Welcome to BIO 202
Human Anatomy and Physiology
with Dr. Fernandez

Please check to make sure you are in the correct course sections:

• Lecture (14950)    MW  9:30-10:45am   LS 104
• Lab (14885)        MW  8:00-9:20am   LS 310
OR
• Lab (14859)        MW  11:00-12:20pm LS 310
Endocrine System

Chapter 17

• Mechanisms of Cell Communication
• Endocrine vs Exocrine
• Neuro-endocrine Relationship
• Major Organs of the Endocrine System
• Hormones and their Actions
• Eicosanoids and Paracrine Signaling
• Endocrine Disorders
Overview of Cell Communication

• Communication among cells is necessary for coordinating important cell activities like growth maintenance and reproduction.

• Mechanisms of cell communication include:
  – gap junctions
    • pores in cell membranes that signaling chemicals can move through from cell to cell
  – neurotransmitters
    • released from neuron travels across a small gap to a 2nd cell
  – hormones
    • Classical definition of a hormone is a chemical messenger that travels in the bloodstream
  – paracrine hormones
    • chemical messengers secreted into tissue fluids that effect nearby cells
Endocrine System

• Major endocrine organs include the:
  – pineal gland
  – pituitary gland
  – thyroid gland
  – parathyroid glands
  – thymus
  – adrenal glands
  – pancreas

• Endocrine System is composed of all of the major endocrine glands and hormone-secreting cells of other organs including the brain, heart, kidneys, organs of the digestive system, and reproductive organs.
Major Organs of the 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)
Differences between Exocrine Glands and Endocrine Glands

• Exocrine Glands
  – Exocrine glands have ducts that carry a secretion to a body surface or an organ cavity.
  – Exocrine glands produce extracellular effects.
  – Example: sweat glands release sweat onto the skin.

• Endocrine Glands
  – Endocrine glands do not have ducts.
  – Endocrine glands release hormones into intercellular space and can be absorbed into the blood.
  – Endocrine glands produce intracellular effects in target cells that will change the target cell’s metabolism.
  – Example: insulin is a hormone that causes cells to absorb glucose that is used as fuel for cell metabolism.
Exocrine Gland:
- Chemical Secretions
- Skin Surface
- Chemicals produced by the gland

Endocrine Gland:
- Blood in Capillaries
- Hormones are secreted into blood
Components of the Endocrine System

- Endocrine Glands secrete hormones into the interstitial space between cells.
- Hormones can be carried in the bloodstream as "chemical messengers" that produce a response in target cells of another tissue or organ.
- Target Cells respond to hormones by having a complementary receptor that matches a particular hormone.
- A hormone may stimulate or inhibit a target cell.
Similarities between the Nervous System and Endocrine System

• Several chemicals function as both hormones and neurotransmitters:
  – examples: norepinephrine, antidiuretic hormone (vasopressin)

• Both systems can have overlapping effects on the same target cells:
  – norepinephrine (from nervous system) and glucagon (from endocrine system) both cause glycogen hydrolysis in liver that elevates blood sugar levels.

• Systems regulate each other:
  – neurons can trigger hormone secretion
  – hormones can stimulate or inhibit neurons

• The term Neuroendocrine is used to describe overlapping functions of nervous and endocrine tissues.
Communication is similar in the Nervous System and the Endocrine System.
Differences between the Nervous System and Endocrine System

• 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 more slowly (hormone release in seconds or days) and effect may continue for weeks

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

• Area of effect:
  – nervous system effects are very specific (one cell or organ)
  – endocrine system usually has more general, widespread effects on many organs
Major Organs of the 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)
Hypothalamus
Hypothalamus

- Hypothalamus is a funnel-shaped structure composed of clusters of neurons in the floor and walls of third ventricle
  - these clusters of neurons in the brain are called “nuclei”
- The hypothalamus regulates many functions carried out by the pituitary gland including regulating:
  - body temperature, reproductive functions, growth of tissues, maintenance of tissues, stress management and other functions
- The hypothalamus regulates the pituitary gland through releasing hormones and release-inhibiting hormones (see next slide)
### Hypothalamus / Pituitary Axis

