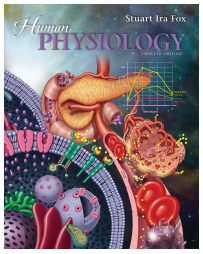
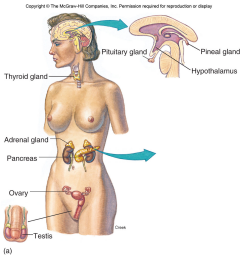


Chapter 11

Endocrine Glands: Secretion and Action of Hormones

Lecture PowerPoint

I. Endocrine Glands and Hormones



Endocrine Glands

- Ductless
- Secrete hormones into the blood
- Hormones are carried to target cells having receptors for those hormones.
- Many organs secrete hormones other than those discussed in this chapter:
  - Heart, liver, kidneys, adipose tissue

Summary of Endocrine System

Table 11.1 | A Partial Listing of the Endocrine Glands

Endocrine Gland	Major Hormones	Primary Target Organs	Primary Effects
Adipose tissue	Leptin	Hypothalamus	Suppresses appetite
Adrenal cortex	Glucocorticoids Aldosterone	Liver and muscles Kidneys	Glucocorticoids influence glucose metabolism; aldosterone promotes Na^+ retention, K^+ excretion
Adrenal medulla	Epinephrine	Heart, bronchioles, and blood vessels	Causes adrenergic stimulation
Heart	Atrial natriuretic hormone	Kidneys	Promotes excretion of Na^+ in the urine
Hypothalamus	Releasing and inhibiting hormones	Anterior pituitary	Regulates secretion of anterior pituitary hormones
Small intestine	Secretin and cholecystokinin	Stomach, liver, and pancreas	Inhibits gastric motility and stimulates bile and pancreatic juice secretion
Islets of Langerhans (pancreas)	Insulin Glucagon	Many organs Liver and adipose tissue	Insulin promotes cellular uptake of glucose and formation of glycogen and fat; glucagon stimulates hydrolysis of glycogen and fat
Kidneys	Erythropoietin	Bone marrow	Stimulates red blood cell production
Liver	Somatomedins	Cartilage	Stimulates cell division and growth
Ovaries	Estradiol-17β and progesterone	Female reproductive tract and mammary glands	Maintains structure of reproductive tract and promotes secondary sex characteristics
Parathyroid glands	Parathyroid hormone	Bone, small intestine, and kidneys	Increases Ca^{2+} concentration in blood
Pineal gland	Melatonin	Hypothalamus and anterior pituitary	Affects secretion of gonadotrophic hormones
Pituitary, anterior	Trophic hormones	Endocrine glands and other organs	Stimulates growth and development of target organs; stimulates secretion of other hormones
Pituitary, posterior	Antidiuretic hormone Oxytocin	Kidneys and blood vessels Uterus and mammary glands	Antidiuretic hormone promotes water retention and vasoconstriction; oxytocin stimulates contraction of uterus and mammary secretory units
Skin	1,25-Dihydroxyvitamin D_3	Small intestine	Stimulates absorption of Ca^{2+}
Stomach	Gastrin	Stomach	Stimulates acid secretion
Testes	Testosterone	Prostate, seminal vesicles, and other organs	Stimulates secondary sexual development
Thymus	Thymopoietin	Lymph nodes	Stimulates white blood cell production
Thyroid gland	Thyroxine (T_4) and triiodothyronine (T_3); calcitonin	Most organs	Thyroxine and triiodothyronine promote growth and development and stimulate basal rate of cell respiration (basal metabolic rate or BMR); calcitonin may participate in the regulation of blood Ca^{2+} levels

Chemical Classification of Hormones

- Amines, derived from tyrosine and tryptophan
  - Examples: hormones from the adrenal medulla, thyroid, and pineal glands
- Polypeptides and proteins
  - Examples: antidiuretic hormone, insulin, and growth hormone

