

Endocrine System: Overview

- Acts with nervous system to coordinate and integrate activity of body cells
- Influences metabolic activities via **hormones** transported in blood
- Response slower but longer lasting than nervous system
- **Endocrinology**
 - Study of hormones and endocrine organs

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Endocrine System: Overview

- Controls and integrates
 - Reproduction
 - Growth and development
 - Maintenance of electrolyte, water, and nutrient balance of blood
 - Regulation of cellular metabolism and energy balance
 - Mobilization of body defenses

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Endocrine System: Overview

- **Exocrine glands**
 - Nonhormonal substances (sweat, saliva)
 - Have ducts to carry secretion to membrane surface
- **Endocrine glands**
 - Produce hormones
 - Lack ducts

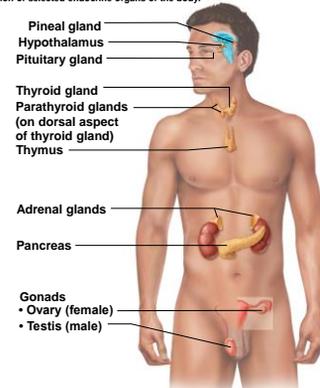
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Endocrine System: Overview

- **Endocrine glands: pituitary, thyroid, parathyroid, adrenal, and pineal glands**
- **Hypothalamus is neuroendocrine organ**
- Some have exocrine and endocrine functions
 - **Pancreas, gonads, placenta**
- Other tissues and organs that produce hormones
 - Adipose cells, thymus, and cells in walls of small intestine, stomach, kidneys, and heart

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Figure 16.1 Location of selected endocrine organs of the body.



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Chemical Messengers

- **Hormones:** long-distance chemical signals; travel in blood or lymph
- **Autocrines:** chemicals that exert effects on same cells that secrete them
- **Paracrines:** locally acting chemicals that affect cells other than those that secrete them
- Autocrines and paracrines are local chemical messengers; not considered part of endocrine system

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Chemistry of Hormones

- Two main classes
 - **Amino acid-based hormones**
 - Amino acid derivatives, peptides, and proteins
 - **Steroids**
 - Synthesized from cholesterol
 - Gonadal and adrenocortical hormones

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Mechanisms of Hormone Action

- Hormones act at receptors in one of two ways, depending on their chemical nature and receptor location
 1. Water-soluble hormones (all amino acid-based hormones except thyroid hormone)
 - Act on plasma membrane receptors
 - Act via G protein second messengers
 - Cannot enter cell

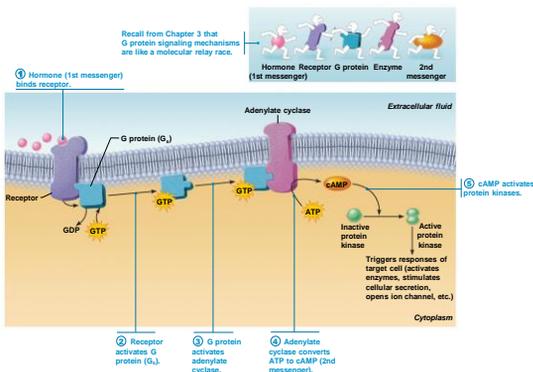
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Mechanisms of Hormone Action

2. Lipid-soluble hormones (steroid and thyroid hormones)
 - Act on intracellular receptors that directly activate genes
 - Can enter cell

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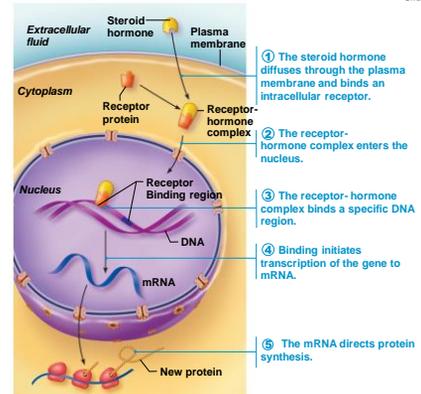
Figure 16.2 Cyclic AMP second-messenger mechanism of water-soluble hormones.



