**THE ENDOCRINE SYSTEM**

**Endocrine Glands**

**Functions**

Same as nervous system: communication and control

Slower acting than nervous system

Effects are longer lasting

**Hormones**

Chemicals that influence or control the activity of a specific tissue or organ

Secreted by endocrine glands directly into blood or lymph

Exocrine glands secrete into body cavities or onto surfaces

Interact only with target cells – cells with receptors for the specific hormone

Peptide

Amino acids, peptides, proteins

Steroid

Derived from cholesterol; therefore are lipid soluble and can pass through the plasma membrane

**How Hormones Function**

**Peptide**

Bind to receptors on the plasma membrane (cell surface)

Action is mediated through 2nd messengers

The hormone itself is the first messenger

Binding to the receptors activates a second messenger inside the cell

The second messenger causes intracellular effects



**Steroids**

Bind to an intracellular receptor

Hormone – receptor complex activates gene transcription, cause a protein to be manufactured



**Hormone Control**

Three mechanisms control release of hormones:

**Humoral**

Controlled by concentration of substances in the blood

**Hormonal**

Controlled by the action of other hormones

Stimulating or inhibiting hormones interact with other endocrine glands/tissues to control release of their hormones

**Neural**

Sensory input from the body stimulates sympathetic or parasympathetic activity or stimulates neuroendocrine cells to release their hormones

**Feedback Loops**

Negative Feedback Inhibition

Most common

Response to a stimulus reduces or removes the stimulus

Examples:

Low blood volume stimulates release of ADH, water is retained, blood volume rises, signal to release ADH is removed (low blood volume), ADH is no longer released

TRH TSH T4/T3 (explain with TSH/anterior pituitary)



Positive Feedback Loops

Exaggerate the response until the episode is terminated

Example: Oxytocin

**Hypothalamus and Pituitary Gland**

**Hypothalamus**

Regulates internal environment, maintains homeostasis

Has centers to control heart rate, body temperature, and water balance

Also regulates the activity of the pituitary gland

Releases hormones which stimulate and inhibit release of anterior pituitary hormones

Manufactures posterior pituitary hormones

Connected to the pituitary by a stalk (infundibulum)



**Posterior Pituitary**

Stores hormones made in hypothalamus

Cell bodies (nuclei) make the hormones

Axons extend down infundibulum to posterior pituitary

Hormones are stored in axon terminals

Secretes the hormones in response to neural stimuli received at the hypothalamus

Antidiuretic hormone (ADH) or vasopressin

Promotes reabsorption of water at the kidneys, prevents dehydration

Stimulated by high blood osmolarity, sensed in the hypothalamus

Diabetes insipidus – inability to produce ADH

Oxytocin

Stimulates uterine contraction during labor

Release is stimulated by movement of baby into and down birth canal

Stimulates release of milk during nursing (contraction of myoepithelial cells)

Release is stimulated by suckling

**Anterior Pituitary**

Connected to hypothalamus by capillary portal system

Makes and stores hormones; secretes hormones in response to stimulus from hypothalamus

Growth hormone (GH)

Stimulates growth, affects height

Produced in greatest quantities during childhood but needed in adults to promote protein synthesis and normal cell division for repair and replacement

Dwarfism – hyposecretion during childhood, normal proportions but very small

Gigantism – hypersecretion in childhood, child grows into a giant, usually suffers from diabetes mellitus (excess GH interferes with insulin activity)



Acromegaly – hypersecretion I adulthood, epiphyseal plates have sealed so long bones no longer lengthen but jaw, browridges, nose, fingers,and toes continue to grow



Prolactin (PRL)

Stimulates milk production by the mammary glands

Produced only after childbirth

Thyroid stimulating hormone (TSH)

Stimulates thyroid to produce thyroxine

Adrenocorticotropic hormone (ACTH)

Stimulates adrenal cortex to produce cortical hormones

Gonadotropic hormones

Stimulate the gonads (ovaries and testes)

Follicle stimulating hormone (FSH)

Lutinizing hormone (LH)

Proopiomelanocortin

A prohormone that must be cleaved to be active

When cleaved gives rise to at least 3 active proteins

ACTH

Melanocyte stimulating hormone (MSH)

      Stimulates melanin production in lower vertebrates

      Probably more important as a neurotransmitter in humans

      UV irradiation is the more important stimulator of melanin production in humans

b-endorphin

**Thyroid and Parathyroid Glands**

**Thyroid**

Attached to trachea just inferior to the larynx

Thyroid cartilage is the Adam’s apple

Composed of follicles

Spherical structures surrounded by thyroid cells

Contain thyroglobulin – protein precursor of thyroid hormone

Requires iodine to finish making thyroid hormone

Iodine is actively transported to thyroid gland

Concentration may be 25x higher than elsewhere in the body

Produces thyroxin (thyroid hormone)