Chemical Classification of Hormones

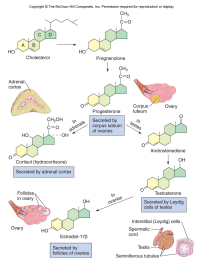
- Glycoproteins are long polypeptides bound to a carbohydrate.
  - Examples: follicle-stimulating and luteinizing hormones
- Steroids are lipids derived from cholesterol
  - Examples: testosterone, estradiol, progesterone, cortisol
  - Secreted by adrenal cortex and gonads

Hormone Classifications

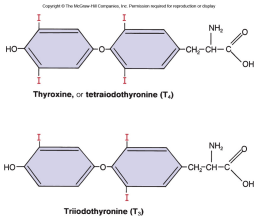
- Polar hormones: water soluble
  - Cannot pass through plasma membranes
  - Must be injected if used as a drug
- Nonpolar: insoluble in water
  - Often called lipophilic hormones
  - Can enter target cells directly
  - Include steroids and thyroid hormone
  - Can be taken orally in pill form

Nonpolar Hormones

Biosynthetic Pathway for Steroid Hormones



Structural Formulas for Thyroid Hormone



Prohormones and Prehormones

- Prohormones are inactive hormones that must be cut and spliced together to be active.
  - Example: insulin
- Prehormones are inactive hormones that must be modified within their target cells.

Prohormones and Prehormones

Table 11.3 | Conversion of Prehormones into Biologically Active Derivatives

Endocrine Gland	Prehormone	Active Products	Comments
Skin	Vitamin D_3	1,25-Dihydroxyvitamin D_3	Conversion (through hydroxylation reactions) occurs in the liver and the kidneys.
Testes	Testosterone	Dihydrotestosterone (DHT)	DHT and other 5α-reduced androgens are formed in most androgen-dependent tissue.
		Estradiol-17β (E_2)	E_2 is formed in the brain from testosterone, where it is believed to affect both endocrine function and behavior; small amounts of E_2 are also produced in the testes.
Thyroid	Thyroxine (T_4)	Triiodothyronine (T_3)	Conversion of T_4 to T_3 occurs in almost all tissues.

Hormones Are Like Neurotransmitters

- Hormones and neurotransmitters both interact with specific receptors.
- Binding to a receptor causes a change within the cell.
- There are mechanisms to turn off target cell activity.
  - The signal is either removed or inactivated.

Hormone Interactions

- A target cell is usually responsive to several different hormones.
  - Hormones may be antagonistic, synergistic, or permissive.
  - How a cell responds depends on the amount of hormone and the combination of all hormones.

Synergistic Effects

- Occur when two or more hormones work together to produce a particular effect
  - Effects may be additive, as when epinephrine and norepinephrine each affect the heart in the same way.
  - Effects may be complementary, as when each hormone contributes a different piece of an overall outcome.
    - For example, producing milk requires estrogen, prolactin, and oxytocin.

Permissive Effects

- Occur when one hormone makes the target cell more responsive to a second hormone
  - Exposure to estrogen makes the uterus more responsive to progesterone.

Antagonistic Effects

- Occur when hormones work in opposite directions.
  - Insulin and glucagon both affect adipose tissue.
  - Insulin stimulates fat storage, while glucagon stimulates fat breakdown.

Hormone Half-life

- The half-life of hormones circulating in the blood ranges from minutes to hours.
  - Most hormones are removed from the blood by the liver.
  - Thyroid hormone circulates for several days.

Hormone Concentration

- Tissues only respond when hormone concentrations are at a certain “normal” level.
  - At higher pharmacological concentrations, effects may be different from normal.
  - High concentrations may result in binding to receptors of related hormones.
  - This can result in widespread side effects.

Priming Effects/Upregulation

- Some target cells respond to a particular hormone by increasing the number of receptors it has for that hormone.
- This makes it more sensitive to subsequent hormone release.

Desensitization and Down Regulation

- Prolonged exposure to high concentrations of hormone may result in a decreased number of receptors for that hormone.
  - Occurs in adipose cells in response to high concentrations of insulin
- To avoid desensitization, many hormones are released in spurts, called pulsatile secretion.

