Chapter 10 Endocrine System

The two major systems responsible for the regulation of homeostasis (performed by all the organ systems) are the nervous system and the endocrine system. While the nervous system acts more quickly it has short-term effects. The endocrine system, which is composed of a group of glands placed throughout the body, releases chemicals (hormones) that must travel through the circulatory system to reach a target tissue or organ causing that tissue or organ to effect a regulatory change. This is a much slower process but the effect is more long-term.

I. Main Functions
   A. Growth, metabolism, and maturation of many tissues and organs
   B. Ionic Regulation – regulates ion concentrations in the blood (blood chemistry)
   C. Water Balance – regulates water balance by controlling solute concentrations
   D. Heart rate & Blood Pressure Regulation
   E. Blood Glucose Regulation
   F. Immune System Regulation
   G. Reproductive Function Control
   H. Uterine Contractions & Milk Release

II. Chemical Signals (ligands) – are molecules released from one location that move to another location to produce a response – 2 classes
   A. Intracellular – are produced in one part of a cell and travel to another part of the same cell
   B. Intercellular – are produced and released by one cell, carried in intercellular (interstitial) fluid, and bind to receptors on some other cells (not all cells have the same receptor sites) – these ligands are placed in functional categories on the basis of the tissue they are secreted from and the tissue/s they regulate
      1. Autocrine – are secreted (released) by cells to have a local effect influencing the activity of the same cell type that secreted them – examples eicosanoids (prostaglandins, thromboxanes, prostacyclins, and leukotrienes) released from smooth muscle and platelets in response to inflammation, causing blood vessel dilation and blood clot formation
      2. Paracrine – produced and secreted by a wide variety of tissues to effect other tissue types in the same area (locally) – examples histamine and prostaglandins

* Because certain chemicals function in several of the above categories they are studied in conjunction with Endocrine and Neuro-chemicals

3. Neuromodulators & Neurotransmitters – related to the nervous system – produced and secreted by neurons – released across the synaptic cleft or small extracellular spaces to influence postsynaptic cells – examples acetylcholine and epinephrine
4. Pheromones – secreted into the environment (outside the body) to modify physiology and behavior of other individuals – mostly seen in animals and relate to reproduction
5. Neurohormones (produced by neurons and function like a hormone – examples oxytocin and antidiuretic hormone) and Hormones (examples – thyroid hormone, growth hormone, insulin, epinephrine, estrogen, progesterone, testosterone) – related to endocrine system - secreted into the blood, travel some distance to a target tissue/organ to influence specific activities
III. **Hormones** – chemical messengers in the **endocrine system** – intercellular chemical signals produced within and secreted by the endocrine glands – transported by blood some distance to target tissues/organs – attach to receptor sites (molecules) on the target to effect a change in activity – broken down in the liver and excreted in the urine

A. **Hormone Chemistry** – 2 basic chemical base types

1. **Proteins** – which can range from; a simple **amino acid**, to a **polypeptide** (20 to less than 100 **amino acids**), to a full protein (greater than 100 **amino acids**) – most bind to membrane bound receptors (exception- peptide hormones secreted by the thyroid that diffuse) – when bound to its receptor on a cell membrane one of two things happens: ¹ it alters the permeability of the cell membrane; ² it can activate a “first messenger-second messenger” system where the **protein hormone** is the **first messenger** bound to the cell membrane activating a **regulatory substance** as the **second messenger** which activates enzymes that effect a change by **catalyzing** (changing the rate at which reactions occur) chemical reactions

2. **Lipid** (steroids) – derived from **cholesterol** – have structures that vary only slightly among the different types – produced mostly by the **adrenal cortex** and **gonads** (ovaries and testes) – all diffuse across the cell membrane and bind to **intracellular receptors** in the cytoplasm or nucleoplasm (activates genes in the DNA of the nucleus, which activate synthesis of mRNA that, through transcription and translation, produce a protein) - steroid hormones are mostly responsible for initiating or changing the rate of protein synthesis

   a. **Eicosanoids** – are derived from the fatty acid **arachidonic acid** and include; prostaglandins (Paracrine), thromboxanes, prostacyclins, and leukotrienes

3. **Four Main Effects of Hormones on Target Tissues**
   a. Initiates Protein Synthesis
   b. Changes Rate of Protein Synthesis
   c. Changes Rate of Secretions of Cells
   d. Alters the Permeability of the cell membrane allowing certain substances to move in and/or out of the cell

B. **Regulation of Secretions** – operate on a **negative feedback mechanism** that keeps the body functioning within a narrow range of values (margin) - regulated by one or more of 3 methods

