hormone- mediator molecule that is released in one part of the body but regulates activity of cells in other parts of the body. Both neurotransmitters and hormones exert their effects by binding to receptors on or in their “target cells”. Can act as both neurotransmitter+hormone

nervous system acts on specific muscles and glands, but hormones can take several minutes or more to cause a response, and their influence is much broader

exocrine glands- secrete products into ducts that carry secretions into body cavities, into lumen of an organ, or to outer surface of body. (ie sudoriferous, sebaceous, mucous, and digestive glands)
endocrine glands secrete products/hormones into interstitial fluid surrounding the secretory cells. Depend on cardiovascular system to distribute their products, so they are often the most vascular tissues of the body.

Hormones influence their target cells by chemically binding to specific protein receptors. Receptors are constantly being synthesized and broken down. Usually btwn 2000-100,000 receptors for particular hormone. If hormone is present in excess, number of receptors may decrease in down regulation (makes less sensitive).
When hormone is deficient, number of receptors may increase (up regulation) making it more sensitive to a hormone.

If a hormone is prevented from interacting with its receptors, the hormone cannot perform its normal functions (drugs)

most endocrine hormones are circulating hormones- pass from secretory cells, then into interstitial fluid and then into blood. Others, called local hormones, act locally on neighboring cells or on their individual cell. (paracrines act on neighboring cells. Autocrines act on the same cell that secreted it).

Interleukin-2- released by helper T cells during immune responses, helps activate other nearby immune cells, a paracrine effect. Also stimulates the same cell to proliferate. Generates more helper T cells.

Nitric Oxide- NO- released by endothelial cells lining blood vessels. Causes relaxation of nearby smooth muscle fibers in blood vessels, causing vasodilation (increase blood vessel diameter)

local hormones usually are inactivated quickly. Circulating hormones may linger in blood, eventually being inactivated by liver and excreted by the kidneys.

Lipid Soluble Hormones-
steroid and thyroid hormones, and Nitric Oxide. Steroid hormones are derived from cholesterol. Thyroid hormones (T3 and T4)- attaching iodine to amino acid tyrosine

water soluble-
amine hormones- decarboxylating/modifying certain amino acids. Retain amino group
catecholamines (epinephrine, norepinephrine, dopamine)- synthesized by modifying tyrosine. Histamine synthesized from amino acid histidine by mast cells and platelets. Serotonin and melatonin derived from tryptophan
peptide hormones- antidiuretic hormone and oxytocin. Protein hormones- growth hormones and insulin. Thyroid stimulating hormone (glycoprotein hormones)
eicosanoid hormones derived from arachidonic acid. Prostaglandins and leukotrienes.
Most water soluble hormones circulate in free form. Most lipid soluble hormones are bound to transport proteins. 0.1%-10% lipid soluble hormones are not bound to transport proteins. These are free fractions.

Action of Lipid soluble hormone- diffuses thru blood, through lipid bilayer. If it's a target cell, binds to/activates receptors within cytosol or nucleus. Alters gene expression. New messenger RNA forms, leaves nucleus, enters
cytosol. Directs synthesis of new protein, often an enzyme, on ribosomes. Alter the cells activity, causing responses typical of that hormone.

Action of water soluble hormone- bind to receptors (integral transmembrane proteins) protruding from target cell surface. Acts as first messenger. Causes production of second messenger inside the cell, where specific hormone stimulated responses take place. (eg cyclic AMP cAMP)

Hormone interactions
permissive effect- actions of some hormones on target cells require a simultaneous or recent exposure to a second hormones
synergistic effect- effect of 2 hormones acting together is greater/more extensive than each acting alone
antagonistic effects- opposing the actions of one another

Hormone secretion is regulated by signals from nervous system, chemical changes in the blood, other hormones.

Hypothalamus and Pituitary Gland
hypothalamus is major link btwn nervous and endocrine systems. Its cells synthesize at least 9 different hormones, and pituitary gland secretes seven. Play roles in virtually all aspects of growth, development, metabolism, and homeostasis.

