Chapter 17
Endocrine System Components

- endocrine system
- endocrinology
- endocrine glands
- hormones
Comparison of Endocrine and Exocrine Glands

- **exocrine glands**
  - have ducts – ‘external secretions’
  - extracellular effects (food digestion)

- **endocrine glands**
  - no ducts
  - fenestrated capillary networks
  - ‘internal secretions’
  - intracellular effects

- **liver acts like both**
Comparison of Nervous and Endocrine Systems (Differences)

• internal communication
  – nervous - both electrical and chemical
  – endocrine - only chemical

• speed and persistence of response
  – nervous – quick, short lived response
  – endocrine – slow, long term response

• adaptation to long-term stimuli
  – nervous - response declines (adapts quickly)
  – endocrine - response persists (adapts slowly)

• area of effect
  – nervous - targeted and specific
  – endocrine - general, widespread effects
Communication by the Nervous and Endocrine Systems

(a) Nervous system

(b) Endocrine system
Nervous and Endocrine Systems (Similarities)

- chemicals that are both hormones and neurotransmitters
  - norepinephrine, cholecystokinin, thyrotropin-releasing hormone, dopamine and antidiuretic hormone

- neuroendocrine cells secrete hormones into the bloodstream
  - oxytocin and catecholamines

- overlapping effects on same target cells
  - norepinephrine and glucagon cause glycogen hydrolysis in liver

- systems regulate each other

- target organs or cells
Hypothalamus & Pituitary Gland
Hypothalamus & Pituitary Gland

infundibulum
Pituitary Gland (Hypophysis)

- **adenohypophysis** (anterior pituitary)
  - arises from hypophyseal pouch (outgrowth of pharynx)
- **neurohypophysis** (posterior pituitary)
  - downgrowth from brain
Adenohypophysis & Neurohypophysis

- **adenohypophysis** - anterior three-quarters of pituitary
  - anterior lobe (pars distalis)
  - pars tuberalis small mass of cells adhering to stalk
    - linked to hypothalamus by hypophyseal portal system
- **neurohypophysis** - posterior one-quarter of the pituitary
  - median eminence, infundibulum, and the posterior lobe (pars nervosa)
  - nerve tissue, not a true gland
Posterior Pituitary Hormones

Nuclei of hypothalamus:
- Paraventricular nucleus
- Supraoptic nucleus

Optic chiasm

Adenohypophysis:
- Pars tuberalis
- Anterior lobe

Neurohypophysis:
- Median eminence
- Hypothalamo-hypophyseal tract
- Stalk (infundibulum)
- Posterior lobe

- Oxytocin
- Antidiuretic hormone
Hypophyseal Portal System

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Hypothalamic hormones
- Gonadotropin-releasing hormone
- Thyrotropin-releasing hormone
- Corticotropin-releasing hormone
- Prolactin-inhibiting hormone
- Growth hormone–releasing hormone
- Somatostatin

Anterior lobe hormones
- Follicle-stimulating hormone
- Luteinizing hormone
- Thyroid-stimulating hormone (thyrotropin)
- Adrenocorticotropic hormone
- Prolactin
- Growth hormone
Histology of Pituitary Gland

(a) Anterior pituitary

(b) Posterior pituitary

- Chromophobe
- Basophil
- Acidophil
- Unmyelinated nerve fibers
- Glial cells (pituicytes)
Anterior Pituitary Hormones

- **Gonadotropin hormones** that target gonads
  - FSH (follicle stimulating hormone)
    - stimulates secretion of ovarian sex hormones, development of ovarian follicles, and sperm production
  - LH (luteinizing hormone)
    - stimulates ovulation, stimulates corpus luteum to secrete progesterone, stimulates testes to secrete testosterone

- **TSH (thyroid stimulating hormone)**
  - stimulates secretion of thyroid hormone

- **ACTH (adrenocorticotropic hormone)**
  - stimulates adrenal cortex to secrete glucocorticoids

- **PRL (prolactin)**
  - after birth stimulates mammary glands to synthesize milk, enhances secretion of testosterone by testes

- **GH (growth hormone)**
  - stimulates mitosis and cellular differentiation
Posterior Pituitary Hormones