II. Mechanisms of Hormone Action

Hormone Receptors

- Hormones bind to receptors on or in target cells.
  - Binding is highly specific.
  - Hormones bind to receptors with a high affinity.
  - Hormones bind to receptors with a low capacity.

Hormones That Bind to Receptors in the Nucleus

- Lipophilic steroid hormones and thyroid hormone:
  - Travel to target cells attached to carrier proteins
  - At the target cell, dissociate from the carrier protein and diffuse across the plasma membrane
  - Receptors are found within the nucleus and are called nuclear hormone receptors.

Hormones That Bind to Receptors in the Nucleus

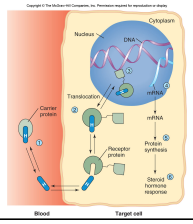
- These hormones activate genetic transcription by serving as transcription factors.
  - The effect of these hormones is therefore to produce new proteins, usually enzymes that change metabolism inside the cell.

Nuclear Hormone Receptors

- Two regions:
  - Ligand-binding domain
  - DNA-binding domain
- Binding of the hormone activates the DNA-binding domain, and it binds to a hormone response element on the DNA.
- Modern science has identified many "orphan" receptors without a known ligand.

Steroid Hormone Action

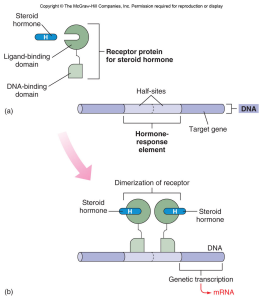
- Receptors located in cytoplasm
- After binding, they translocate to the nucleus and bind to DNA.



Steroid Hormone Action

- Hormone response elements have two "half-sites."
- Two ligand-bound receptors must bind.
  - Called dimerization; this forms a homodimer.

Steroid Hormone Action



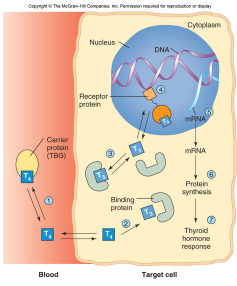
Coactivators and Corepressors

- Molecules are needed in addition to the steroid hormone.
- They bind to the nuclear receptor proteins at specific regions.
- This changes the effect of a given hormone in different cells.

Thyroid Hormone Action

- Thyroxine (T_4) travels to target cells on thyroxine-binding globulin (TBG).
  - Inside the target cell, it is converted to T_3.
  - Receptor proteins are located inside the nucleus bound to DNA.

Thyroid Hormone Action

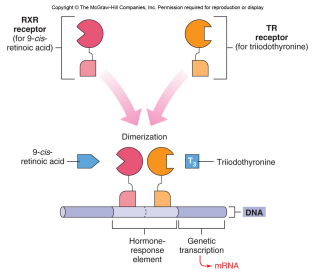


Thyroid Hormone Action

– The hormone response element on the DNA has two half-sites, one for a T_3 receptor and one for a 9-*cis*-retinoic acid receptor.

– Binding of these molecules forms a heterodimer.

Thyroid Hormone Action



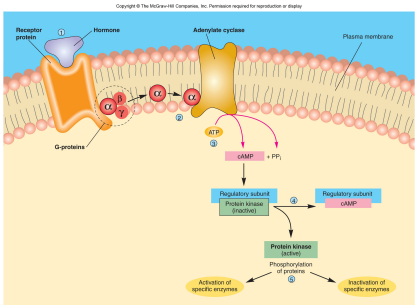
Hormones That Use 2nd Messengers

- These hormones cannot cross the plasma membrane, so they bind to receptors on the cell surface.
- There are three possible 2nd messenger mechanisms:
  - Adenylate cyclase
  - Phospholipase C
  - Tyrosine kinase

Adenylate Cyclase/cAMP System

- Used by epinephrine and norepinephrine
  - Binds to a β-adrenergic receptor
  - G-protein dissociates
  - Activates adenylate cyclase
  - Uses ATP to make cAMP
  - cAMP activates protein kinase
  - Protein kinase phosphorylates proteins in the target cell to alter cell metabolism
  - cAMP inactivated by phosphodiesterase

