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
  – gap junctions
    • pores in cell membrane along which signalling chemicals move from cell to cell
  – neurotransmitters
    • released from neurons to travel across gap to 2nd cell
  – paracrine (local) hormones
    • secreted into tissue fluids to effect nearby cells
  – hormones (strict definition)
    • chemical messengers that travel in the bloodstream
Components of Endocrine System

• Hormone
  – chemical messenger secreted into bloodstream, stimulates response in another tissue or organ

• Target cells
  – have receptors for hormone

• Endocrine glands
  – produce hormones

• Endocrine system
  – includes endocrine organs (thyroid, pineal, etc)
  – includes hormone producing cells in organs such as brain, heart and small intestine
Endocrine Organs

- Major organs of endocrine system
  - Hypothalamus
  - Pituitary gland
  - Pineal gland
  - Thyroid gland
  - Parathyroid glands (on dorsal aspect of thyroid gland)
  - Thymus
  - Adrenal glands
  - Pancreas
  - Gonads
    - Ovaries (female)
    - Testes (male)
Endocrine vs. Exocrine Glands

• Exocrine glands
  – ducts carry secretion to body surface or other organ cavity
  – extracellular effects (food digestion)
• Endocrine glands
  – no ducts, release hormones into tissue fluids, have dense capillary networks to distribute hormones
  – intracellular effects, alter target cell metabolism
• Endocrine system
  – all endocrine glands and hormone-secreting cells of other organs (brain, heart, small intestine, etc.)
Differences in Nervous and Endocrine Systems

• Means of communication
  – nervous system has both electrical and chemical methods
  – endocrine system has only chemical methods

• Speed and persistence of response
  – nervous system reacts quickly (1 - 10 msec) and stops quickly
  – endocrine system reacts slowly (hormone release in seconds or days), effect may continue for weeks

• Adaptation to long-term stimuli
  – nervous system adapts quickly and response declines
  – endocrine system has more persistent responses

• Area of effect
  – nervous system effects are targeted and specific (one organ)
  – endocrine system may have general, widespread effects on many organs
Communication by the Nervous & Endocrine Systems
Similarities in Nervous and Endocrine Systems

- Several chemicals function as both hormones and neurotransmitters
  - norepinephrine, cholecystokinin, thyrotropin-releasing hormone, dopamine and antidiuretic hormone
- Some hormones secreted by neuroendocrine cells (neurons)
  - oxytocin and catecholamines
- Both systems with overlapping effects on same target cells
  - norepinephrine and glucagon cause glycogen hydrolysis in liver
- Systems regulate each other
  - neurons trigger hormone secretion
  - hormones stimulate or inhibit neurons
Hypothalamus

• Shaped like a flattened funnel, forms floor and walls of third ventricle
• Regulates primitive functions from water balance to sex drive
• Many functions carried out by pituitary gland
Pituitary Gland (Hypophysis)

• Suspended from hypothalamus by stalk (infundibulum)

• Location and size
  – housed in sella turcica of sphenoid bone
  – 1.3 cm diameter
Embryonic Development of Pituitary

(a) Embryo at 4 weeks

(b) Sagittal section of 4-week embryo

(c) 8 weeks

(d) Fetus

Telencephalon
Diencephalon
Neurohypophyseal bud
Hypophyseal pouch
Primitive oral cavity

Dura mater
Sella turcica
Posterior lobe
Pars intermedia
Anterior lobe
Sphenoid bone
Roof of pharynx
Pituitary Gland Anatomy and Hormones of the Neurohypophysis

Nuclei of hypothalamus
- Paraventricular nucleus
- Supraoptic nucleus

Third ventricle of brain
Floor of hypothalamus

Optic chiasm

Median eminence
Hypothalamo-hypophyseal tract

Pars tuberalis
Anterior lobe
Adenohypophysis

Stalk
Posterior lobe
Neurohypophysis

Oxytocin
Antidiuretic hormone
Hypothalamo-Hypophyseal Portal System

- Gonadotropin-releasing hormone controls FSH + LH release
- Thyrotropin-releasing hormone
- Corticotropin-releasing hormone
- Prolactin-releasing hormone
- Prolactin-inhibiting hormone
- GH-releasing hormone
- Somatostatin