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Figure 16.3 Direct gene activation mechanism of lipid-soluble hormones.



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Target Cell Specificity

- Target cells must have specific receptors to which hormone binds, for example
 - ACTH receptors found only on certain cells of adrenal cortex
 - Thyroxin receptors are found on nearly all cells of body

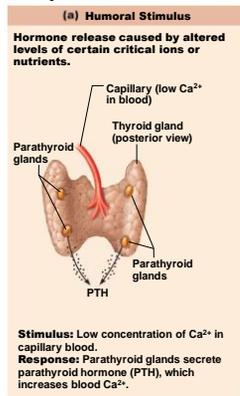
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Target Cell Activation

- Hormones influence number of their receptors
 - **Up-regulation**—target cells form more receptors in response to low hormone levels
 - **Down-regulation**—target cells lose receptors in response to high hormone levels

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Figure 16.4a Three types of endocrine gland stimuli.



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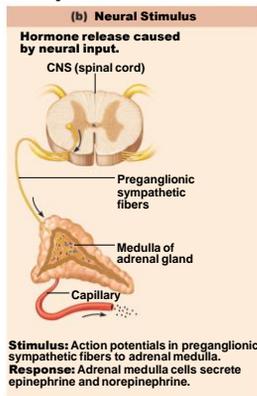
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Neural Stimuli

- Nerve fibers stimulate hormone release
 - Sympathetic nervous system fibers stimulate adrenal medulla to secrete catecholamines

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Figure 16.4b Three types of endocrine gland stimuli.



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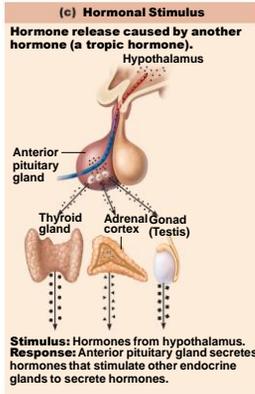
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Hormonal Stimuli

- Hormones stimulate other endocrine organs to release their hormones
 - Hypothalamic hormones stimulate release of most anterior pituitary hormones
 - Anterior pituitary hormones stimulate targets to secrete still more hormones
 - Hypothalamic-pituitary-target endocrine organ feedback loop: hormones from final target organs inhibit release of anterior pituitary hormones

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Figure 16.4c Three types of endocrine gland stimuli.



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Nervous System Modulation

- Nervous system modifies stimulation of endocrine glands and their negative feedback mechanisms
 - Example: under severe stress, hypothalamus and sympathetic nervous system activated
 - → body glucose levels rise
- Nervous system can override normal endocrine controls

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Duration of Hormone Activity

- Limited
 - Ranges from 10 seconds to several hours
 - Effects may disappear as blood levels drop
 - Some persist at low blood levels

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Interaction of Hormones at Target Cells

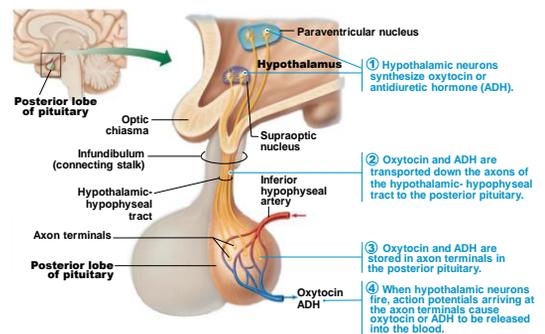
- Multiple hormones may act on same target at same time
 - **Permissiveness:** one hormone cannot exert its effects without another hormone being present
 - **Synergism:** more than one hormone produces same effects on target cell → amplification
 - **Antagonism:** one or more hormones oppose(s) action of another hormone

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The Pituitary Gland and Hypothalamus