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<td>TRH: Thyrotropin-releasing H.</td>
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<td>CRH: Corticotropin-releasing H.</td>
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<td>GnRH: Gonadotropin-releasing H.</td>
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<td>Somatostatin</td>
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<td>PIH: Prolactin-inhibiting H. (dopamine)</td>
<td>inhibits PRL secretion</td>
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Pituitary Gland (Hypophysis)

- The Pituitary is connected to the hypothalamus by a stalk called the infundibulum.
- The Pituitary is located in the sella turcica of the sphenoid bone of the skull.
- The Pituitary Gland is about 1.3 cm (about ½ inch) diameter
- 3 lobes of the Pituitary Gland:
  - Anterior Lobe (pars distalis, adenohypophysis) develops from oral ectoderm of the roof of the embryonic mouth (pharynx) forming Rathke’s (hypophyseal) pouch.
  - Posterior Lobe (pars nervosa, neurohypophysis) develops from a neurohypophyseal bud of neural ectoderm from the floor of the diencephalon.
  - Intermediate Lobe (pars intermedia) tissue is induced from oral ectoderm that contacts neural ectoderm.
Representation of the actual size of embryos from zygote to the eighth week of development.

http://missinglink.ucsf.edu/Lm/IDS_101_embryology_basics/CoreText.htm
Embryonic Development of Pituitary

(a) Embryo at 4 weeks

(b) Sagittal section of 4-week embryo

Telencephalon
Diencephalon
Neurohypophyseal bud
Hypophyseal pouch
Primitive oral cavity

(c) 8 weeks

(d) Fetus

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

Nuclei of hypothalamus

- Paraventricular nucleus
- Supraoptic nucleus

Optic chiasm

- Pars tuberalis
- Anterior lobe
- Adenohypophysis

Median eminence

- Hypothalamo-hypophyseal tract

Stalk

Posterior lobe

Floor of hypothalamus

Third ventricle of brain

Adenohypophysis

Oxytocin

Antidiuretic hormone

← anterior           posterior →
Pituitary Hormones of the Posterior Lobe

- Posterior Lobe produces, stores and releases two hormones:
  - Oxytocin (OT)
  - Vasopressin (Antidiuretic Hormone – ADH)

- OT and Vasopressin are produced by neurons in the hypothalamus and are transported down axons to the posterior lobe
- OT is produced by the paraventricular nucleus
- Vasopressin is produced by the supraoptic nucleus
- Note similarity in molecular structure of the two hormones
Posterior Lobe Hormone Actions:

- **Vasopressin (ADH)**
  - targets kidneys to ↑ water retention, reduce urine production
  - called vasopressin because it can cause vasoconstriction
  - also functions as a neurotransmitter in the brain

- **Oxytocin**
  - stimulates labor contractions during childbirth
  - stimulates flow of milk during lactation
  - promotes emotional bonding between lactating mother and infant
  - promotes feelings of sexual satisfaction and emotional bonding between partners
  - surge of oxytocin is released during sexual arousal and orgasm causing smooth muscle contractions in uterus and propulsion of semen
Pituitary Intermediate Lobe

- Melaonotroph cells of the intermediate lobe produce Melanocyte-Stimulating Hormone (MSH)
  - Intermediate Lobe is present in human fetuses but quickly degenerates into non-functional cysts in adults.
  - Human brain neurons produce a large prohormone, POMC (pro-opiomelanocortin), which is cleaved into several smaller products including MSH, ACTH, endorphins, b-lipotrophic hormone and other neurohormones. MSH functions as a neurotransmitter in the human brain.
  - In other animals, MSH stimulates pigment cells to produce more melanin pigment which can darken skin, hair or feathers.
6 Hormones of the Anterior Lobe