- Hormones secreted by hypothalamus, travel in portal system to anterior pituitary
- Hormones (red box) secreted by anterior pituitary (under control of hypothalamic releasers and inhibitors)
Pituitary Hormones - Anterior Lobe

• Tropic hormones target other endocrine glands
  – gonadotropins target gonads, FSH (follicle stimulating hormone) and LH (luteinizing hormone)
  – TSH (thyroid stimulating hormone)
  – ACTH (adrenocorticotropic hormone)

• PRL (prolactin)

• GH (growth hormone)
Anterior Pituitary Hormones

- Principle hormones and target organs shown
- Axis - refers to way endocrine glands interact
Pituitary Hormones - Posterior Lobe

- Stores and releases OT and ADH
- OT (oxytocin) and ADH produced in hypothalamus, transported down to posterior lobe by hypothalamo-hypophyseal tract
Pituitary Hormone Actions:
Anterior Lobe Hormones

• FSH (secreted by gonadotrope cells)
  – ovaries, stimulates development of eggs and follicles
  – testes, stimulates production of sperm

• LH (secreted by gonadotrope cells)
  – females, stimulates ovulation and corpus luteum to secrete progesterone and estrogen
  – males, stimulates interstitial cells of testes to secrete testosterone

• TSH (secreted by thyrotropes)
  – stimulated growth of gland and secretion of TH
Pituitary Hormone Actions:
Anterior Lobe Hormones

• ACTH or corticotropin (secreted by corticotropes)
  – regulates response to stress, stimulates adrenal cortex to secrete of corticosteroids that regulate glucose, fat & protein metabolism

• PRL (secreted by lactotropes)
  – female, milk synthesis after delivery
  – male, ↑ LH sensitivity, thus ↑ testosterone secretion

• GH or somatotropin – see next 2 slides
Growth Hormone

• Secreted by somatotropes of anterior pituitary
• Promotes tissue growth
  – directly affects mitosis and cellular differentiation
  – indirectly stimulates liver to produce IGF-I somatomedins
    • half-life of 20 hours compared to 20 minutes for GH
• Functions of GH-IGF
  – protein synthesis
    • ↑DNA transcription for ↑mRNA production, proteins synthesized
    • enhances amino acid transport into cells, ↓protein catabolism
  – lipid metabolism
    • stimulates FFA and glycerol release from adipocytes, protein sparing
  – CHO metabolism
    • glucose sparing effect = less glucose used for energy
  – Electrolyte balance
    • promotes Na⁺, K⁺, Cl⁻ retention, Ca²⁺ absorption
Growth Hormone and Aging

- **Childhood and adolescence**
  - bone, cartilage and muscle growth

- **Adulthood**
  - increase osteoblastic activity and appositional growth affecting bone thickening and remodeling
  - blood concentration decrease by age 75 to ¼ of that of adolescent

- **Levels of GH**
  - higher during first 2 hours of deep sleep, after high protein meals, after vigorous exercise
  - lower after high CHO meals
Pituitary Hormone Actions:  
Posterior Lobe Hormones

• ADH
  – targets kidneys to $\uparrow$ 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
  – 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
Control of Pituitary: Feedback from Target Organs

• **Negative feedback**
  – $\uparrow$ target organ hormone levels inhibits release of tropic hormones

• **Positive feedback**
  – stretching of uterus $\uparrow$ OT release, causes stretching of uterus $\uparrow$ OT release, until delivery
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 $\uparrow$ in SAD + PMS, $\downarrow$ by phototherapy
  - depression, sleepiness, irritability and carbohydrate craving
Thymus

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

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

• Thyroid follicles
  – filled with colloid and lined with simple cuboidal epith. (follicular cells) that secretes 2 hormones, \( T_3 + T_4 \)
  – Thyroid hormone
    • \( \uparrow \) body’s metabolic rate and \( O_2 \) consumption
    • calorigenic effect - \( \uparrow \) heat production
    • \( \uparrow \) heart rate and contraction strength
    • \( \uparrow \) respiratory rate
    • stimulates appetite and breakdown CHO, lipids & proteins