Occurs and is secreted in two forms, T4 and T3

Denotes number of iodine atoms attached

T3 is more active, T4 is eventually converted to T3 at the target cell surface

Hypothyroidism

Low levels of thyroxin in the blood

Causes

Low or absent TSH - Low or absent TRH – hypothalamic problem or TRH released but no TSH released – pituitary problem

Inability of TSH to stimulate thyroid follicle cells – Hasimoto’s thyroiditis: autoimmune attack on the thyoid destroys the gland

Lack of iodine – thyroglobulin (colloid) builds up in follicles but no thyroxine can be made

Effects

Simple goiter – swelling of the thyroid due to lack of iodine, used to be common in the midwest



Myxedema – in adults, lethargy, weight gain slow bradycardia, low body temperature (all due to decreased BMR), loss of hair, puffiness of skin

Cretinism – in children or infants, due to failure of thyroid to develop properly; leads to short, stocky stature and mental retardation



Treatments

Simple goiter – iodized salt

Myxedema and cretinism – synthetic thyroxine; however infants suffering from thyroid dysfunction must receive treatment within first 2 months to avoid mental retardation

Hyperthyroidism – Grave’s disease

Enlargement and overactivity of thyroid

Increased BMR; increased heart rate, exopthalmic goiter due to edema in eye socket and swelling of extrinsic eye muscles

Autoimmune stimulation of TSH receptors

Surgery or radioablation followed by synthetic thyroxine therapy

Calcitonin

Produced by  parafollicular cells located between follicles

Regulates blood calcium levels by stimulating uptake of calcium by bone



**Parathyroids**

Four small glands located on the posterio-lateral aspect of the thyroid

Produce parathyroid hormone (PTH)

Regulates blood calcium levels by stimulating the release of calcium from bone when blood calcium levels are low

**Adrenal Glands**

Located on top of kidneys

**Adrenal medulla**

1.   Stimulated by the sympathetic nervous system

2.   Produces epinephrine (adrenalin) and norepinephrine (noradrenalin)

a.    Responsible for flight or flight syndrome

b.   Stimulate increases in blood glucose levels, metabolic rate, breathing rate, heart rate, cardiac contractile force, vasodilation of blood vessels feeding skeletal muscle, bronchiodilation, and vasoconstriction of blood vessels to the digestive tract

**Adrenal cortex**

Stimulated by ACTH from pituitary in response to stress

ACTH release stimulated by the hypothalamus remember

Secretes glucocorticoids, mineralocorticoids, and low levels of gonadocorticoids (sex hormones)

Glucocorticoids (cortisol is major) promotes

Hydrolysis of proteins to release amino acids which are then converted to glucose

Mobilization of fatty acids for energy

Glucose sparing reactions

Anti-inflammatory also

Mineralocorticoids

Aldosterone is major

Regulates sodium re-absorption by the kidney (which is balanced by potassium excretion)

Water follows sodium, so aldosterone is water-conserving

Secreted in response to the renal enzyme renin, which is secretedby the kidneys in response to low blood pressure or high blood osmolarity

Renin converts angiotensinogen to ATI, which is then converted to ATII, which stimulates aldosterone release, vasoconstriction, and ADH release





Disorders of the Adrenal Cortex

Addison’s Disease -  low levels of gluco- and mineralocorticoids

Susceptible to severe blood glucose drops due to no cortisol

Low sodium levels, low blood volume, susceptible to severe dehydration

Bronzing of the skin – feedback mechanisms fouled up, MSH produced in high quantities.





Cushing’s Syndrome – high levels of adrenal cortex hormones

Tendency to develop diabetes mellitus, decrease in muscular protein, increase in subcutaneous fat, hypernatriemia, increased blood volume, hypertension, moon face (edema) and possible virilization in women



**Pancreas**

**Islets of Langerhans**

Endocrine portion of gland

Exocrine function for most of gland (digestive enzymes)



**Insulin**

Promotes uptake and usage of glucose by cells

Promotes glycogen synthesis

Promotes buildup of fats and proteins

Inhibits use of fats and proteins as an energy source

Secretion stimulated by high blood glucose levels

Lowers blood glucose levels to normal limits

**Glucagon**

Opposite effects of insulin

Secreted in response to low blood glucose levels

Raises blood glucose levels by stimulating breakdown of glycogen



**Diabetes Mellitus**

Most common hormonal disease

Due to either lack of insulin or inability of insulin to stimulate cells to take up glucose

Hallmarks:

Polyuria – glucose levels exceed ability of kidney to reabsorb, spill into urine, act as an osmotic stimulatory of water movement into urine

Polydipsia – thirst to replace lost fluid leads to high fluid intake

Polyphagia – hunger because cells can’t use available glucose

Ketosis, metabolic acidosis

Due to utilization of fats for energy since glucose can’t be used

Type I

Insulin-dependent (used to be called juvenile onset)