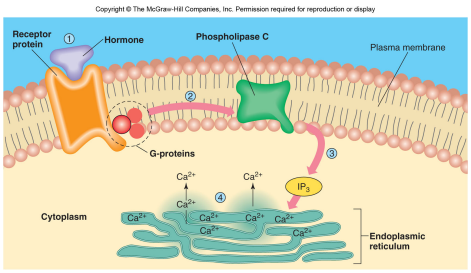
Adenylate Cyclase/cAMP System



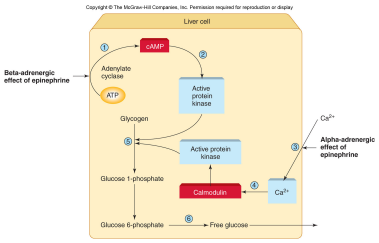
Phospholipase C System

- Used by epinephrine in some cells
  - Bind to α-adrenergic receptors
  - G-protein dissociates
  - Activates phospholipase C
  - Produces IP_3 and DAG
  - Liberates Ca^{2+} from the endoplasmic reticulum
  - Ca^{2+} activates calmodulin
  - Activates protein kinases to modify enzymes

Phospholipase C System



Two Systems for Epinephrine

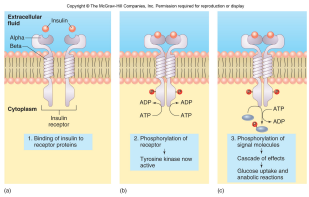


Tyrosine Kinase System

- Insulin uses this.
  - The receptor is also the enzyme tyrosine kinase.
  - The ligand-binding site is on the outside of the cell, and the enzyme faces the cytoplasm.
  - The enzyme portion is activated via phosphorylation.

Tyrosine Kinase System

- The activated receptor phosphorylates insulin receptor substrate molecules.
- This activates a cascade of enzymatic activity.

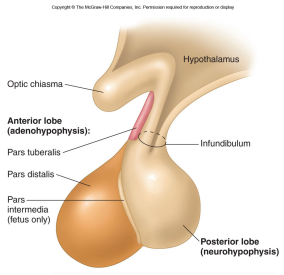


III. Pituitary Gland

Pituitary Gland

- Attached to the hypothalamus by the infundibulum
- Divided into an anterior lobe (adenohypophysis) and a posterior lobe (neurohypophysis)

Pituitary Gland



Pituitary Hormones

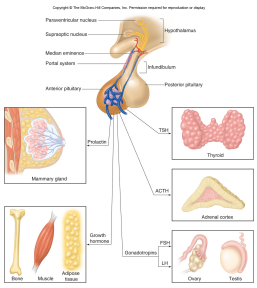
- Secreted by the anterior lobe
- Trophic hormones stimulate hormone secretion in other glands:
  - Growth hormone (GH)
  - Thyroid-stimulating hormone (TSH)
  - Adrenocorticotropic hormone (ACTH)
  - Follicle-stimulating hormone (FSH)
  - Luteinizing hormone (LH)
  - Prolactin (PRL)

Anterior Pituitary Hormones

Table 11.6 | Anterior Pituitary Hormones

Hormone	Target Tissue	Principal Actions	Regulation of Secretion
ACTH (adrenocorticotropic hormone)	Adrenal cortex	Stimulates secretion of glucocorticoids	Stimulated by CRH (corticotropin-releasing hormone); inhibited by glucocorticoids
TSH (thyroid-stimulating hormone)	Thyroid gland	Stimulates secretion of thyroid hormones	Stimulated by TRH (thyrotropin-releasing hormone); inhibited by thyroid hormones
GH (growth hormone)	Most tissue	Promotes protein synthesis and growth; lipolysis and increased blood glucose	Inhibited by somatostatin; stimulated by growth hormone-releasing hormone
FSH (follicle-stimulating hormone)	Gonads	Promotes gamete production and stimulates estrogen production in females	Stimulated by GnRH (gonadotropin-releasing hormone); inhibited by sex steroids and inhibin
PRL (prolactin)	Mammary glands and other sex accessory organs	Promotes milk production in lactating females; additional actions in other organs	Inhibited by PIH (prolactin-inhibiting hormone)
LH (luteinizing hormone)	Gonads	Stimulates sex hormone secretion; ovulation and corpus luteum formation in females; stimulates testosterone secretion in males	Stimulated by GnRH; inhibited by sex steroids