• C (calcitonin or parafollicular) cells
  – produce calcitonin that \( \downarrow \) blood \( Ca^{+2} \), promotes \( Ca^{+2} \) deposition and bone formation especially in children
Histology of the Thyroid Gland

- Thyroid follicle
- Follicular cells
- C cells
- Colloid
Parathyroid Glands

- PTH release
  - ↑ blood Ca\(^{+2}\) levels
  - promotes synthesis of calcitriol
    - ↑ absorption of Ca\(^{+2}\)
    - ↓ urinary excretion
    - ↑ bone resorption

![Parathyroid Glands diagram](image)
Adrenal Gland

Adrenal gland
Kidney
Adrenal cortex
Adrenal medulla
Connective tissue capsule
Zona fasciculata
Zona reticularis
Zona glomerulosa
Adrenal Medulla

• Sympathetic ganglion innervated by sympathetic preganglionic fibers
  – consists of modified neurons called chromaffin cells
  – stimulation causes release of (nor-)epinephrine
• Hormonal effect is longer lasting
  – increases BP and heart rate
  – increases blood flow to skeletal muscle
  – increases pulmonary air flow
  – decreases digestion and urine formation
  – stimulates gluconeogenesis and glycogenolysis
• Stress causes medullary cells to stimulate cortex
Adrenal Cortex

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

- Corticosteroids
  - mineralocorticoids (zona glomerulosa)
    - control electrolyte balance, aldosterone promotes Na\(^+\) retention and K\(^+\) excretion
  - glucocorticoids (zona fasciculata)
    - especially cortisol, stimulates fat + protein catabolism, gluconeogenesis (from a.a.’s + FA’s) and release of fatty acids and glucose into blood
    - anti-inflammatory effect becomes immune suppression with long-term use
  - sex steroids (zona reticularis)
    - androgen (including DHEA which other tissues convert to testosterone) and estrogen (important after menopause)
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 $\beta$ cells)
  - secreted after meal with carbohydrates raises glucose blood levels
  - stimulates glucose and amino acid uptake
  - nutrient storage effect (stimulates glycogen, fat and protein synthesis)
  - antagonizes glucagon
Pancreatic Hormones 2

• **Glucagon (from $\alpha$ cells)**
  – secreted in very low carbohydrate and high protein diet or fasting
  – stimulates glycogenolysis, fat catabolism (release of FFA’s) and promotes absorption of amino acids for gluconeogenesis

• **Somatostatin from delta ($\delta$) cells)**
  – secreted with rise in blood glucose and amino acids after a meal
  – paracrine secretion = modulates secretion of $\alpha + \beta$ cells

• **Hyperglycemic hormones raise blood glucose**
  – glucagon, epinephrine, norepinephrine, cortisol & corticosterone

• **Hypoglycemic hormones lower blood glucose**
  – insulin
Histology of Ovary

Follicles = egg surrounded by granulosa cells
Ovary

• Granulosa cells in wall of ovarian follicle
  – produces estradiol, first half of menstrual cycle

• Corpus luteum: follicle after ovulation
  – produces estradiol and progesterone for 12 days or 8-12 weeks with pregnancy

• Functions of estradiol and progesterone
  – development of female reproductive system and physique including bone growth
  – regulate menstrual cycle, sustain pregnancy
  – prepare mammary glands for lactation

• Both secrete inhibin: suppresses FSH secretion
Histology of Testis

Seminiferous tubules produce sperm.
Testes

• Interstitial cells (between seminiferous tubules)
  – produce testosterone and estrogen

• Functions
  – development of male reproductive system and physique
  – sustains sperm production and sex drive

• Sustentacular sertoli cells
  – secrete inhibin which suppresses FSH secretion which stabilizes sperm production rates
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

- Synthesized from cholesterol – differs in functional groups attached to 4-ringed steroid backbone
Hormone Synthesis: Peptides