• produced in hypothalamus
  – transported by hypothalamo-hypophyseal tract to posterior lobe
  – releases hormones when hypothalamic neurons are stimulated

• **ADH** (antidiuretic hormone)
  – increases water retention thus reducing urine volume and prevents dehydration
  – also called vasopressin because it can cause vasoconstriction

• **OT** (oxytocin)
  – surge of hormone released during sexual arousal and orgasm
    • stimulate uterine contractions and propulsion of semen
  – promotes feelings of sexual satisfaction and emotional bonding between partners
  – stimulates labor contractions during childbirth
  – stimulates flow of milk during lactation
  – promotes emotional bonding between lactating mother and infant
Control of Pituitary Secretion

• rates of secretion are not constant
  – regulated by hypothalamus, other brain centers, and feedback from target organs

• **Hypothalamic and Cerebral Control**
  – **anterior lobe control** - releasing hormones and inhibiting hormones from hypothalamus
    • in cold weather, pituitary stimulated by hypothalamus to release TSH, leads to generation of body heat
  – **posterior lobe control** - neuroendocrine reflexes
    • **neuroendocrine reflex** - hormone release in response to nervous system signals
    • suckling infant ★ stimulates nerve endings ★ hypothalamus ★ posterior lobe ★ oxytocin ★ milk ejection
    • hormone release in response to higher brain centers
    • milk ejection reflex can be triggered by a baby's cry
    • emotional stress can affect secretion of gonadotropins, disrupting ovulation, menstruation, and fertility
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
TRH to Pituitary (Thyroid-stimulating hormone, TSH)

1. TRH (Thyrotropin-releasing hormone) stimulates the release of TSH.
2. TSH stimulates the production of thyroid hormone.
3. Thyroid hormone feeds back to inhibit TSH production.
4. Thyroid hormone also stimulates target organs.
5. Negative feedback inhibition of TSH production.
6. Negative feedback inhibition of TRH production.

Stimulatory effect:
- Green arrows indicate stimulatory effects.
- TSH stimulation of thyroid hormone production.
- Thyroid hormone stimulation of target organs.

Inhibitory effect:
- Red arrows indicate inhibitory effects.
- Negative feedback inhibition of TSH production.
- Negative feedback inhibition of TRH production.
Growth Hormone

• GH has widespread effects on the body tissues
  – especially cartilage, bone, muscle, and fat

• induces liver to produce growth stimulants
  – insulin-like growth factors (IGF-I) or somatomedins (IGF-II)
    • stimulate target cells in diverse tissues
    • IGF-I prolongs the action of GH
    • hormone half-life – the time required for 50% of the hormone to be cleared from the blood
      – GH half-life 6 – 20 minutes       - IGF-I half-life about 20 hours

• protein synthesis increases -- boosts transcription of DNA, production of mRNA, amino acid uptake into cells, suppresses protein catabolism

• lipid metabolism increased – fat catabolized by adipocytes (protein-sparing effect) – provides energy for growing tissues
Growth Hormone

• carbohydrate metabolism – by mobilizing fatty acids for energy, GH produces glucose-sparing makes glucose available for glycogen synthesis and storage

• electrolyte balance – promotes Na⁺, K⁺, & Cl⁻ retention by kidneys, enhances Ca²⁺ absorption in intestine

− bone growth, thickening, and remodeling influenced, especially during childhood and adolescence
− secretion high during first two hours of sleep
− can peak in response to vigorous exercise
− GH levels decline gradually with age
− average 6 ng/ml during adolescence, 1.5 ng/mg in old age
  • lack of protein synthesis contributes to aging of tissues and wrinkling of the skin
  • age 30, average adult body is 10% bone, 30% muscle, 20% fat
  • age 75, average adult body is 8% bone, 15% muscle, 40% fat
Pineal Gland

- after age 7, it undergoes involution (shrinkage)
  - down 75% by end of puberty
  - tiny mass of shrunken tissue in adults

- circadian rhythms of daylight and darkness
  - synthesizes melatonin from serotonin during the night
    - fluctuates seasonally with changes in day length