Anterior Pituitary Hormones



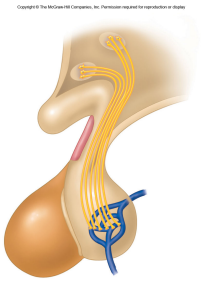
Posterior Pituitary

- Stores and releases two hormones made in the pituitary gland:
  - Antidiuretic hormone (ADH), which promotes the retention of water in the kidneys
  - Oxytocin, which stimulates contractions in childbirth

Hypothalamic Control of the Posterior Pituitary

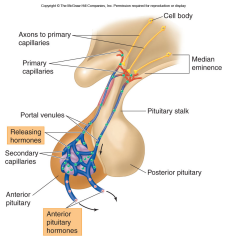
- ADH and oxytocin are produced by the supraoptic and paraventricular nuclei of the hypothalamus.
- They are transported along axons of the hypothalamo-hypophyseal tract to the posterior pituitary.
- Release is controlled by neuroendocrine reflexes.

Hypothalamic Control of the Posterior Pituitary



Hypothalamic Control of the Anterior Pituitary

- The anterior pituitary is controlled via releasing and inhibiting hormones transported through the hypothalamo-hypophyseal portal system.



Hypothalamic Control of Anterior Pituitary

- Corticotropin-releasing hormone (CRH)
- Gonadotropin-releasing hormone (GRH)
- Prolactin-inhibiting hormone (PIH)
- Somatostatin
- Thyrotropin-releasing hormone (TRH)
- Growth hormone–releasing hormone (GHRH)

Hypothalamic Control of Anterior Pituitary

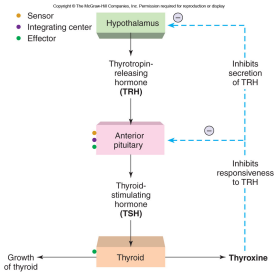
Table 11.7 | Hypothalamic Hormones Involved in the Control of the Anterior Pituitary

Hypothalamic Hormone	Structure	Effect on Anterior Pituitary
Corticotropin-releasing hormone (CRH)	41 amino acids	Stimulates secretion of adrenocorticotropic hormone (ACTH)
Gonadotropin-releasing hormone (GnRH)	10 amino acids	Stimulates secretion of follicle-stimulating hormone (FHS) and luteinizing hormone (LH)
Prolactin-inhibiting hormone (PIH)	Dopamine	Inhibits prolactin secretion
Somatostatin	14 amino acids	Inhibits secretion of growth hormone
Thyrotropin-releasing hormone (TRH)	3 amino acids	Stimulates secretion of thyroid-stimulating hormone (TSH)
Growth hormone-releasing hormone (GHRH)	44 amino acids	Stimulates growth hormone secretion

Feedback Control of Anterior Pituitary

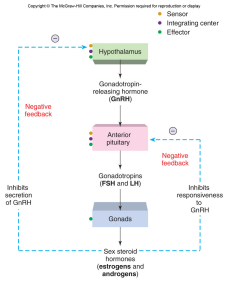
- The final product regulates secretion of pituitary hormones.
  - Inhibition can occur at the pituitary gland level, inhibiting response to hypothalamic hormones.

Feedback Control of Anterior Pituitary



Feedback Control of Anterior Pituitary

– Inhibition can occur at the hypothalamus level, inhibiting secretion of releasing hormones.