Pituitary- 1-1.5cm, lies in hypophyseal fossa of sella turcica of sphenoid bone. Attached to hypothalamus by infundibulum. Has anterior and posterior pituitary. Anterior pituitary (adenohypophysis) about 75% of total weight. In adults, two parts- pars distalis (larger) and pars tuberalis (forms a sheath around infundibulum)

posterior pituitary (neurohypophysis)- neural tissue. Two parts- pars nervosa (larger bulbar portion and infundibulum). Also pars intermedia atrophies during human fetal development.

Superior hypophyseal arteries branches of internal carotid arteries, bring hypothalamus blood. Primary plexus of hypophyseal portal system.

Anterior pituitary hormones that act on other endocrine glands are called tropic hormones/tropins

Anterior pituitary cells-
somatotrophs secrete HGH. Stimulates several tissues to secrete IGFs which stimate general body growth and regulate aspects of metabolism
thyrotrophs secrete thyroid stimulating hormones (thyrotropin). Controls secretions+other activities of thyroid gland
gonadotrophs FSH and Luteinizing hormones. Stimulate secretion of estrogens+ progesterone and the maturation of oocytes in ovaries, and stimulate sperm production and secretion of testosterone in the testes.
Lactotrophs- secrete prolactin, which initiates milk production in mammary glands.
Corticotrophs- secrete adrenocorticotropic hormone, stimulates adrenal cortex to secrete glucocorticiods like cortisol.


Somatotrophs are cotrolled mainly by 2 hypothalamic hormones- growth hrmone releasing hormone GHRH and
growth hormone inhibiting hormone GHIH. Major regulator of these is blood glucose level. Promote secretion of HGH- decreased fatty acids, increased amino acids in blood, deep sleep, increased activity in sympathetic division of autonomic nervous system (stress/vigorous exercise), glucagon, estrogens, cortisol, insulin.

Excess secretion of HGH may have diabetogenic effect due to beta cell burnout (greatly decreased capacity of pancreatic beta cells to synthesize and secrete insulin)- causes diabetes mellitus (lack of insulin activity)

THYROID STIMULATING HORMONE- triiodothyronine (T3) and thyroxine (T4). Negative feedback. FSH-gonadotropin releasing hormone from the hypothalamus stimulates FSH release. Surpressed by estrogens in females and testosterone in males thru negative feedback systems.

LH-triggers ovulation, release of secondary oocyte by an ovary. FSH and LH stimulate secretion of estrogens by ovarian cells. Controlled by gonadotropin releasing hormone.

Prolactin- with other hormones, initiates+maintains milk production. Ejection of milk from mammary glands depends on oxytocin. Regulated by hypothalamus. Prolactin inhibiting hormone (dopamine) sucking action of nursing infant causes reduction in hypothalamic secretion of PIH

Posterior Pituitary- stores and releases 2 hormones synthesized by the neuronal cell bodies of both the paraventricular and supraoptic nuclei- oxytocin and antidiurectic hormone. Stored in posterior pituitary until nerve impulses trigger exocytosis and release the hormone.

Stretching of cervix during delivery stimulates release of oxytocin, enhances contraction of smooth muscle cells in wall of uterus. After delivery, stimulates milk ejection from mammary glands

anti diuretic hormone- decreases urine production. Causes kidneys to remove more water to the blood. In its absence, urine output increases more than 10 fold.

High blood osmotic pressure (or decreased blood volume) from dehydration, hemorrhage, diarrhea, or excessive sweating stimulates Osmoreceptors in hypothalamus that monitor blood osmotic pressure.

Secretion of ADH can be altered in other ways- pain, stress, trauma, anxiety, acetylcholine, nicotine, drugs like morphine, tranquilizers, and anesthetics stimulate ADH secretion.