1. FSH (follicle stimulating hormone)
2. LH (luteinizing hormone)
3. TSH (thyroid stimulating hormone)
4. ACTH (adrenocorticotropic hormone)
5. PRL (prolactin)
6. GH (growth hormone)
6 Anterior Pituitary Hormones and their Target Organs

- Axis refers to the regulatory interactions between the hypothalamus, pituitary and other endocrine glands.
Gonadotropin-releasing hormone controls FSH + LH release
Thyrotropin-releasing hormone
Corticotropin-releasing hormone
Prolactin-releasing hormone
Prolactin-inhibiting hormone
GH-releasing hormone
Somatostatin

Releasing and inhibiting hormones secreted by the hypothalamus are absorbed by hypothalamic capillaries that drain into portal venules that connect to capillaries in the anterior pituitary.
Actions of Anterior Lobe Hormones

• **FSH** (secreted by gonadotrope cells)
  – female: stimulates development of follicles in ovaries
  – male: stimulates production of sperm in testes

• **LH** (secreted by gonadotrope cells)
  – female: stimulates ovulation and maintains the corpus luteum to secrete progesterone and estrogen
  – male: stimulates interstitial cells of testes to secrete testosterone

• **TSH** (secreted by thyrotrope cells)
  – stimulates growth of thyroid gland and the secretion of thyroid hormone
Actions of Anterior Lobe Hormones continued:

- **ACTH** (secreted by corticotropes)
  - regulates response to chronic stress, stimulates adrenal cortex to secrete corticosteroids that regulate glucose, fat and protein metabolism

- **PRL** (secreted by lactotropes)
  - female: milk production by mammary glands
  - male: enhances secretion of testosterone by testes

- **GH** (secreted by somatotropes)
  - see next 2 slides for functions of GH
Growth Hormone

- GH is also called somatotropin
- GH is secreted by somatotropes of the anterior pituitary
- GH promotes tissue growth through multiple mechanisms:
  - directly affects mitosis and cellular differentiation
  - stimulates liver to produce Insulin-like Growth Factors (IGF) that are also called somatomedins.
  - IGFs last 60x longer than GH (20 hours vs 20 minutes)
- Functions of GH and IGF:
  - \( \uparrow \) protein synthesis and \( \downarrow \) protein catabolism
  - \( \uparrow \) lipid metabolism which spares proteins and carbohydrates
  - Electrolyte balance: promotes Na\(^+\), K\(^+\), Cl\(^-\) retention and Ca\(^{+2}\) absorption
Growth Hormone and Aging

• During childhood and adolescence GH causes bone, cartilage and muscle growth

• GH in adults:
  – increases osteoblastic activity and appositional growth resulting in bone thickening and remodeling

• GH in old age:
  – blood concentration of GH normally decreases by age 75 to ¼ of that of adolescents
  – low GH in old age results in decrease protein synthesis that can cause wrinkling of skin and less muscle strength and muscle mass

• Levels of GH
  – are higher after high protein meals, after vigorous exercise, and during the first 2 hours of deep sleep
  – GH also increases after trauma
Growth Hormone Disorders

Hypersecretion of growth hormone during childhood can lead to gigantism.

Robert Pershing Wadlow (in 1938, at age 20 with actresses Maureen O’Sullivan, left, and Ann Morris) had grown to a record height of 8’11” by the time of his death at age 22.

Smithsonian August 2005 p. 76.
Robert Pershing Wadlow with his mother at his side in 1939.
In 2008, Leonid Stadnik was named the world's tallest man. Standing at 8 feet, 5 inches. Here he walks near his home in the tiny village of Podolyantsi in central Ukraine.
Growth Hormone Disorders continued

- Hypersecretion of growth hormone in old age leads to **acromegaly**.
  - Symptoms of acromegaly include thickening of hand, foot, jaw and brow bones and growth of soft tissues particularly in the nose and ears.
There are over 200 different types of dwarfism, all of which involve bone growth disorders (osteodysplasia) that result in short stature (adult height less than 4 ft. 10 in. tall).

Primordial Dwarfism is a group of disorders in which growth is proportional but severely delayed, beginning in the womb. This results in some of the smallest people in the world.