1. **Body Chemistry Levels** – secretion of some hormones is triggered by levels of certain chemicals in blood (examples – **insulin** is triggered by blood glucose levels, **parathyroid hormone** is triggered by calcium blood levels)

2. **Hormones** – secretion of some hormones is triggered by other hormones (example – **pituitary hormones** trigger release of **sex hormones**)

3. **Nervous System** – secretion of some hormones is controlled by the nervous system (example – nervous stimulation of the **adrenal medulla** triggers release of **epinephrine**)

IV. **Endocrine Glands & Their Hormones** – consist of ductless glands that secrete hormones directly into the circulatory system

A. **Pituitary Gland** (hypophysis) – about the size of a pea – sits in the **sella turcica** (Turkish saddle – see cranial bones) – connected to the **hypothalamus** by the **infundibulum** – historically though to be the **master** gland – is divided into 2 lobes – releases 9 different hormones

   1. **Anterior Pituitary** (adenohypophysis) – made of glandular epithelial cells derived from the embryonic oral cavity – secretion of hormones controlled by **releasing factors** (neurohormones) produced by nerve cells in the
hypothalamus which travel to the **anterior pituitary** by the **hypothalamic-hypophyseal portal system** (a group of capillaries and veins within the anterior portion of the **pituitary gland** and the **infundibulum**) - 7 main hormones secreted

a. **Growth Hormone (GH)** – target tissue is most tissues of the body – **effects**; increasing protein synthesis, breaking down of fats, and releasing of fatty acids from cells – influences the liver to produce and secrete **somatomedins** (protein chemical signals, which bind to cells of other tissue (like bone and cartilage) stimulating growth), neurons synapse with capillaries by releasing vesicles filled with releasing factors that disperse into the capillaries by **exocytosis** and are carried to the **anterior pituitary gland** – stimulates uptake of amino acids into cells giving them more raw materials to manufacture tissues with (3 main tissues effected; muscle, bone, and adipose)

- hyposecretion – causes **pituitary dwarfism** (normal proportionally, just remaining small)
- hypersecretion – causes **giantism** (increased bone length) during growth phase or **acromegaly** (increased bone diameter) after adult hood is reached

b. **Prolactin (PRL)** – target tissue the **mammarys** (modified apocrine sweat glands) in the breast – **effects**; stimulates milk production in females before giving birth, stimulates interstitial cells in the testes to become more sensitive to ICSH or LH in males

c. **Thyroid stimulating hormone (TSH)** – target tissue the **thyroid gland** – **effect,** causes the thyroid to secrete more thyroid hormones – activated by (driver) iodine levels in the blood

d. **Adrenocorticotropic hormone (ACTH)** – target tissue the **adrenal cortex** of the **adrenal gland** – **effect,** to increase secretion of hormones by the adrenal cortex (mainly cortisol) – **activated by** (driver) stress

e. **Gonadotropins** – target tissue the **gonads** (testes and ovaries) – **effect,** to regulate the growth, development, and function of the gonads – activated by a single releasing hormone from the hypothalamus – 2 hormones (3 names)

  - **Luteinizing hormone (LH)** – in females targets the ovaries to **ovulate** (release of an oocyte) and increase secretion of **estrogen** and **progesterone** – in males LH is called **interstitial cell-stimulating hormone (ICSH)** which targets the interstitial cells of the testes to secrete more **testosterone**

  - **Follicle-stimulating hormone (FSH)** – stimulates the development of **follicles** (maturation into an oocyte) in the ovaries and **sperm** (increased production) in the testes

g. **Melanocyte-stimulating hormone (MSH)** – targets melanocytes – **effect,** synthesis of melanin (in fetus only)

2. **Posterior Pituitary (neurohypophysis)** – made of nervous tissue – nerve cell bodies in the **hypothalamic nuclei** (nuclei detect and regulate ionic and chemical levels in the body) have axons extending down through the **infundibulum** to the posterior pituitary – production of the 2 hormones released by the posterior pituitary happen in the nuclei of the hypothalamus and are transported down the axons where they synapse with capillaries in the posterior pituitary

a. **Antidiuretic hormone (ADH)** – target tissue the **kidneys** – effects; increased water reabsorption in the kidneys = decreased urine output, **vasopressin** (blood vessel constriction) – **activated by** (driver) low blood pressure
b. Oxytocin (OT) – target tissue the smooth muscle of the uterus and melanocytes in the mammarys - effects; uterine contractions for birth and milk “let-down”