- may regulate timing of puberty in humans

- seasonal affective disorder (SAD) occurs in winter or northern climates
  - symptoms - depression, sleepiness, irritability and carbohydrate craving
  - Treatment - 2 to 3 hours of exposure to bright light each day
Pineal Gland
Thymus

- thymus plays a role in three systems: endocrine, lymphatic, and immune
- bilobed gland in the mediastinum superior to the heart
  - goes through involution after puberty
- site of **maturation of T cells** important in immune defense
- secretes hormones (**thymopoietin**, **thymosin**, and **thymulin**) that stimulate development of other lymphatic organs and activity of T-lymphocytes
Thyroid Gland Anatomy

- **thyroid follicles** – sacs that compose most of thyroid
  - contain protein rich **colloid**
  - **follicular cells** – simple cuboidal epithelium that lines follicles

- secretes **thyroxine** ($T_4$) and **triiodothyronine** ($T_3$)
  - increases metabolic rate, $O_2$ consumption, heat production (**calorogenic effect**), appetite, growth hormone secretion, alertness and quicker reflexes

- **parafollicular (C or clear) cells** secrete **calcitonin** with rising blood calcium
  - stimulates osteoblast activity and bone formation
thyroid follicles are filled with colloid and lined with simple cuboidal epithelial cells (follicular cells).
Thyroid Histology

Thyroid follicles

Follicular cells

Colloid

Parafollicular (C) cells
Parathyroid Glands

- secrete parathyroid hormone (PTH)
  - increases blood $\text{Ca}^{2+}$ levels
    - promotes synthesis of calcitriol
    - increases absorption of $\text{Ca}^{2+}$
    - decreases urinary excretion
    - increases bone resorption
Adrenal Gland

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(a) Adrenal gland
Suprarenal vein
Kidney

Adrenal cortex
Adrenal medulla

(b) Connective tissue capsule
Adrenal cortex
Zona glomerulosa
Zona fasciculata
Zona reticularis
Adrenal medulla
Adrenal (Suprarenal) Glands
Adrenal Medulla

- **endocrine gland** and **sympathetic ganglion** of sympathetic nervous system
  - modified sympathetic postganglionic neurons called **chromaffin cells**
  - release **catecholamines** (epinephrine and norepinephrine) and a trace of **dopamine** directly into the bloodstream

- **effect is longer lasting than neurotransmitters**
  - increases alertness and prepares body for physical activity –
    - mobilize high energy fuels, lactate, fatty acids, and glucose
    - **glycogenolysis** and **gluconeogenesis** boost glucose levels
    - **glucose-sparing effect** because inhibits insulin secretion
      - muscles use fatty acids saving glucose for brain
  - increases blood pressure, heart rate, blood flow to muscles, pulmonary air flow and metabolic rate
  - decreases digestion and urine production
Adrenal Cortex

• secretes 5 major steroid hormones from three layers of glandular tissue
  – zona glomerulosa (thin, outer layer)
    • secretes mineralocorticoid – regulate the body’s electrolyte balance
  – zona fasciculata (thick, middle layer)
    • secretes glucocorticoids
  – zona reticularis (narrow, inner layer)
    • secretes sex steroids
Adrenal Histology

- adrenal gland
- capsule
- zona glomerulosa
- zona fasciculata
- zona reticularis
- adrenal medulla
Categories of Corticosteroids

• mineralocorticoids – zona glomerulosa
  – regulate electrolyte balance
  – aldosterone

• glucocorticoids – zona fasciculata
  – regulate metabolism of glucose and other fuels
  – Cortisol
  – helps body adapt to stress and repair tissues
  – anti-inflammatory effect becomes immune suppression with long-term use

• sex steroids – zona reticularis
  – androgens
  – estradiol
Adrenal Gland Interactions

- medulla and cortex of adrenal gland are not functionally independent
- medulla atrophies without the stimulation of cortisol
- some chromaffin cells of medullary origin extend into the cortex
  - they stimulate the cortex to secrete corticosteroids when stress activates the sympathetic nervous system
Pancreas Histology

- exocrine digestive gland and endocrine cell clusters (pancreatic islets).
Pancreatic Hormones