Higher Brain Functions

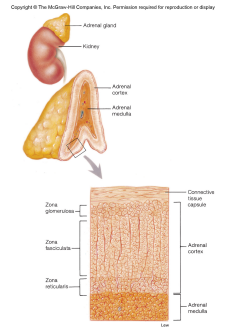
- Since the hypothalamus receives input from higher brain regions, emotions can alter hormone secretion.
  - At least six brain regions and olfactory neurons send axons to the GHRH-producing neurons.
  - Stressors increase CRH production.

IV. Adrenal Glands

Adrenal Glands

- Found atop the kidneys
- Consist of an outer adrenal cortex and an inner adrenal medulla that function as separate glands

Adrenal Glands



Adrenal Glands

- The adrenal medulla secretes epinephrine and norepinephrine in response to neural stimulation from the hypothalamus.
- The adrenal cortex secretes steroid hormones in response to ACTH

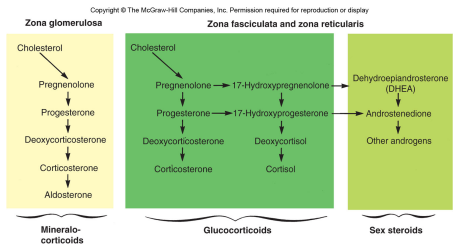
Corticosteroids

- Made from cholesterol
- Three categories:
  - Mineralocorticoids regulate Na^+ and K^+ balance.
    - Example: aldosterone
  - Glucocorticoids regulate glucose metabolism.
    - Example: cortisol
  - Sex steroids are weak androgens that supplement those made in the gonads.

Regions of the Adrenal Cortex

- Zona glomerulosa
- Zona fasciculata
- Zona reticularis

Regions of the Adrenal Cortex



Adrenal Medulla Hormones

- Epinephrine and norepinephrine
  - Activated with sympathetic response
  - Have effects similar to sympathetic innervation but lasting 10 times longer
  - Increase cardiac output, respiratory rate, and mental alertness; dilate coronary blood vessels; elevate metabolic rates

Stress and the Adrenal Gland

- Stress increases secretion of ACTH, which results in increased glucocorticoid release.
- This is called the *general adaptation syndrome.*
  - Good for proper recovery after stress, such as an illness or trauma.
  - Cortisol helps inhibit the immune system so it does not overrespond.

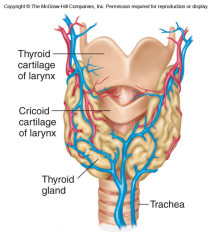
Stress and the Adrenal Gland

  - Chronic stress leads to an increased risk of illness.
  - Cortisol may act on higher brain regions, contributing to depression and anxiety.
  - By stimulating the liver to release glucose, insulin receptors may become resistant, making it harder to treat people with diabetes.

V. Thyroid and Parathyroid Glands

Thyroid Gland

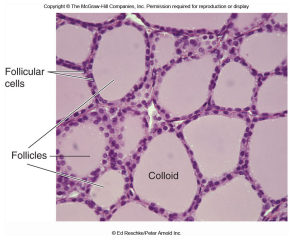
- Located just below the larynx



Thyroid Gland

- Consists of hollow spaces called thyroid follicles lined with simple cuboidal epithelium composed of follicular cells
  - Interior of the follicles is filled with a fluid called colloid.
  - Outside of the follicles are parafollicular cells.

Thyroid Gland



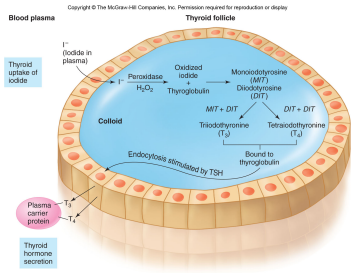
Production of Thyroid Hormone

- Thyroglobulin is made by the follicular cells.
- Thyroid follicles actively accumulate iodine and secrete it into the colloid.
- The iodine is attached to tyrosines within the thyroglobulin molecule.
  - One iodine produces monoiodotyrosine (MIT).
  - Two iodines produce diiodotyrosine (DIT).

