Endocrine System

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1 Introduction

The endocrine system is integral to the regulation of the body's activities. It plays a key role in the growth, development, and regulation of metabolism through the release of chemical messengers, called hormones, into the bloodstream. In this handout, we will discuss the complexities of the mammalian endocrine system. We highly recommend reading the cell biology handouts before reading this one to achieve a complete understanding of the material. A quick note before we begin with the fun stuff: Text in the color blue often indicates information that is often not necessary for success on the Open Exam.

1.1 Classes of Hormones

1.1.1 Peptide Hormones

This subset of hormones is often composed of short peptide/protein chains. In addition, they are synthesized into **prohormones**, which are hormone precursors. Prohormones are composed of inactivated peptide hormones and are synthesized by adding peptide chains to their receptor-binding sites. Different post-translational modifications (e.g., cleavage) will often activate these hormones.

- They tend to be lipophobic and **hydrophilic** (i.e., water-soluble) due to their polar chemical structure.
  - Their hydrophilic nature allows for free transportation in the blood.
  - Their lipophobic characteristics allow these hormones to bind to membrane-bound receptors, which activate secondary messengers to relay the signal.
- Examples include insulin, glucagon, gastrin, and parathyroid hormone.

1.1.2 Lipid-derived Hormones

This subset can be further divided into *eicosanoids* and **steroid hormones**. Eicosanoids will be covered in further detail in the immune system handout.

- Steroid hormones are often synthesized from **cholesterol** and can be differentiated by their unique side chains.
- They are **hydrophobic** and lipophilic (fat-soluble), which is a result of their nonpolar chemical structure.
  - Due to the aforementioned properties, steroid hormones require carrier proteins for transportation in the blood.
  - Their lipophilicity allows them to pass through the plasma membrane via passive diffusion to relay a signal.
  - As a result, they often bind to **cytoplasmic** or **nuclear** receptors, meaning these hormones tend to act as transcription factors.
- Examples include testosterone, estrogen, cortisol (stress-related hormone) and aldosterone.

1.1.3 Amino Acid-derived Hormones

- These hormones are relatively small molecules that are akin, in structure, to the fundamental building blocks of proteins: amino acids.
- They are synthesized from the aromatic amino acids **tryptophan** and **tyrosine**.
- Some notable examples of tyrosine-based hormones are the **thyroid** hormones and **catecholamines** (e.g., epinephrine, norepinephrine, and dopamine).
- Tryptophan, on the other hand, is used to synthesize **melatonin**, which is produced in the **pineal gland** and plays a role in regulating sleep.

2 Feedback Systems

2.1 Negative Feedback Loops

- In a negative feedback loop, the response *reduces* the initial stimulus.
- For instance, in the thyroid, secretion of T3 and T4 act on the anterior pituitary gland to inhibit thyroid-stimulating hormone (TSH) release.
- Another example is the inhibin feedback system. Follicle-stimulating hormone (FSH) stimulates the secretion of inhibin, which then dampens FSH release.

2.2 Positive Feedback Loop

- Positive feedback loops serve to *reinforce* a stimulus.
- For instance, in the milk let-down reflex, the secretion of oxytocin leads to suckling, which further increases oxytocin and prolactin levels.

3 Hormones of the Hypothalamus

Now that we understand the different classes of hormones, let's get into the specific types of hormones of the **hypothalamus**, an endocrine gland that is situated on the undersurface of the brain.

Table 1. **Major hypothalamic releasing and inhibiting hormones**			
Hypothalamic hormone secreted	**Target anterior pituitary cells**	**Anterior pituitary gland secretion/release**	**Physiological result**
Growth hormone-releasing hormone	Somatotrophs	Growth hormone	Stimulates growth
Growth hormone-inhibiting hormone	Somatotrophs	Inhibits growth hormone secretion	Inhibits growth
Prolactin-releasing hormone (hypothetical)	Lactotrophs	Prolactin	Thought to stimulate lactation
Prolactin-inhibiting hormone (hypothetical)	Lactotrophs	Inhibits prolactin secretion	Thought to inhibit lactation
Thyrotropin-releasing hormone	Thyrotrophs	Thyroid-stimulating hormone	Stimulates release of T3 and T4 (thyroxine), thereby increasing metabolism
Corticotropin-releasing hormone	Corticotrophs	Adrenocorticotropic hormone	Regulates glucocoticoids, mineralocorticoid and androgen secretion by the adrenal cortex
Gonadothropin-releasing hormone	Gonadotrophs	Luteinising hormone	Stimulates ovulation/progesterone secretion in females and testosterone secretion in males
Gonadothropin-releasing hormone	Gonadotrophs	Follicle-stimulating hormone	Stimulates maturation of ovarian follicles in females and spermatogenesis in males

Figure 1: Hypothalamic Hormones (Source: Nursing Times)