• **somatostatin** secreted by D or **delta (δ)** cells
  – partially suppresses secretion of glucagon and insulin
  – inhibits nutrient digestion and absorption which prolongs absorption of nutrients

• **pancreatic polypeptide** secreted by PP cells or **F cells)**
  – inhibits gallbladder contraction and secretion pancreatic digestive enzymes

• **gastrin** secreted by **G cells**
  – stimulates stomach acid secretion, motility and emptying
Hormones Affecting Glucose Metabolism

• **hyperglycemic hormones** raise blood glucose concentration
  – glucagon, growth hormone, epinephrine, norepinephrine, cortisol, and corticosterone

• **hypoglycemic hormones** lower blood glucose
  – insulin
The Gonads

- **ovaries** and **testes** are both endocrine and exocrine
  - **exocrine** product – whole cells - eggs and sperm (**cytogenic glands**)
  - **endocrine** product - gonadal hormones – mostly steroids

- **ovarian** hormones
  - estradiol, progesterone, and inhibin

- **testicular** hormones
  - testosterone, weaker androgens, estrogen and inhibin
Histology of Ovary and Testis

(a) Ovary
- Granulosa cells (source of estrogen)
- Egg nucleus
- Egg
- Theca

(b) Testis
- Blood vessels
- Seminiferous tubule
- Germ cells
- Connective tissue wall of tubule
- Sustentacular cells
- Interstitial cells (source of testosterone)

Follicle - egg surrounded by granulosa cells and a capsule (theca)
Endocrine Functions of Other Organs

• skin
  – keratinocytes convert a cholesterol-like steroid into cholecalciferol using UV from sun

• liver
  – converts cholecalciferol into calcidiol
  – secretes angiotensinogen (a prohormone)
    • precursor of angiotensin II (a regulator of blood pressure)
  – secretes 15% of erythropoietin (stimulates bone marrow)
  – hepcidin – promotes intestinal absorption of iron
  – source of IGF-I that controls action of growth hormone

• kidneys
  – converts calcidiol to calcitriol, the active form of vitamin D
    • increases Ca\(^{2+}\) absorption by intestine and inhibits loss in the urine
  – secretes renin that converts angiotensinogen to angiotensin I
    • angiotensin II created by converting enzyme in lungs
      – constricts blood vessels and raises blood pressure
  – produces 85% of erythropoietin –
    • stimulates bone marrow to produce RBCs
Endocrine Functions of Other Organs

• **heart**
  – cardiac muscle secretes **atrial natriuretic peptide (ANP)** in response to an increase in blood pressure
  – decreases blood volume and blood pressure by increasing Na$^+$ and H$_2$O output by kidneys
  – opposes action of angiotensin II

• **stomach and small intestine** secrete at least ten hormones
  – coordinate digestive motility and glandular secretion
  – cholecystokinin, gastrin, Ghrelin, and peptide YY

• ...and many others.
Hormone Chemistry

- three chemical classes
  - **steroids**
    - derived from cholesterol
    - secreted by gonads and adrenal glands
    - estrogens, progesterone, testosterone, cortisol, corticosterone, aldosterone, DHEA, and calcitriol
  - **peptides and glycoproteins**
    - created from chains of amino acids
    - secreted by pituitary and hypothalamus
    - oxytocin, antidiuretic hormone, releasing and inhibiting hormones, and anterior pituitary hormones
  - **monoamines (biogenic amines)**
    - derived from amino acids
    - secreted by adrenal, pineal, and thyroid glands
    - epinephrine, norepinephrine, melatonin, and thyroid hormone

- all hormones are made from either cholesterol or amino acids with carbohydrate added to make glycoproteins.
Hormone Synthesis: Steroid Hormones

- synthesized from cholesterol – differs in functional groups attached to 4-ringed steroid backbone

Figure 17.16
Peptides

• synthesized in same way as any protein

• at first is an inactive preprohormone

• first several amino acids is a signal peptide that guides it into cisterna of rough endoplasmic reticulum

• signal peptide removed to form prohormone

• Golgi does final transformation to hormone packaged for secretion
Hormone Synthesis: Insulin

• begins as **proproinsulin**, then becomes **proinsulin**

• when **connecting peptide** is removed, two polypeptide chains are formed that make up insulin