Production of Thyroid Hormone

- Enzymes within the colloid attach MIT and DIT together:
  - DIT + DIT = T_4
  - DIT + MIT = T_3
- These are still bound to thyroglobulin.
  - They dissociate from thyroglobulin when the thyroid gland is stimulated by TSH.

Production of Thyroid Hormone



Action of Thyroid Hormone

- Stimulates protein synthesis
- Promotes maturation of the nervous system
- Increases rates of cellular respiration
  - Elevates basal metabolic rate

Calcitonin

- Made by the parafollicular cells
- Inhibits dissolution of calcium from bone and stimulates excretion of calcium in the kidneys to lower blood calcium levels

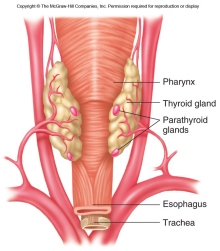
Diseases of the Thyroid

- Iodine deficiency leads to overstimulation of the thyroid gland (no negative feedback on pituitary gland) and growth of a goiter.
- It also leads to hypothyroidism: low metabolic rates, weight gain and lethargy, poor adaptation to cold stress, and myxedema (accumulation of fluids in subcutaneous connective tissues).

Diseases of the Thyroid

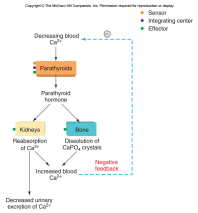
Parathyroid Glands

- Embedded in the back of the thyroid gland



Parathyroid Glands

- Secrete parathyroid hormone
  - Hormone promotes a rise in blood calcium by acting on bones, kidneys, and intestine

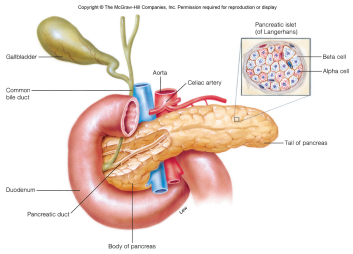


VI. Pancreas and Other Endocrine Glands

Pancreas

- The pancreas is both an endocrine and an exocrine gland.
- Endocrine cells are located in islets of Langerhans.
  - Alpha cells: glucagon
  - Beta cells: insulin

Pancreas



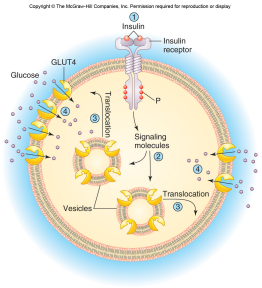
Insulin

- Insulin is secreted by beta cells when blood glucose levels rise after a sugary meal.
- Its purpose is to lower blood glucose levels to the “normal” range.

Action of Insulin

- Insulin binds to receptors on target cells.
  - Vesicles with GLUT4 carrier proteins bind to membrane.
  - Glucose diffuses through GLUT4 channels.
  - Occurs in adipose tissue, skeletal muscle, and the liver.

Action of Insulin



Insulin

- Indirectly stimulates the enzyme glycogen synthase in liver and skeletal muscles to promote sugar storage
- Stimulates adipose tissue to store fat

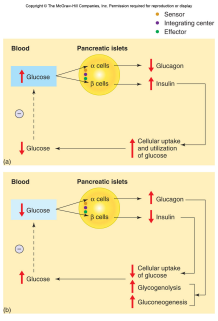
Glucagon

- Antagonistic to insulin
- Secreted by alpha cells when blood glucose levels are low
- Purpose is to raise blood glucose levels to a “normal” range

Action of Glucagon

- Stimulates liver to hydrolyze glucagon into glucose and release it into the blood
- Stimulates gluconeogenesis, conversion of noncarbohydrates into glucose
- Stimulates lipolysis in adipose tissue so fat is released and used as a fuel source instead of glucose