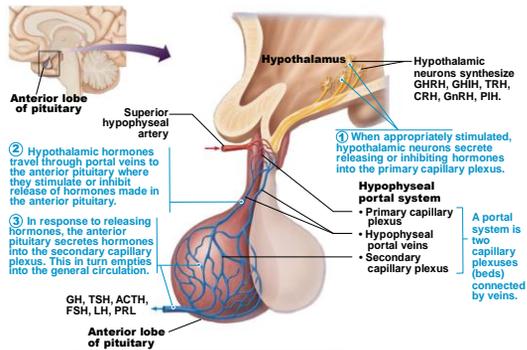
- **Pituitary gland (hypophysis)** has two major lobes
 - **Posterior pituitary (lobe)**
 - Neural tissue
 - **Anterior pituitary (lobe)** (adenohypophysis)
 - Glandular tissue

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Figure 16.5a The hypothalamus controls release of hormones from the pituitary gland in two different ways (1 of 2).
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Figure 16.5b The hypothalamus controls release of hormones from the pituitary gland in two different ways (2 of 2).
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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

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

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Anterior Pituitary Hormones

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

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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)

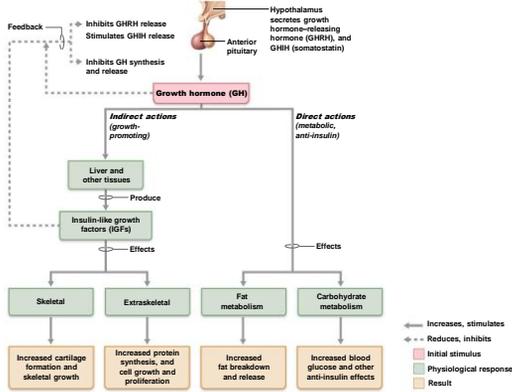
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Homeostatic Imbalances of Growth Hormone

- **Hypersecretion**
 - In children results in **gigantism**
 - In adults results in **acromegaly**
- **Hyposecretion**
 - In children results in **pituitary dwarfism**

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Figure 16.6 Growth-promoting and metabolic actions of growth hormone (GH).



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Figure 16.7 Disorders of pituitary growth hormone.



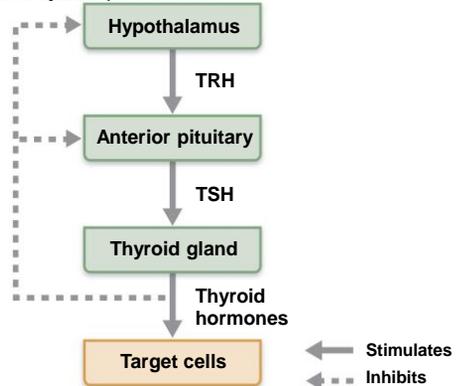
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Thyroid-stimulating Hormone (Thyrotropin)

- 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

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Figure 16.8 Regulation of thyroid hormone secretion.



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Adrenocorticotrophic 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

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Gonadotropins

- Follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
- Secreted by gonadotropic cells of anterior pituitary
- FSH stimulates gamete (egg or sperm) production
- LH promotes production of gonadal hormones
- Absent from the blood in prepubertal boys and girls

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Thyroid Gland

- Two lateral lobes connected by median mass called **isthmus**
- Composed of follicles that produce glycoprotein **thyroglobulin**
- Colloid (fluid with thyroglobulin + iodine) fills lumen of follicles and is precursor of thyroid hormone
- **Parafollicular cells** produce the hormone **calcitonin**

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Thyroid Hormone (TH)

- Actually two related compounds
 - T_4 (thyroxine); has 2 tyrosine molecules + 4 bound iodine atoms
 - T_3 (triiodothyronine); has 2 tyrosines + 3 bound iodine atoms
- Affects virtually every cell in body