The individual pictured has Majewski osteodysplastic primordial dwarfism (MOPD) Type II. Only about 100 individuals worldwide have been identified as having MOPD type II. Both males and females of all ethnic backgrounds are affected. Some families have more than one child with MOPD Type II, which suggests that the disorder is inherited in an autosomal recessive manner.

Pineal Gland (Epiphysis)

- Shaped like a PINE CONE
- The pineal gland secretes **melatonin** in darkness.
- The pineal is inhibited by light.
- Pinealocytes convert tryptophan into serotonin during the day (in bright light), then converts serotonin into melatonin at night (in darkness).
- Peak melatonin secretion in humans occurs at 1-5 years old.
- Melatonin inhibits puberty in humans. Levels drop 75% at puberty.
- Melatonin levels are correlated with human activity cycles (biorhythms).
- High melatonin levels are correlated with SAD and PMS with symptoms including:
  - depression
  - sleepiness, irritability
  - carbohydrate craving
- Melatonin levels may be manipulated by phototherapy and can reduce the affects of jet lag.
- In other animals, high levels of melatonin inhibit reproduction and inhibit melanogenesis which affects seasonal reproductive timing, and fur or feather color.
Pineal Gland (Epiphysis)
Pineal Gland
Histology
Melatonin Secretion

- Pineal gland
- Sympathetic neurons
- Retinohypothalamic tract
- Suprachiasmatic nucleus (the "biological clock")
- Superior cervical ganglion

**Inhibition**
- During the day, light inhibits melatonin secretion.

**Stimulation**
- During the night, darkness stimulates melatonin secretion.

[Chemical structure of melatonin]
Winter: Long nights, pinealocytes uninhibited, high levels of melatonin inhibit pigment cells and gonads.
Summer: Long days, pinealocytes inhibited, low levels of melatonin, uninhibited pigment cells and gonads.
Thymus

- Location: mediastinum, superior to heart
- Involution after puberty (converts to fibrous connective tissue and adipose)
- Secretes the hormones **Thymosin** and **Thymopoietin** that regulate development of T-lymphocytes (type of white blood cell)
Thymus Gland

adult thymus

infant thymus
Athymic Nude Mice play an important role in immunology research and cancer research.

These mouse colonies must be maintained in absolutely sterile conditions.
Severe Combined Immunodeficiency Disease

- Hereditary lack of T and B lymphocytes
- Extreme vulnerability to opportunistic infection
Thyroid Gland Anatomy

- Thyroid gland is located on the anterior and lateral sides of trachea.
- 2 large lobes of thyroid tissue are connected by an isthmus of thyroid tissue.
- Thyroid gland is highly vascular and receives a large volume of blood flow.
Thyroid Gland Histology

- Follicular cells
- Colloid of thyroglobulin
- C (calcitonin) cells
- Follicle
Cells of the Thyroid Gland

- **Thyroid Follicles**
  - Spheres of simple cuboidal cells (follicular cells) filled with a colloid of 2 thyroid hormones, $T_3$ and $T_4$ bound to thyroglobulin
  - $T_3 = \text{triiodothyronine}$  $T_4 = \text{tetraiodothyronine}$
  - $T_3$ contains 3 iodine atoms, $T_4$ contains 4 iodine atoms
  - Follicles produce 90% $T_4$ and 10% $T_3$
  - $T_3$ is more potent than $T_4$
  - In circulation and in cells, $T_4$ is broken down into $T_3$
  - Thyroid hormone functions:
    - ↑ metabolic rate, $O_2$ consumption and heat production
    - ↑ heart rate and respiratory rate
    - stimulates appetite and breakdown of carbohydrates, lipids and proteins

- **C-cells** (calcitonin cells or parafollicular cells)
  - cells are located in between the follicles.
  - cells produce the hormone calcitonin that ↓ blood $Ca^{+2}$ and promotes $Ca^{+2}$ deposition in bone, especially in children.
Thyroid Hormone Synthesis