Pancreas doesn’t produce insulin

Genetic predisposition, due to autoimmune destruction of islet cells

Type II

Non-insulin dependent (formerly adult onset)

Also has genetic risk factors but etiology is different

Due to inability of insulin to stimulate cells even though it is present

Obesity is a risk factor

Can usually be controlled with diet and exercise

Complications of diabetes

Blindness, kidney disease, circulatory disorders (heart disease and strokes), risk of diabetic coma

Gestational -  due to placental hormonal influences on insulin activity, usually disappears after childbirth

**Other Endocrine Glands**

**Testes and Ovaries**

**Testosterone**

Male sex hormone

Essential for normal development and functioning of the male sex organs

Growth of penis and testes at puberty

Maturation of sperm

Stimulates development of secondary sex characteristics

Facial, axillary, and pubic hair

Enlargement of larynx and vocal cords – voice change

Stimulates skeletal muscle development and closure of epiphyseal plates

Contributes to greater strength in males as compared to females

Stimulates secretion of sebaceous and sweat glands

Acne

Body odor

Contributes to pattern baldness (DHT)

Stimulates sex drive

Can contribute to aggressivness

Therapeutic use

      Prevent muscular atrophy in long term illness

      Promote healing in burn and surgery patients (GH may be better)

      Used to treat rare forms of anemia and breast cancer

Abuse

      Doses at 10 to 100x therapeutic promote great gains in muscle mass when paired with resistance exercise

      Negative feedback inhibition of GnRH release causes testes to atrophy, sperm counts and sex drive to drop

      High androgen levels cause acne, baldness, and agression (‘roid rage)

      Promote liver and kidney damage, including cancer, dysregulation of lipoprotein metabolism (leads to heart disease), and inability to regulate fluid balance (steroid bloat, which leads to hypertension, which also contributes to heart disease and risk of stroke

      When discontinued hypothalamus doesn’t resume release of GnRH, prostate enlarges, gynecomastia may occur

      Women may develop male sexual characteristics; stop ovulataing or menstruating, grow facial and body hair, lose hair from the scalp, and experience breast reduction and clitoral enlargement



**Estrogen and Progesterone**

Estrogen secreted at puberty stimulates growth of the uterus and vagina, required for egg maturation

Stimulates female secondary sex characteristics

Body hair and fat distribution

Breast enlargement (promotes growth and maintains size)

Promotes closure of epiphyseal plates, enlargement of pelvic girdle

Stimulates higher HDL levels (protective against heart disease)

Feminizes the brain

Estrogen and progesterone together regulate menstrual cycle and breast development (maturation to milk-producing glands), maintain the uterus during pregnancy

**Thymus Gland**

Located in upper thoracic cavity (neck along trachea to mediastinum)

Largest in children, atrophies with age until nearly gone by early 20’s

Site of T cell maturation

Produces thymosins

Hormones that stimulate T cell maturation

May be good therapeutic agents for treatment of immunodeficiencies (including AIDS)

**Pineal Gland**

Cone shaped gland in the roof of the third ventricle

Smaller than the pituitary, atrophies with age

Innervated through the optic chiasma (light sensitive)

Produces melatonin (don’t confuse with melanin)

Secreted in response to declining light levels

Regulates sleep-wake cycles (promotes sleep)

Jet lag (take it on the west to east trip, lets your body go to sleep on local eastern time when it is still awake on the earlier western time)



High amounts contribute to SAD

      Treat with bright light therapy to cause breakdown

Inhibits secretion of FSH and LH

Lower animals

      Sex organs enlarge in the summer

      Mating occurs in the fall

      Young are born in the spring

Humans – children with tumors that destroy the pineal gland go through early puberty

**Endocrine Tissues**

Non-glandular tissues which secrete hormones

**Heart**

Atrial natriuretic hormone (ANH) secreted by atria in response to high blood volume

Also secreted by cells in the aorta, ventricles, lungs, and pituitary

Promotes renal excretion of sodium and water to lower blood volume and thus pressure

**Stomach and Small Intestine**

Secrete peptide hormones that regulate digestive activity

**Pancreas** already mentioned

**Paracrine Factors**

**Growth factors**

Platelet-derived growth factor

Secreted from platelets and other cell types

Promotes wound healing

Promotes increases in some cells in nervous system

Epidermal growth factor

Stimulates growth of epidermis

Nerve growth factor

Stimulates growth of neurons

Tumor angiogenesis factor

Promotes vascularization of tumors (secreted by tumors)

**Prostaglandins**

Derived from arachadonic acid

Many different kinds, many different effects

Blood clotting/inhibition of blood clotting

Generally promote inflammation; inhibited by aspirin, acetaminophen, or ibuprofen

Inhibit synthesis

**Effects of Aging**

Most endocrine glands shrink with age but maintain function

Most common problems with thyroid and pancreas (Graves disease and diabetes)