THYROID- stores its product in large quantities- 100 day supply follicular cells produce thyroid hormines. Parafollicular cells produce calcitonin, which helps regulate calcium homeostasis

increase Basal metabolic rate- rate of oxygen consumption under standard conditions by stimulating cellular oxygen to produce ATP. Cellular metabolism of carbs, lipids, and proteins increases. Also, second major effect of thyroid hormones is to stimulate synthesis of additional NA-K pumps which use large amounts of ATP. More heat is given off, and body temp rises. CALORIGENIC EFFECT. Maintenance of normal body temperatures. Thyroid hormones enhance some actions of catecholamines (norepinephrine and epinephrine), upregulate beta receptors- hyperthyroidism include increased heart rate, more forceful heartbeats, and increased blood pressure. Accelerate body growth- nervous and skeletal systems

thyrotropin-releasing hormone from hypothalamus and Thyroid stimulating hormone from anterior pituitary
stimulate synthesis of thyroid hormones

**Calcitonin** can decrease level of calcium in blood by inhibiting action of osteoclasts (cells which break down bone extracellular matrix). Secretion is controlled by a negative feedback system.

**PARATHYROID GLANDS**
more numerous CHIEF cells- produce parathyroid hormone (parathormone). Other cell is oxyphil cell parathyroid hormone is major regulator of levels of Ca$^{2+}$ and Mg$^{2+}$ and phosphate HPO$_4^{2-}$ ions in blood. Specific action of PTH is to increase number and activity of osteoclasts- elevated bone resorption which releases Ca$^{2+}$ and phosphates into blood. Also, acts on kidneys by slowing rate these are lost from blood in urine. Also promotes formation of hormone calcitriol, active form of vit D. increases the rate of Ca$^{2+}$, phosphate, and Mg$^{2+}$ absorption from GI tract

blood calcium level directly controls secretion of calcitonin and PTH via negative feedback loops that do not involve pituitary.

ADRENAL GLANDS- suprarenal glands, superior to each kidney in retroperitoneal space. Adrenal cortex is 80-90% of the gland, with small centrally located adrenal medulla. Adrenal cortex produces steroid hormones. Complete loss of adrenocortical hormones leads to death due to dehydration and electrolyte imbalances in a few days to a week, unless hormone replacement therapy. Adrenal medulla produces norepiniephrine, epinephrine, and small amt of dopamine

Adrenal cortex-zouter zone- ona glomerulosa- secrete mineralocorticoids which affect mineral homeostasis. Middle zone- zona fasciculata- wides of 3 zones with long straight column cells. Secrete glucocorticoids, primarily cortisol, affect glucose homeostasis. Inner zone- zona reticularis, branching cords, synthesize small amounts of weak androgens.

Mineralocorticoids- aldosterone- regulates homeostasis of sodium ions and potassium ions, help adjust blood pressure and volume. Promotes excretion of H$^+$ in urine, removal of acids helps prevent acidosis. This is controlled by renin angiotensin aldosterone RAA pathway

Glucocorticoids- regulate metabolism and resistance to stress include cortisol, corticosterone, and cortisone. Of these 3 released by zona fasciculata, cortisol is most abundant (95%) -protein breakdown, mainly in muscle fibers, increasing liberation of amino acids into blood stream. Glucose formation- liver cells may convert certain amino acids or lactic acid to glucose. Lipolysis- breakdown of triglycerides and release of fatty acids from adipose tissue into the blood resistance to stress. Additional glucose supplied by liver cells provides ready source of ATP to combat a range of stresses light exercise, fasting, fright, temp extremes, high altitude, bleeding, infection, surgery, trauma, disesase. Raise blood pressure. Anti inflammatory effects- inhibit white blood cells that participate in inflammatory responses. Also retard tissue repair. Depression of immune responses (prescribed for organ transplant recipients to retard tissue rejection)

controlled via typical negative feedback system
low levels of glucocorticoids stimulate neurosecretory cells in hypothalamus to secrete corticotropin releasing hormone, promotes release of ACTH from anterior pituitary

androgens-
drenal cortex secretes small amounts of weak androgens. Dehydroepiandrosterone DHEA major androgen
secreted. After puberty in males, testosterone released in much greater quantities by testes, so secretion by adrenal gland is usually so low their effects are insignificant. In females, adrenal androgens play important roles, promoting libido and are converted to estrogens by other tissues. After menopause, all female estrogens come from this conversion. Adrenal androgens also stimulate growth of axillary + pubic hair.