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 $T_3$ and $T_4$ into the blood

The figure illustrates the process of thyroglobulin synthesis and secretion in thyroid follicles, involving iodide absorption, thyroglobulin synthesis, iodine incorporation, hydrolysis, and finally release of $T_3$ and $T_4$ into the blood.
Thyroid Hormone Synthesis

(3) Iodine added to a tyrosine forms monoiodothyronine (MIT). (4) Iodine added to MIT forms diiodothyronine (DIT). (5) DIT + MIT = T₃.
(6) Lysosome enzymes cleave T₃ from the thyroglobulin. Arrows indicate where adding another iodine would form T₄.
Thyroid Hormone Effects

• T₃ and T₄ dissociate from thyroxine-binding globulin (TBG), leave bloodstream and enter target cell. T₄ is converted into T₃.

• T₃ can
  – bind to receptors on mitochondria that ↑ rate of aerobic respiration
  – activate ribosomes that ↑ protein synthesis
  – enter the nucleus and activate genes and ↑ protein synthesis

• Example: one protein that can be produced is Na⁺-K⁺ ATPase and the activity of this protein generates heat
Thyroid Hormone Transport and Effects

TBG \rightarrow T_{3} \rightarrow T_{4} \rightarrow Tissue fluid

Various metabolic effects

Protein synthesis

mRNA \rightarrow DNA

T_{3} \rightarrow Target cell

Blood
High thyroid hormone levels inhibit release of tropic hormones (TRH, TSH).
Thyroid Gland Disorders

• Congenital hypothyroidism (↓ TH)
  – infant suffers abnormal bone development, thickened facial features, low body temperature, lethargy, brain damage. Can be treated with synthroid.

• Myxedema (adult hypothyroidism, ↓ TH)
  – low metabolic rate, sluggishness, sleepiness, weight gain, puffy face, constipation, dry skin and hair, cold sensitivity, ↑ blood pressure and tissue swelling

• Graves Disease (a type of hyperthyroidism)
  – antibodies mimic TSH, ↑ TH secretion, exophthalmos

• Endemic Goiter (goiter = enlarged thyroid gland)
  – dietary iodine deficiency, low TH, low - feedback, ↑ TSH
Congenital Hypothyroidism

Congenital hypothyroidism results from chronically low levels of TH. Infants suffer abnormal bone development, thickened facial features, low body temperature, lethargy, brain damage. Can be treated with synthroid.
Myxedema (adult hypothyroidism) chronically low TH results in low metabolic rate, sluggishness, sleepiness, weight gain, puffy face, constipation, dry skin and hair, cold sensitivity, increased blood pressure and tissue swelling.
Exophthalmos – a symptom of Graves’ Disease

Graves Disease (a type of hyperthyroidism) results from production of antibodies that mimic TSH resulting in increased TH secretion.
Endemic Goiter (goiter = enlarged thyroid gland) due to dietary iodine deficiency results in low TH synthesis and reduced feedback resulting in increased TSH and thyroid growth.
Parathyroid Glands

- Multiple lobes of tissue on the posterior surface of the thyroid gland. There may also be other ectopic sites.
- Produces Parathyroid Hormone (PTH or parathormone)
  - PTH increases blood Ca^{+2} levels and synthesis of calcitriol (Vitamin D) resulting in:
    - ↑ absorption of Ca^{+2}
    - ↓ urinary Ca^{+2} excretion
    - ↑ urinary PO^{-4} excretion
    - ↑ bone erosion
Parathyroid Disorders

• Hypoparathyroid
  – usually results from surgical excision during thyroid surgery
  – can result in fatal tetany in 3-4 days from low Ca$^{+2}$

• Hyperparathyroid
  – Excess PTH secretion can result from a tumor
  – causes soft, fragile and deformed bones, extremely high blood Ca$^{+2}$, and renal calculi (kidney stones).
Adrenal (Suprarenal) Glands
Adrenal Gland