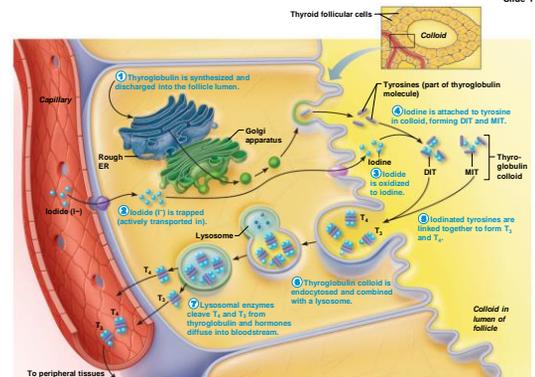
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Thyroid Hormone

- Major metabolic hormone
- Increases metabolic rate and heat production (calorigenic effect)
- Regulation of tissue growth and development
 - Development of skeletal and nervous systems
 - Reproductive capabilities
- Maintenance of blood pressure

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Figure 16.10 Synthesis of thyroid hormone.



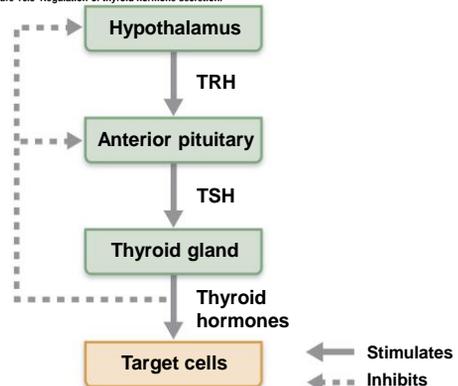
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Transport and Regulation of TH

- T_4 and T_3 transported by thyroxine-binding globulins (TBGs)
- Both bind to target receptors, but T_3 is ten times more active than T_4
- Peripheral tissues convert T_4 to T_3

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Figure 16.8 Regulation of thyroid hormone secretion.

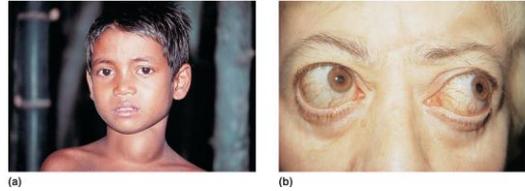


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Homeostatic Imbalances of TH

- Hyposecretion in adults—**myxedema**; **goiter** if due to lack of iodine
- Hyposecretion in infants—**cretinism**
- Hypersecretion—most common type is **Graves' disease**

Figure 16.11 Thyroid disorders.



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Calcitonin

- Produced by parafollicular (C) cells
- No known physiological role in humans
- Antagonist to parathyroid hormone (PTH)
- At higher than normal doses
 - Inhibits osteoclast activity and release of Ca^{2+} from bone matrix
 - Stimulates Ca^{2+} uptake and incorporation into bone matrix

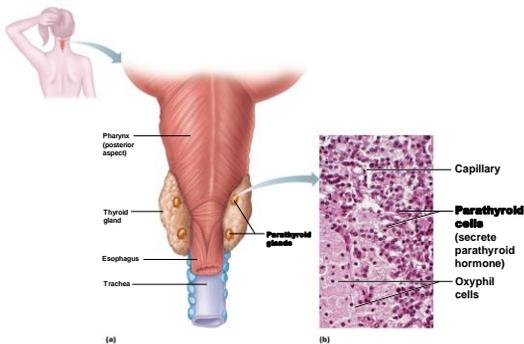
Parathyroid Glands

- Four to eight tiny glands embedded in posterior aspect of thyroid
- Contain oxyphil cells (function unknown) and parathyroid cells that secrete **parathyroid hormone (PTH)** or parathormone
- PTH—most important hormone in Ca^{2+} homeostasis

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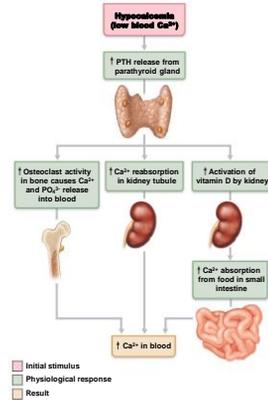
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Figure 16.12 The parathyroid glands.