Adrenal Medulla- inner region of adrenal gland- modified sympathetic ganglion of autonomic nervous system. Hormone producing cells called chromaffin cells. Hormone release can occur very quickly.- synthesizes epinephrine and norepinephrine (80% and 20%) impulses from hypothalamus stimulate sympathetic preganglionic neurons which stimulate chromaffin cells to secrete epinephrine and norepinephrine. Augment flight or fight response- increase output of heart, which increases blood pressure. Also increase blood flow to heart, liver, skeletal muscles, and adipose tissue, dilate airway to lungs, increase blood levels of glucose and fatty acids.

PANCREAS
acini-produce digestive enzymes which flow into GI tract through ducts amongst the acini are pancreatic islets. Abundant capillaries

Alpha cells- 17%- secrete glucagon
Beta cells- 70%- secrete insulin
Delta cells 7%- secrete somatostatin- acts in paracrine manner to inhibit insulin and glucagon release. May also act as circulating hormone to slow absorption of nutrients from GI tract. Inhibits secretion of GH
F cells are the remainder pancreatic islet cells- secrete pancreatic polypeptide- inhibits somatostatin secretion NEGATIVE FEEDBACK SYSTEM

insulin secretion also stimulated by acetylcholine, amino acids arginine and leucine, glucose dependent insulinotrophic peptide released by enteroendocrine cells of small intestines when glucose in GI tract

OVARIES AND TESTES
ovaries produce estrogens (estradiol and estrone) and progesterone. With FSH and LH, regulate menstrual cycle, maintain pregnancy, and prepare mammary glands for lactation. Ovaries also produce inhibin, protein hormone that inhibits FSH. During pregnancy, ovaries and placenta produce peptide hormone relaxin which increase flexibility of pubic symphysis to help dilate uterine cervix. Testes-testosterone- descent of testes before birth, regulates production of sperm, and male secondary characteristics like beard growth and deepening of voice. Also produce inhibin.

PINEAL GLANDS AND THYMUS-
pineal gland secretes melatonin, amine hormone derived from serotonin. Sets body's biological clock.

Thymus- thymosin, thymic humoral factor, thymic factor, and thymopoietin- promote maturation of T cells (white blood cells that destroy microbes and foreign substances) and may retard aging process.

Eicosanoids- prostaglandins and leukotrienes- found in virtually all body cells except red blood cells. Act as local hormones in response to chemical or mechanical stimuli. Thromboxane is a modified prostaglandins that constricts blood vessels and promotes platelet activation. Present only briefly. Bind to receptors on target cell plasma membranes and stimulate or inhibit synthesis of second messengers like cyclic AMP.
Leukotrienes stimulate chemotaxis (attraction to chemical stimulus) of white blood cells and mediate inflammation.
Prostaglandins alter smooth muscle contraction, glandular secretions, blood flow, reproductive processes, platelet function, respiration, nerve impulse, transmission, lipid metabolism, and immune responses.
Growth factors- cell growth, division, tissue development, growth, repair.

STRESS RESPONSE (18.14)
body's homeostatic mechanisms attempt to counteract stress.
Flight or fight, initiated by nerve impulses from hypothalamus, mobilizes resources for immediate physical activity. Glucose and oxygen to most active organs (brain, skeletal muscles, heart). Reduces blood flow to kidneys, promotes release of renin, RAA pathway set in motion. Aldosterone causes kidneys to retain Na+ --> water retention, elevates blood pressure

Resistance Reaction (2nd stage)- initiated by hypothalamic releasing hormones. Longer lasting. Cricotropin releasing hormone, GHRH, thyrotropin-releasing hormone. Repair damage cells. Reduce inflammation. Helps body continue fighting a stressor for longer, generally through the stressor, and our bodies return to normal. If resistance stage fails to combat stressor, move to state of exhaustion

WITH AGING
PTH increases with fall in calcitonin levels, heighten age related decrease in bone mass osteoporosis. Pancreas releases insulin more slowly and receptor sensitivity to glucose declines.

DISEASES