Adrenal Gland *in situ* on kidney

Cross Section
Adrenal Medulla

- Postganglionic sympathetic neurons innervated by sympathetic preganglionic fibers.
  - consists of modified neurons called chromaffin cells
  - stimulation causes release of adrenaline into bloodstream
- Responds to ACUTE stress (fight or flight)
- Hormonal effect is relatively long lasting (minutes) compared to nervous system (fractions of a second).
  - increases BP and heart rate
  - increases blood flow to skeletal muscle
  - increases pulmonary air flow
  - stimulates gluconeogenesis and glycogenolysis
  - decreases digestion and urine formation
Adrenal Cortex

- Response to CHRONIC stress (long duration – weeks or more)
- Three Layers - (outer) zona glomerulosa, (middle) zona fasciculata, (inner) zona reticularis
- All three layers produce Corticosteroids from cholesterol
  - Zona Glomerulosa produces the mineralocorticoid aldosterone
    - controls electrolyte balance by conserving Na⁺
  - Zona Fasciculata produces the glucocorticoids cortisol, corticosterone and cortisone
    - cortisol stimulates fat and protein catabolism, gluconeogenesis (from amino acids and fatty acids) and release of fatty acids and glucose into blood
    - anti-inflammatory effect suppresses the immune system
  - Zona Reticularis produces the sex steroids testosterone and estrogen
    - important source of estrogen in women after after menopause
All steroid hormones are synthesized from cholesterol – the various hormones differ in functional groups attached to a 4-ringed steroid backbone.
Adrenal Cortex Disorders

- **Cushing’s Syndrome** is excessive secretion of cortisol
  - can be caused by pituitary hypersecretion of ACTH, ACTH-secreting tumor, over activity of adrenal cortex
  - causes hyperglycemia, hypertension, weakness, edema
  - muscle and bone loss occurs with protein catabolism
  - buffalo hump and moon face caused by abnormal fat deposition between shoulders and in face

- **Adrenogenital Syndrome (AGS)**
  - adrenal androgen hypersecretion causes enlargement of external sexual organs in children and early onset of puberty
  - can cause masculinizing effects on females (deeper voice, beard growth, male-like genitalia)
Pancreas location is retroperitoneal and inferior and dorsal to stomach.
Products of the Pancreas

- 98% of pancreas is EXOCRINE – produces digestive enzymes and bicarbonate from acinar tissue.
- 2% of pancreas is ENDOCRINE – produces at least 5 hormones – best understood are insulin, glucagon and somatostatin.
- Endocrine tissue is in 1-2 million pancreatic islets of Langerhans.
Pancreatic Hormones

• Insulin (from $\beta$ cells)
  – insulin is secreted when blood sugar levels are high as in after a meal
  – insulin receptors are on most cells of the body
  – insulin stimulates cells to take up glucose and amino acids
  – insulin antagonizes glucagon

• Glucagon (from $\alpha$ cells)
  – glucagon is secreted when blood glucose levels are low as it is between meals
  – glucagon stimulates glycogenolysis (breakdown of glycogen), fat catabolism (release of free fatty acids) and promotes absorption of amino acids for gluconeogenesis (production of glucose from amino acids)

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

• Hyperglycemic hormones raise blood glucose: glucagon, epinephrine, norepinephrine, cortisol and corticosterone

• Hypoglycemic hormone, insulin, lowers blood glucose
Diabetes Mellitus

- Diabetes Mellitus is a disease resulting from the hyposecretion or inaction of insulin.

- Extremely high blood glucose levels can exceed the kidney tubule transport maximum of glucose reabsorption and cause osmotic diuresis: glucose remains in urine, osmolarity increases and draws water into urine.
Diabetes Mellitus

