AGS)
  - adrenal androgen hyperssecretion accompanies Cushing
  - causes enlargement of external sexual organs in children & early onset of puberty
  - masculinizing effects on women (deeper voice & beard growth)

Diabetes Mellitus

- Signs and symptoms of hyposecretion of insulin
  - polyuria, polydipsia, polyphagia
  - hyperglycemia, glycosuria, ketonuria
    - osmotic diuresis: blood glucose levels rise above transport maximum of kidney tubules, glucose remains in urine, osmolarity ↑ and draws water into urine
  - Transport maximum of glucose reabsorption
    - kidney tubules can not reabsorb glucose fast enough if no insulin is present
    - osmotic diuresis results due to excess glucose and ketones in tubules

Types of Diabetes Mellitus

- Type I (IDDM) - 10% of cases
  - some cases have autoimmune destruction of β cells, diagnosed about age 12
  - treated with diet, exercise, monitoring of blood glucose and periodic injections of insulin or insulin pump
- Type II (NIDDM) - 90%
  - insulin resistance
    - failure of target cells to respond to insulin
    - 3 major risk factors are heredity, age (40+) and obesity
  - treated with weight loss program of diet and exercise,
    - oral medications improve insulin secretion or target cell sensitivity

Pathology of Diabetes

- Acute pathology: cells cannot absorb glucose, rely on fat and proteins (weight loss + weakness)
  - fat catabolism ↑ FFA’s in blood and ketone bodies
  - ketonuria promotes osmotic diuresis, loss of Na^+ + K^+
  - ketoacidosis occurs as ketones ↓ blood pH
    - if continued causes dyspnea and eventually diabetic coma
- Chronic pathology
  - chronic hyperglycemia leads to neuropathy and cardiovascular damage from atherosclerosis
    - retina and kidneys (common in type I), atherosclerosis leading to heart failure (common in type II), and gangrene

Hyperinsulinism

- From excess insulin injection or pancreatic islet tumor
- Causes hypoglycemia, weakness and hunger
  - triggers secretion of epinephrine, GH and glucagon
    - side effects: anxiety, sweating and ↑ HR
- Insulin shock
  - uncorrected hyperinsulinism with disorientation, convulsions or unconsciousness