B. Parathyroid Glands – four small glands embedded in the posterior wall of the thyroid gland – secrete 1 hormone
1. Parathyroid hormone (PTH) – target tissue the osteoclasts of the bone, digestive system, and kidneys – effect: increase calcium (Ca²⁺) levels by; increased bone break down by the osteoclasts, increased Ca²⁺ absorption in the digestive system by increasing active vitamin D synthesis (calcium uptake is dependent on vitamin D), increased reabsorption of Ca²⁺ in the kidneys – functions on a negative feedback loop – activated by (driver) low blood or serum calcium (Ca²⁺)

C. Thyroid Gland – is highly vascular - works in a negative feedback mechanism with the hypothalamus – formed by 2 lobes, located on either side of the trachea and connected by a narrow band called the isthmus, consisting of many follicles (small hollow spheres of simple cuboidal epithelium each filled with a protein-rich colloid called thyroglobin that the hormones $T_3$ and $T_4$ are attached to – storage area for hormones, between the follicles is a network of loose connective tissue, capillaries, and parafollicular cells (produce the hormone calcitonin)
1. $T_3$ and $T_4$ - produced by the follicular cells of the follicles – target tissue; most tissues of the body – effect; regulate cellular metabolism (influencing heart rate & contraction strength and respiratory rate to meet oxygen and nutrient needs, stimulates appetite and brake down of nutrients) – activated by TSH (hormone produced by the anterior pituitary) with the driver being iodine levels (hypothalamus monitors serum iodine levels) – requires iodine for synthesis (iodine added to salt)
   a. Tetraiodothyroxine ($T_4$) – most abundant of the 2 – contains 4 iodine atoms – also called Thyroxine
   b. Triiodothyroxine ($T_3$) – most potent of the 2 – contains 3 iodine atoms
2. Calcitonin – produced by the parafollicular cells – target tissue the bone (inhibits osteoclasts and stimulates osteoblasts) – effect; to lower blood calcium

D. Adrenal Glands (suprarenal glands) – 2 small glands located superior to each kidney and composed of 2 distinct types of tissue
1. Adrenal Cortex – outer portion of the adrenal gland – composed of glandular tissue derived from the same epithelial tissue as the gonads embryonically – 3 basic classes of steroid hormones secreted
   a. Glucocorticoids – helps regulate blood nutrient levels – secretion levels controlled by the hypothalamus (which secretes a releasing hormone) in conjunction with the anterior pituitary (which secretes ACTH adrenocorticotrophic hormone) – major hormone is cortisol (which functions in the increased breakdown of protein & fat converting them into glucose & fatty acids to be used as energy, also reduces the inflammatory response) – target tissue the liver (gluconeogenesis) – drivers stress and low blood glucose
   b. Mineralocorticoids – helps regulate blood volume and levels of potassium ($K^+$) and sodium ($Na^+$) in the blood – major hormone aldosterone (which causes the kidneys to retain Na⁺ thereby retaining water which increases blood volume = increased blood pressure) – target tissue the kidneys (primarily), but also intestines, sweat glands, and salivary glands – drivers low blood pressure or high blood osmolality
• The Renin-Angiotensin Mechanism: Kidneys detect a drop in blood pressure → kidneys release renin (which acts as an enzyme) → converts angiotensinogen (a blood protein produced by the liver) into angiotensin I → angiotensin I is acted on by angiotensin-converting enzyme (produced in the lungs) converting it to angiotensin II (active version) which causes blood vessel constriction and increased aldosterone (mineralocorticoid produced by the adrenal cortex) → causes the kidneys to excrete K⁺ and retain Na⁺ → ↑ blood volume → ↑ B/P

• 3 targets of Angiotensin II
  o The hypothalamus – to increase parasympathetic stimulation of the salivary glands
  o The circulatory system – systemic vasoconstriction
  o The adrenal cortex – release of aldosterone

  c. Androgens – derivatives of estrogen and testosterone – produced in minuet quantities – responsible for some male characteristics – increases female sex drive and influences some female characteristics (mainly hair growth in pubic and Axillary regions)

2. Adrenal Medulla – inner portion of the adrenal glands – derived from embryonic neuronal tissue – produces catacolamines (which prepare the body for vigorous physical activity) – called ‘fight-or-flight’ hormones – released in response to sympathetic stimulation by the autonomic nervous system – drivers are stress and low blood glucose levels – effects: ¹ increased heart rate, ² vasodilation of the vessels that supply blood to the muscles, ³ vasoconstriction (shunting) of blood vessels that supply the skin and internal organs, ⁴ increased break down of glycogen to glucose and release of fatty acids to increase metabolism, ⁵ increase of respirations
  a. epinephrine – principal hormone released by the adrenal medulla (80%) – also called adrenalin
  b. norepinephrine – used by sympathetic postganglions – makes up the other 20% of catacolamines released