Signs and symptoms of Diabetes Mellitus
- polyuria, polydipsia, polyphagia
- hyperglycemia, glycosuria, ketonuria
- blood glucose levels up to 100 mg/dL are considered normal. (mg/dL = milligrams per deciliter)
- Diabetes is typically diagnosed when fasting blood glucose levels are 126 mg/dL or higher.
- Glucose is a major source of energy for most cells of the body. Some cells (for example, brain and red blood cells), are almost totally dependent on blood glucose as a source of energy. The brain requires that glucose concentrations in the blood remain within a certain range in order to function normally. Concentrations of less than 30 mg/dL or greater than 300 mg/dL can produce confusion or unconsciousness.
- Ketones are a metabolic breakdown product of fatty acid metabolism. Some cells will use fatty acids for fuel if glucose is not available and produce ketones as waste.
Types of Diabetes Mellitus

• Type I (insulin dependent diabetes mellitus = IDDM)
  – 10% of diabetes mellitus cases
  – Caused by autoimmune destruction of $\beta$ cells
  – Usually diagnosed at about age 12
  – Treated with diet, exercise, monitoring of blood glucose and periodic injections of insulin (new delivery methods include pumps and inhalers).

• Type II (non-insulin dependent diabetes mellitus = NIDDM)
  – 90% of diabetes mellitus cases
  – Patients develop insulin resistance which is a failure of target cells to respond to insulin due to receptor downregulation (see next slide).
  – 3 major risk factors are heredity, age (40+) and obesity
  – Treated with programs for weight loss through diet and exercise.
  – Some patients are helped by oral medications (like glucophaghe) that decrease intestinal absorption of glucose, decrease hepatic glucose production and improve target cell sensitivity to insulin.
Receptor Regulation on Target Cells

- **Down-regulation**: Long-term exposure to high levels of a hormone can result in target cells reducing the number of receptors to the hormone as in Type II Diabetes.

- **Up-regulation**: results from chronically low levels of hormone.
Pathology of Diabetes

• Acute pathology: cells cannot absorb glucose, so instead they rely on fat and proteins resulting in weight loss and weakness.
  – fat catabolism $\uparrow$ FFA’s and ketones in blood
  – ketonuria promotes osmotic diuresis, loss of $\text{Na}^+$, $\text{K}^+$
  – ketoacidosis occurs as ketones $\downarrow$ blood pH

• Chronic pathology:
  – chronic hyperglycemia leads to neuropathy and cardiovascular damage:
    • retina and kidney damage (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 causes disorientation, convulsions or unconsciousness because the brain requires a constant supply of glucose.
Gonadal Hormones: the Ovary

Follicle = egg surrounded by granulosa cells
(source of estrogen)
(source of estrogen and progesterone)

Egg (ovum)
Granulosa cells
Ovulation
Corpus luteum
Ovary

- Granulosa cells in wall of ovarian follicle
  - stimulated by follicle-stimulating hormone (FSH)
  - produce **estrogen** during the menstrual cycle
- Corpus Luteum: follicle after ovulation
  - stimulated by luteinizing hormone (LH)
  - produces **estrogen** and **progesterone** for 12 days if no fertilization or 8-12 weeks with pregnancy
- Functions of estrogen and progesterone
  - development of female reproductive system and physique including bone growth
  - regulates menstrual cycle, sustains pregnancy
  - prepares mammary glands for lactation
Gonadal Hormones: the Testis
Testes

• Interstitial Cells (Leydig cells)
  – between seminiferous tubules
  – Stimulated by LH and FSH
  – produce **testosterone** (and small amounts of estrogen)
  – testosterone causes development of male reproductive system and physique
  – sustains sperm production and sex drive

• Sustentacular Cells (Sertoli cells)
  – secrete **inhibin** which regulates sperm production rate.
Chemical Classification of Hormones

• **Steroid Hormones** are all derived from cholesterol
  – aldosterone, cortisol, cortisone, corticosterone, progesterone, testosterone, estrogen, calcitrol

• **Oligopeptides** are chains of 3-10 amino acids
  – angiotensin II, vasopressin (ADH), GnRH, Oxytocin, TRH

• **Polypeptides** are chains of 14-199 amino acids
  – ACTH, atrial naturitic peptide, calcitonin, CRH, glucagon, growth hormone, GHRH, insulin, PTH, PRL, somatostatin

• **Glycoproteins** are two amino acid chains with a carbohydrate
  – FSH, LH, TSH, HCG, inhibin

• **Monoamines or Biogenic Amines** are all made from the amino acid tyrosine except melatonin which is made from tryptophan
  – dopamine, epinephrine, norepinephrine, serotonin, melatonin, T₃, T₄
Transport and Action of Hormones

- Hydrophobic hormones (steroids and thyroid hormone) are carried in the blood on carrier proteins to increase their solubility. Free hormone can penetrate plasma membrane and enter the nucleus.