Figure 17.17
Monoamines

• **melatonin** is synthesized from amino acid **tryptophan**, and other monoamines from amino acid **tyrosine**
  – **thyroid hormone** is composed of 2 tyrosines
Thyroid Hormone Synthesis

Figure 17.18

1. Iodide absorption and oxidation
2. Thyroglobulin synthesis and secretion
3. Iodine added to tyrosines of thyroglobulin
4. Thyroglobulin uptake and hydrolysis
5. Release of T₄ and a small amount of T₃ into the blood
T₃ and T₄ Synthesis

• follicular cells
  – absorb *iodide (I⁻) ions* from blood and store in lumen as a reactive form of iodine
  – synthesize *thyroglobulin* and store in lumen
    • forms colloid
    • contains lots of tyrosine
  – tyrosine and iodine combine to form thyroxine (T₄) bound to thyroglobulin
  – stored in follicle

• TSH
  – stimulates follicular cells to remove T₄ from thyroglobulin for release into plasma
  – most T₃ is produced in liver or by target cells removing an iodine from circulating T₄
  – 95% T₄ and 5% T₃
Hormone Receptors

- Hormones stimulate only those cells that have receptors for them.
- **Receptors** are protein or glycoprotein molecules:
  - on plasma membrane, in the cytoplasm, or in the nucleus.
- **Receptors** act like switches turning on metabolic pathways when hormone binds to them.
- Usually each target cell has a few thousand receptors for a given hormone.
- Receptor-hormone interactions exhibit **specificity** and **saturation**:
  - specific receptor for each hormone
  - saturated when all receptor molecules are occupied by hormone molecules.
Hormone Mode of Action

- **hydrophobic hormones**
  - penetrate plasma membrane and enter nucleus
  - act directly on the genes changing target cell physiology
  - estrogen, progesterone, thyroid hormone act on nuclear receptors
  - take several hours to days to show effect due to lag for protein synthesis

- **hydrophilic hormones**
  - cannot penetrate into target cell
  - must stimulate physiology indirectly

Figure 17.20
Thyroid Hormone

- Thyroid hormone enters target cell by diffusion – mostly as $T_4$ with little metabolic effect.
- Within target cell, $T_4$ is converted to more potent $T_3$.
- $T_3$ enters target cells and binds to receptors in chromatin.
- Activates genes:
  - Make a muscle protein (myosin) enhancing cardiac muscle response to sympathetic stimulation.
  - Strengthening heartbeat.

Figure 17.21
Peptides and Catecholamines: Hydrophilic

• hormone binds to cell-surface receptor
• receptor linked to second messenger system on other side of the membrane
• activates G protein which
• activates adenylate cyclase
• produces cAMP
• activates or inhibits enzymes
• metabolic reactions:
  – synthesis
  – secretion
  – change membrane potentials

2. G protein activates adenylate cyclase.

3. Adenylate cyclase produces cAMP.

4. cAMP activates protein kinases.

5. Protein kinases phosphorylate enzymes. This activates some enzymes and deactivates others.

6. Activated enzymes catalyze metabolic reactions with a wide range of possible effects on the cell.
Enzyme Amplification

- Hormones are extraordinarily potent chemicals.
- One hormone molecule can trigger the synthesis of many enzyme molecules.
- Very small stimulus can produce very large effect.
- Circulating concentrations very low.

Figure 17.24
Modulation of Target Cell Sensitivity

- Target cell sensitivity adjusted by changing the number of receptors
  - up-regulation means number of receptors is increased
    - sensitivity is increased
  - down-regulation reduces number of receptors
    - cell less sensitive to hormone
    - happens with long-term exposure to high hormone concentrations

Figure 17.25
Hormone Interactions

• most cells sensitive to more than one hormone and exhibit interactive effects

• synergistic effects
  – multiple hormones act together for greater effect
    • synergism between FSH and testosterone on sperm production

• permissive effects
  – one hormone enhances the target organ’s response to a second later hormone
    • estrogen prepares uterus for action of progesterone

• antagonistic effects
  – one hormone opposes the action of another
    • insulin lowers blood glucose and glucagon raises it
Hormone Clearance