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Figure 16.13 Effects of parathyroid hormone on bone, the kidneys, and the intestine.



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Homeostatic Imbalances of PTH

- **Hyperparathyroidism** due to tumor
 - Bones soften and deform
 - Elevated Ca^{2+} depresses nervous system and contributes to formation of kidney stones
- **Hypoparathyroidism** following gland trauma or removal or dietary magnesium deficiency
 - Results in tetany, respiratory paralysis, and death

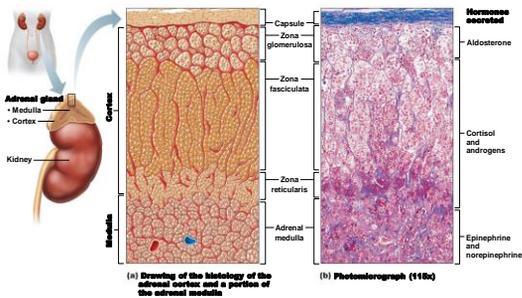
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Adrenal (Suprarenal) Glands

- Paired, pyramid-shaped organs atop kidneys
- Structurally and functionally are two glands in one
 - **Adrenal medulla**—nervous tissue; part of sympathetic nervous system
 - **Adrenal cortex**—three layers of glandular tissue that synthesize and secrete corticosteroids

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Figure 16.14 Microscopic structure of the adrenal gland.



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Homeostatic Imbalances of Aldosterone

- **Aldosteronism**—hypersecretion due to adrenal tumors
 - Hypertension and edema due to excessive Na^+
 - Excretion of K^+ leading to abnormal function of neurons and muscle

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Glucocorticoids

- Keep blood glucose levels relatively constant
- Maintain blood pressure by increasing action of vasoconstrictors
- **Cortisol (hydrocortisone)**
 - Only one in significant amounts in humans
- Cortisone
- Corticosterone

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Homeostatic Imbalances of Glucocorticoids

- **Hypersecretion—Cushing's syndrome/disease**
 - Depresses cartilage and bone formation
 - Inhibits inflammation
 - Depresses immune system
 - Disrupts cardiovascular, neural, and gastrointestinal function
- **Hyposecretion—Addison's disease**
 - Also involves deficits in mineralocorticoids
 - Decrease in glucose and Na^+ levels
 - Weight loss, severe dehydration, and hypotension

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Figure 16.16 The effects of excess glucocorticoid.



(a) Patient before onset.

(b) Same patient with Cushing's syndrome. The white arrow shows the characteristic "buffalo hump" of fat on the upper back.

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Gonadocorticoids (Sex Hormones)

- Most weak androgens (male sex hormones) converted to testosterone in tissue cells, some to estrogens
- May contribute to
 - Onset of puberty
 - Appearance of secondary sex characteristics
 - Sex drive in women
 - Estrogens in postmenopausal women

Gonadocorticoids

- **Hypersecretion**
 - **Adrenogenital syndrome** (masculinization)
 - Not noticeable in adult males
 - Females and prepubertal males
 - Boys – reproductive organs mature; secondary sex characteristics emerge early
 - Females – beard, masculine pattern of body hair; clitoris resembles small penis

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Adrenal Medulla

- **Medullary chromaffin cells** synthesize epinephrine (80%) and norepinephrine (20%)
- **Effects**
 - Vasoconstriction
 - Increased heart rate
 - Increased blood glucose levels
 - Blood diverted to brain, heart, and skeletal muscle