- Hydrophilic hormones (monoamines and peptides, glycoproteins) are soluble in plasma, but cannot pass through membranes so they must bind to cell-surface receptors.
Steroid Hormones are derived from cholesterol and diffuse easily through the plasma membranes of cells.

Once in the cell, the hormone binds to a receptor forming a hormone-receptor complex.

The complex can bind to DNA in the nucleus and either activate or inhibit the genes.

Activation of genes leads to protein synthesis.
Steroid hormones are not water-soluble. They travel in the blood attached to protein carriers.
Mechanism of Steroid Hormone Action Animation

http://highered.mcgraw-hill.com/sites/0072437316/student_view0/chapter47/animations.html#

Other Endocrine System Animations

http://nhscience.lonestar.edu/biol/ap1int.htm#endocrine
Hydrophilic Hormones using the cAMP Second Messenger

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.

Note: Caffeine inhibits breakdown of cAMP.

ACTH
FSH
LH
PTH
TSH
Glucagon
Calcitonin
Catecholamines
Hydrophilic hormones may also work through a phospholipase-mediated second messenger system.
When a signal molecule such as epinephrine binds to a cell surface receptor protein, it activates a G protein on the inside of the cell.
Eicosanoids

• Diacylglycerol $\rightarrow$ Arachidonic Acid $\rightarrow$ Eicosanoids
• Diacylglycerol is converted into Arachidonic Acid by a phospholipase enzyme and this process can be inhibited by steroidal anti-inflammatory agents like cortisol and corticosterone
• Arachidonic acid is converted into various eicosanoids by 2 enzymes:
  – lipoxygenase converts arachidonic acid into leukotrienes that mediate allergic and inflammatory reactions.
  – cyclooxygenase converts arachidonic acid into prostacyclins, thromboxanes and prostaglandins and can be inhibited by NSAIDs:
    • prostacyclins: produced by blood vessel walls, inhibits blood clotting and vasoconstriction
    • thromboxanes: produced by blood platelets after injury, they override prostacyclin and stimulate vasoconstriction and clotting
    • prostaglandins: diverse group including:
      – PGE’s: relaxes smooth muscle in bladder, intestines, bronchioles, uterus and stimulates contraction of blood vessels
      – PGF’s: opposite effects
Eicosanoid Synthesis

NSAIDs = non-steroidal anti-inflammatory drugs (aspirin, ibuprofen, naproxen, indomethacin) are also called COX inhibitors since they inhibit cyclooxygenase. SAIDs = steroidal anti-inflammatory drugs like cortisol, cortisone.
Eicosanoids and Headaches

- The vascular theory of headaches states that the constriction of peripheral arteries and the dilation of cerebral blood vessels lead to a headache. The vasoconstriction leads to a loss of cerebral oxygen in the blood, therefore, the compensatory mechanism is vasodilation. The dilation and constriction of vessels is sensed as pain.
Endocrine Functions of Other Organs

• Heart produces atrial natriuretic peptide which regulates blood pressure.

• Liver
  – Source of IGF that works with GH.
  – Secretes about 15% of erythropoietin.
  – Secretes angiotensinogen (a prohormone involved in blood pressure regulation).

• Kidneys produce 85% of erythropoietin which stimulates bone marrow to produce RBC’s.

• Stomach and Small Intestines produce 10 enteric hormones that coordinate digestive motility and secretion.

• Placenta secretes estrogen, progesterone and other hormones that regulate pregnancy, stimulate development of fetus and mammary glands.