• hormone signals must be turned off when they have served their purpose

• most hormones are taken up and degraded by liver and kidney
  – excreted in bile or urine

• metabolic clearance rate (MCR)
  – rate of hormone removal from the blood
  – half-life - time required to clear 50% of hormone from the blood
  – faster the MCF, the shorter is the half-life
Endocrine Disorders

• **hyposecretion** – inadequate hormone release

• **hypersecretion** – excessive hormone release
Pituitary Disorders

• hypersecretion of growth hormone (GH)
  – acromegaly - thickening of bones and soft tissues in adults
    • especially hands, feet and face
  – problems in childhood or adolescence
    • gigantism if hypersecretion
    • pituitary dwarfism if hyposecretion – rare since growth hormone is now made by genetically engineered bacteria

From Clinical Pathological Conference Acromegaly, Diabetes, Hypermetabolism, Protein Use and Heart Failure in American Journal of Medicine, 20:133, 1986. Copyright © 1986 by Excerpta Media, Inc.
Thyroid Gland Disorders

- **congenital hypothyroidism** (decreased TH)
  - hyposecretion present at birth
  - treat with oral thyroid hormone

- **myxedema** (decreased TH)
  - adult hypothyroidism
  - treat with oral thyroid hormone

- **goiter** – any pathological enlargement of the thyroid gland
  - **endemic goiter**
    - dietary iodine deficiency, no TH, no feedback, increased TSH stimulates hypertrophy
  - **toxic goiter** (Graves disease)
    - autoantibodies mimic the effect of TSH on the thyroid causing hypersecretion
    - overgrown thyroid produces functional TH
Endemic Goiter

Figure 17.28

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Figure 17.28
Parathyroid Disorders

– hypoparathyroidism
  • surgical excision during thyroid surgery
  • fatal tetany in 3 - 4 days due to rapid decline in blood calcium level

– hyperparathyroidism - excess PTH secretion
  • parathyroid tumor
  • bones become soft, fragile, and deformed
  • $\text{Ca}^{2+}$ and phosphate blood levels increase
  • promotes renal calculi formation
Adrenal Disorders

• Cushing syndrome - excess cortisol secretion
  – hyperglycemia, hypertension, weakness, edema
  – rapid muscle and bone loss due to protein catabolism
  – abnormal fat deposition
Diabetes Mellitus

• most prevalent metabolic disease in world
  – disruption of metabolism due to hyposcretion or inaction of insulin
  – symptoms:
    • polyuria (excess urine output), polydipsia (intense thirst) and polyphagia (hunger)
    • revealed by elevated blood glucose, glucose in urine and ketones in the urine
Types of Diabetes Mellitus

• **Type 1** (IDDM) – 5 to 10% of cases in US
  – **insulin** is always used to treat Type 1
    • insulin injections, insulin pump, or dry insulin inhaler
    • monitoring blood glucose levels and controlled diet
  – hereditary susceptibility if infected with certain viruses (rubella, cytomegalovirus)
  – autoantibodies attack and destroy pancreatic beta cells

• **Type 2** (NIDDM) – 90 to 95% of diabetics
  – problem is **insulin resistance**
    • failure of target cells to respond to insulin
  – risk factors are heredity, age (40+), obesity, and ethnicity – Native American, Hispanic, and Asian
  – treated with weight loss program and exercise
  – oral medications improve insulin secretion or target cell sensitivity
Pathology of Diabetes

• pathogenesis: cells cannot absorb glucose, must rely on fat and proteins for energy needs - weight loss and weakness
  – fat catabolism increases free fatty acids and ketones in blood
    • ketonuria irregular heartbeat, and neurological issues
    • ketoacidosis gasping breathing and diabetic coma

• chronic pathology (chronic hyperglycemia)
  – leads to neuropathy and cardiovascular damage from atherosclerosis and microvascular disease
    • arterial damage in retina and kidneys (common in type I), atherosclerosis leads to heart failure (common in type II)
    • diabetic neuropathy – nerve damage from impoverished blood flow can lead to erectile dysfunction, incontinence, poor wound healing, and loss of sensation from area