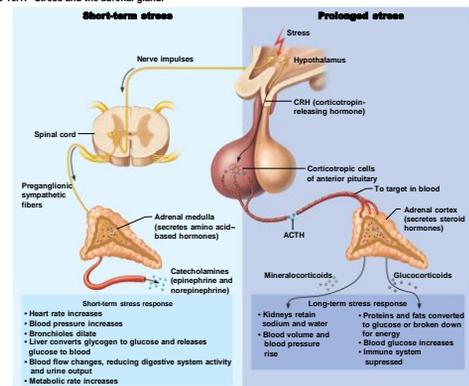
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Adrenal Medulla

- **Hypersecretion**
 - Hyperglycemia, increased metabolic rate, rapid heartbeat and palpitations, hypertension, intense nervousness, sweating
- **Hyposecretion**
 - Not problematic
 - Adrenal catecholamines not essential to life

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Figure 16.17 Stress and the adrenal gland.



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Pineal Gland

- Small gland hanging from roof of third ventricle
- **Pinealocytes** secrete **melatonin**, derived from serotonin
- Melatonin may affect
 - Timing of sexual maturation and puberty
 - Day/night cycles
 - Physiological processes that show rhythmic variations (body temperature, sleep, appetite)
 - Production of antioxidant and detoxification molecules in cells

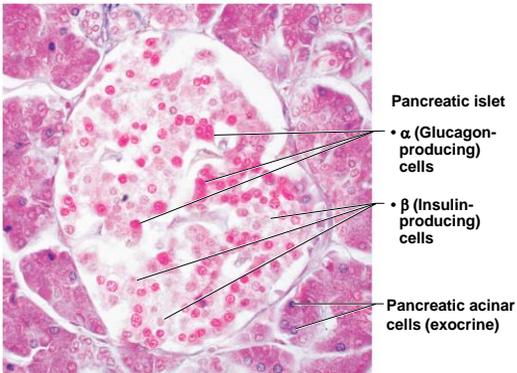
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Pancreas

- Triangular gland partially behind stomach
- Has both exocrine and endocrine cells
 - **Acinar cells** (exocrine) produce enzyme-rich juice for digestion
 - **Pancreatic islets (islets of Langerhans)** contain endocrine cells
 - **Alpha (α) cells** produce **glucagon** (hyperglycemic hormone)
 - **Beta (β) cells** produce **insulin** (hypoglycemic hormone)

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Figure 16.18 Photomicrograph of differentially stained pancreatic tissue.



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Glucagon

- Major target—liver
- Causes increased blood glucose levels
- Effects
 - **Glycogenolysis**—breakdown of glycogen to glucose
 - **Gluconeogenesis**—synthesis of glucose from lactic acid and noncarbohydrates
 - Release of glucose to blood

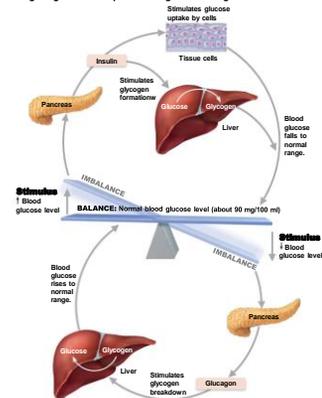
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Insulin

- Effects of insulin
 - Lowers blood glucose levels
 - Enhances membrane transport of glucose into fat and muscle cells
 - Inhibits glycogenolysis and gluconeogenesis
 - Participates in neuronal development and learning and memory
- Not needed for glucose uptake in liver, kidney or brain

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Figure 16.19 Insulin and glucagon from the pancreas regulate blood glucose levels.



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Factors That Influence Insulin Release

- Elevated blood glucose levels – primary stimulus
- Rising blood levels of amino acids and fatty acids
- Release of acetylcholine by parasympathetic nerve fibers
- Hormones glucagon, epinephrine, growth hormone, thyroxine, glucocorticoids
- Somatostatin; sympathetic nervous system

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Homeostatic Imbalances of Insulin