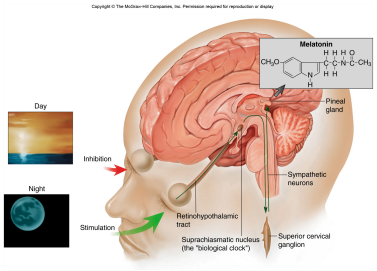
Glucose Homeostasis



Pineal Gland

- Located on roof of third ventricle in the brain
- Secretes the hormone melatonin
- Regulated by the suprachiasmatic nucleus of the hypothalamus
  - Stimulates melatonin production when it gets dark

Pineal Gland



Other Endocrine Glands

- Intestinal tract: Several hormones are made in the organs of the intestinal tract to regulate digestive processes.
- Gonads: Produce testosterone, estrogen, and progesterone
- Placenta

VII. Autocrine and Paracrine Regulation

Autocrine vs. Paracrine Signals

- Both are involved in short-range signaling between neighboring cells within an organ.
  - Autocrine signals: The sender and receiver are the same cell type.
  - Paracrine signals: The sender and receiver are different cell types/tissues.

Autocrine Regulation

- Many regulatory molecules are called cytokines or growth factors.
  - Given specific names depending on where they are found and what they do—for example, lymphokines, neurotrophins
- Most control gene expression in the target cell.

Autocrine and Paracrine Regulators

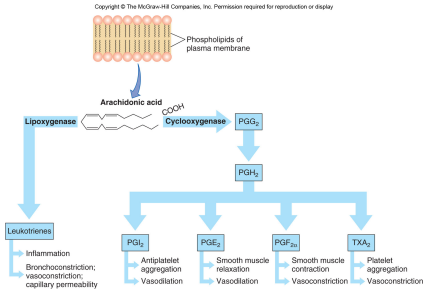
Table 11.9 | Examples of Autocrine and Paracrine Regulators

Autocrine or Paracrine Regulator	Major Sites of Production	Major Actions
Insulin-like growth factors (somatomedins)	Many organs, particularly the liver and cartilages	Growth and cell division
Nitric oxide	Endothelium of blood vessels; neurons; macrophages	Dilation of blood vessels; neural messenger; antibacterial agent
Endothelins	Endothelium of blood vessels; other organs	Constriction of blood vessels; other effects
Platelet-derived growth factor	Platelets; macrophages; vascular smooth muscle cells	Cell division within blood vessels
Epidermal growth factors	Epidermal tissues	Cell division in wound healing
Neurotrophins	Schwann cells; neurons	Regeneration of peripheral nerves
Bradykinin	Endothelium of blood vessels	Dilation of blood vessels
Interleukins (cytokines)	Macrophages; lymphocytes	Regulation of immune system
Prostaglandins	Many tissues	Wide variety (see text)
TNF_{α} (tumor necrosis factor alpha)	Macrophages; adipocytes	Wide variety

Prostaglandins

- Made from arachidonic acid released from phospholipids in the plasma membrane
  - Alternatively, the cell may make leukotrienes.
- Released from almost every cell, with a wide range of function

Formation and Action of Prostaglandins



Functions of Prostaglandins

- Immune system: promote inflammation
- Reproductive system: aid ovulation
- Digestive system: inhibit secretion; stimulate propulsion and absorption
- Respiratory system: aid bronchoconstriction and dilation

Functions of Prostaglandins

- Circulation: affect vasoconstriction and dilation, blood clotting
- Urinary system: increase blood flow to the kidneys, which increases excretion of urine

Prostaglandin Inhibition

- Nonsteroidal anti-inflammatory drugs (NSAIDs):
  - NSAIDs inhibit prostaglandin synthesis by inhibiting the enzyme cyclooxygenase.
  - Side effects include gastric bleeding, kidney problems, and less clotting
  - Aspirin is the most common.

Prostaglandin Inhibition

- COX2 Inhibitors: Celebrex and Vioxx
  - Cyclooxygenase comes in two forms:
    - COX1 is found in the stomach and kidneys.
    - COX2 is involved in inflammation.
  - Newer drugs that inhibit COX2 selectively avoid gastric- and kidney-related side effects.
  - Unfortunately, these drugs increase the chance of stroke and heart attack, so they have been pulled from the market.