E. Pancreas – primary function is exocrine (98% - 99%) as an accessory organ to the digestive system secreting digestive enzymes to aide in the break down of food – only 1% - 2% of its function is endocrine and this portion is performed by the islets of Langerhans or pancreatic islets dispersed (scattered) among the exocrine tissue they help regulate blood glucose levels (set point 80mg/dl to 120mg/dl) and consist of 2 cell types, each secreting a different hormone
  1. Alpha cells – secrete the hormone glucagon which targets the liver (which stores glycogen) increasing the breakdown of glycogen into glucose to increase blood glucose levels – driver is low blood glucose and sympathetic stimulation
  2. Beta cells – secrete the hormone insulin which targets the liver (primarily) but also skeletal muscle, adipose tissue and satiety center (appetite control center of the hypothalamus) – binds to cellular receptors on the cell membranes, making the membrane more permeable to glucose → the glucose then moves into the cell from the blood lowering blood glucose → within the cell glucose is converted into ATP – excess glucose (blood sugar) is converted by insulin into glycogen (energy storage molecule in the liver and muscles) – driver is high blood glucose and parasympathetic stimulation (associated with eating a meal)

F. Gonads (testes & ovaries) – produce and secrete sex hormones (which target tissues responsible for sexual characteristics) along with production and/or maturation of gametes (sex cells; sperm and oocytes)
1. **Testes** – 2 of them – located in the *scrotum* (a flesh sac extending from the base of the penis) – produce and secrete the sex hormone **testosterone**
   a. **Testosterone** – steroid based hormone produced by the *interstitial cells of Leydig* (located between the seminiferous tubules which produce sperm) – *driver* release of ICSH (LH) by the anterior pituitary which is stimulated by release of GnRH by the hypothalamus in a negative-feedback loop triggered by a drop in serum testosterone – **prebirth** is responsible for masculinizing the reproductive organs – **no production from birth to puberty** – **puberty** is responsible for enlarging the male reproductive system, beginning spermatogenesis (production of sperm by the seminiferous tubules, of the testes, stimulated by the release of FSH by the anterior pituitary), development of **secondary male sex characteristics** (distribution of muscle mass, growth of facial and groin hair, deepening of male voice tone), and the male sex drive

2. **Ovaries** – 2 of them – located lateral posterior to the *uterus* – produce and secrete 2 hormones which contribute to the development and function of the female reproductive structures, **female sex characteristics** (enlargement of breasts, distribution of fat that influences the hips and breasts), and the **menstrual cycle** (caused by the cyclical release of ovarian sex hormones)
   a. **Estrogen** – steroid based hormone – primary hormone of the *ovaries* – produced by the *granulose cells* (surround the immature oocyte, also called a *follicle*) – causes endometrium build up – responsible for the proliferative phase of the menstrual cycle – *driver* the release of FSH – **ovulation** (caused by a spike in estrogen in a positive-feedback loop with the hypothalamus in the release of GnRH stimulating release of FSH (begins enlargement and maturation of several follicles)and LH (causes final maturation of one follicle) by the anterior pituitary) – greatly decreases after ovulation then levels off
   b. **Progesterone** – produced by the *corpus luteum* (formed from the granulose cells, after ovulation (release of the oocyte), under the influence of LH) – responsible for the secretory phase of the menstrual cycle causing the endometrium to secrete nutrients in preparation for implantation of a blastocyst (fertilized oocyte)

G. **Thymus Gland** – located in the upper part of the thoracic cavity in the mediastinum just superior to the heart – is a key player in the development of the **immune system** – is a large gland in children and shrinks with aging
   1. **Thymosin** – hormone secreted by the *thymus* – responsible for the maturation of *T lymphocytes* (T-cells) (produced in the red bone-marrow – migrate to the thymus for maturation – function in immunity)

H. **Pineal Gland** – located superior, posterior to the *thalamus* – associated with the epithalamus
   1. **Melatonin** – targets the hypothalamus – regulates sleep and wake cycles and contributes to the onset of puberty by suppressing GnRH production and release

V. **Other Hormones**
   A. **Erythropoietin** – secreted by the *kidneys* in response to *hypoxia* (low blood oxygen levels) – *target* is bone marrow to increase red blood cell production
   B. **Human Chorionic Gonadotropin** – produced and released by cells of the *chorionic villi* (fingerlike projections in the endometrium) within the *placenta* – similar to LH, targets the ovary (the one that released the oocyte) to influence the *corpus luteum* to remain functional (continue secreting progesterone) in order to maintain the endometrium during pregnancy (gestation) – secretion begins shortly after implantation – is the hormone tested for to indicate pregnancy