- Diabetes mellitus (DM)
 - Due to hyposecretion (type 1) or hypoactivity (type 2) of insulin
 - Blood glucose levels remain high → nausea → higher blood glucose levels (fight or flight response)
 - **Glycosuria** – glucose spilled into urine
 - Fats used for cellular fuel → **lipidemia**; if severe → **ketones** (ketone bodies) from fatty acid metabolism → **ketonuria** and **ketoacidosis**
 - Untreated ketoacidosis → hyperpnea; disrupted heart activity and O₂ transport; depression of nervous system → coma and death possible

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Diabetes Mellitus: Signs

- Three cardinal signs of DM
 - **Polyuria**—huge urine output
 - Glucose acts as osmotic diuretic
 - **Polydipsia**—excessive thirst
 - From water loss due to polyuria
 - **Polyphagia**—excessive hunger and food consumption
 - Cells cannot take up glucose; are "starving"

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Homeostatic Imbalances of Insulin

- **Hyperinsulinism:**
 - Excessive insulin secretion
 - Causes **hypoglycemia**
 - Low blood glucose levels
 - Anxiety, nervousness, disorientation, unconsciousness, even death
 - Treated by sugar ingestion

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Table 16.4 Symptoms of Insulin Deficit (Diabetes Mellitus)

ORGAN/TISSUE RESPONSES TO INSULIN DEFICIENCY		RESULTING CONDITIONS		
ORGANS/TISSUES INVOLVED	ORGAN/TISSUE RESPONSES TO INSULIN DEFICIENCY	IN BLOOD	IN URINE	SIGNS AND SYMPTOMS
 Adipose tissue Muscle	Decreased glucose uptake and utilization	Hyperglycemia	Glycosuria Osmotic diuresis	Polyuria (and dehydration, soft eyeballs) Polydipsia (and fatigue, weight loss) Polyphagia
	Glycogenolysis			
 Liver	Protein catabolism and gluconeogenesis			
 Liver Adipose tissue	Lipolysis and ketogenesis	Lipidemia and ketoacidosis	Ketonuria Loss of Na ⁺ , K ⁺ ; electrolyte and acid-base imbalances	Acetone breath Hyperpnea Nausea, vomiting, abdominal pain Cardiac irregularities Central nervous system depression; coma

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Ovaries and Placenta

- Gonads produce steroid sex hormones
 - Same as those of adrenal cortex
- Ovaries produce **estrogens** and **progesterone**
 - Estrogen
 - Maturation of reproductive organs
 - Appearance of secondary sexual characteristics
 - With progesterone, causes breast development and cyclic changes in uterine mucosa
- **Placenta** secretes estrogens, progesterone, and human chorionic gonadotropin (hCG)

Testes

- Testes produce **testosterone**
 - Initiates maturation of male reproductive organs
 - Causes appearance of male secondary sexual characteristics and sex drive
 - Necessary for normal sperm production
 - Maintains reproductive organs in functional state

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Other Hormone-producing Structures

- Heart
 - **Atrial natriuretic peptide (ANP)** decreases blood Na⁺ concentration, therefore blood pressure and blood volume
- Kidneys
 - **Erythropoietin** signals production of red blood cells
 - **Renin** initiates the renin-angiotensin-aldosterone mechanism

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Developmental Aspects

- Hormone-producing glands arise from all three germ layers
- Most endocrine organs operate well until old age
- Exposure to pesticides, industrial chemicals, arsenic, dioxin, and soil and water pollutants disrupts hormone function
- Sex hormones, thyroid hormone, and glucocorticoids are vulnerable to the effects of pollutants
- Interference with glucocorticoids may help explain high cancer rates in certain areas

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Developmental Aspects

- Ovaries undergo significant changes with age and become unresponsive to gonadotropins; problems associated with estrogen deficiency occur
- Testosterone also diminishes with age, but effect is not usually seen until very old age

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Developmental Aspects

- GH levels decline with age - accounts for muscle atrophy with age
- TH declines with age, contributing to lower basal metabolic rates
- PTH levels remain fairly constant with age, but lack of estrogen in older women makes them more vulnerable to bone-demineralizing effects of PTH

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