- **Cellular steps**
  - RER removes a segment forming prohormone
  - Golgi complexes further modifies it into hormone

- **Insulin formation**
  - preproinsulin converted to proinsulin in RER
  - proinsulin split into insulin and C peptide in golgi complex
    - C peptide has its own hormone effects
Hormone Synthesis: Monoamines

• All are synthesized from tyrosine
  – except melatonin which is synthesized from tryptophan

• Thyroid hormone is unusual
  – composed of 2 tyrosine molecules
  – requires a mineral, iodine
Thyroid Hormone Synthesis

1. $I^-$ transported into cell then
2. $I^- +$ thyroglobulin released into lumen
3-5 next slide
6. TSH stimulates pinocytosis, lysosome liberates TH, carried by thyroxine-binding globulin
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
  – **bound hormone** - hormone attached to transport protein, (prolongs half-life to weeks, protects from enzymes and kidney filtration)
  – only **unbound hormone** can leave capillary to reach target cell (half-life a few minutes)

• Transport proteins in blood plasma
  – albumin, thyretin and TGB (thyroxine binding globulin) bind to thyroid hormone
  – steroid hormones bind to globulins (transcortin)
  – aldosterone has no transport protein, 20 min. half-life
Hormone Receptors

- Located on plasma membrane, mitochondria and other organelles, or in nucleus
- Usually thousands for given hormone
  - turn metabolic pathways on or off when hormone binds
- Exhibit specificity and saturation
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

- TH binds to receptors on mitochondria (↑rate of aerobic respiration), on ribosomes and chromatin (↑protein synthesis)
- One protein produced: Na\(^+\)-K\(^+\) ATPase generates heat
Peptides and catecholamines bind to receptors in cell membrane

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
Hormone Clearance

- Hormone signals must be turned off
- Take up and degraded by liver and kidney
- Excreted in bile or urine
- Metabolic clearance rate (MCR)
- Half-life is time required to clear 50% of hormone
Hormone Interactions

• Most cells sensitive to more than one hormone and exhibit interactive effects
• Synergistic effects
• Permissive effects
  – one hormone enhances response to a second hormone
• Antagonistic effects
Stress and Adaptation

• Any situation that upsets homeostasis and threatens one’s physical or emotional well-being causes stress

• Way body reacts to stress called the general adaptation syndrome, occurs in 3 stages
  – alarm reaction
  – stage of resistance
  – stage of exhaustion
Alarm Reaction

- Initial response
- ↑ epinephrine and norepinephrine levels
- ↑ HR and ↑ BP
- ↑ blood glucose levels
- Sodium and water retention (aldosterone)
Stage of Resistance

- After a few hours, glycogen reserves gone
- ↑ ACTH and cortisol levels
- Fat and protein breakdown
- Gluconeogenesis
- Depressed immune function
- Susceptibility to infection and ulcers
Stage of Exhaustion

- Stress that continues until fat reserves are gone
- Protein breakdown and muscle wasting
- Loss of glucose homeostasis
- Hypertension and electrolyte imbalances (loss of $K^+$ and $H^+$)
- Hypokalemia and alkalosis leads to death
Endocrine Disorders

• Variations in hormone concentration and target cell sensitivity have noticeable effects on the body

• Hyposecretion – inadequate hormone release
  – tumor or lesion destroys gland
    • head trauma affects pituitary gland’s ability to secrete ADH
      – diabetes insipidus = chronic polyuria

• Hypersecretion – excessive hormone release
  – tumors or autoimmune disorder
    • toxic goiter (graves disease) – antibodies mimic effect of TSH on the thyroid
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

Age 9  Age 16  Age 33  Age 52
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
Diabetes Mellitus

• Signs and symptoms of hyposcretion 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 $\uparrow$ 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 $\uparrow$ FFA’s in blood and ketone bodies
  – ketonuria promotes osmotic diuresis, loss of $\text{Na}^+ + \text{K}^+$
  – ketoacidosis occurs as ketones $\downarrow$ 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