- The hypothalamus is, in general, responsible for the secretion of hormones that initiate the release of major hormones from the **pituitary gland**.
- **Thyrotropin-releasing hormone (TRH)** is a *peptide* hormone responsible for initiating the release of **thyroid-stimulating hormone (TSH)** and **prolactin (PRL)** by the **anterior pituitary gland**, which will be discussed in the next section.
- **Gonadotropin-releasing hormone (GnRH)** is another peptide hormone that primarily serves to initiate the release of **follicle-stimulating hormone (FSH)** and **luteinizing hormone (LH)** by the **anterior pituitary gland**.
  - Its secretion begins at the onset of puberty, which triggers sexual development and is integral in normal physiology. It is secreted in pulses spaced out in 1-2 hour intervals.
- **Growth hormone-releasing hormone (GHRH)** is another peptide hormone that stimulates cells in the **anterior pituitary** to secrete **growth hormone (GH)**.
- **Corticotropin-releasing hormone (CRH)** is a peptide hormone that acts on the **anterior** lobe of the **pituitary** gland, where it promotes the release of **adrenocorticotropic hormone (ACTH)**.
  - CRH and ACTH are precursors to **cortisol**, a stress-related hormone. They follow the **hypothalamic-pituitary-adrenal (HPA) axis**, an important endocrine pathway.
- **Somatostatin** is a peptide hormone that acts on the **anterior pituitary** to *inhibit* **GH** release and **TSH** release. It is also secreted by the pancreas.
- **Dopamine** is derived from the amino acid **tyrosine** by the enzyme *tyrosine hydroxylase*. Its main function in the hypothalamus is to *inhibit* the release of **prolactin**. In addition, it's known to activate the **reward centers**.

- **Prolactin-releasing hormone (PRLH)** stimulates the secretion of prolactin by the pituitary gland.

4 Pituitary Gland

The pituitary gland is a small pea-shaped endocrine organ that is composed of two lobes, the **anterior** lobe and the **posterior** lobe.

4.1 Anterior Pituitary Gland

The anterior lobe, also known as the adenohypophysis, is responsible for the secretion of 6 hormones.

- The anterior lobe consists of 5 distinct cell types: corticotrophs, thyrotrophs, gonadotrophs, somatotrophs, and lactotrophs.
- **TSH** (**thyrotropin** or **thyroid-stimulating hormone**) is a peptide hormone released by **thyrotrophs**. It targets the secretory cells of the *thyroid*, triggering the release of thyroid hormones.
- **ACTH** (**corticotropin** or **adrenocorticotropic hormone**) is a peptide hormone secreted by **corticotrophs**. It stimulates the release of steroid hormones by the *adrenal cortex*. ACTH targets cells responsible for the release of *glucocorticoids*, which metabolize glucose.
- **Gonadotropins** (e.g., LH and FSH) are peptide hormones, released by **gonadotrophs**, that regulate the activity of the *gonads*.
  - **FSH** (**follitropin** or **follicle-stimulating hormone**) promotes follicle development in females with LH and stimulates the production of *estrogens*.
  - **LH** (**lutropin** or **leutinizing hormone**) induces ovulation in females and stimulates the release of *progestins*. In males, it induces the release of *androgens*, male sex hormones.
- **PRL** (**mammotropin** or **prolactin**) is a peptide hormone secreted by **lactotrophs** to stimulate mammary gland development. In pregnancy, it can stimulate milk production. **Oxytocin**, a hormone released by the posterior pituitary gland, is responsible for milk ejection.
- **GH** (**somatotropin** or **growth hormone**) is a peptide hormone that stimulates cell growth and replication by accelerating protein synthesis. It has two mechanisms: indirect and direct.
  - **Indirect mechanism of GH**: Liver cells respond to GH release by synthesizing and secreting peptide hormones called **somatomedins** and **insulin-like growth factors** (**IGFs**). In turn, these hormones allow for the increased uptake of amino acids and new proteins, causing growth.

- **Direct mechanism of GH**: In epithelial tissue and connective tissue, GH triggers stem cell division and daughter cell differentiation. In adipose tissue, GH increases the lysis of triglycerides This increases the free fatty acid contents of the blood, triggering the glucose-sparing effect. In the liver, GH stimulates glycogen breakdown, releasing glucose into the bloodstream.

- **Melanocyte-stimulating hormone** (**melanotropin** or **MSH**) is a peptide hormone secreted by **melanotrophs**. It's responsible for the creation of melanocytes in the skin, increasing their production of melanin. MSH controls skin pigmentation in reptiles, fish, amphibians, and many mammals. Their role as a pigmentary hormone in humans is complicated and contested.

Anterior pituitary hypersecretory conditions	
GH hypersecretion	Insulin resistance Diabetes mellitus
ACTH hypersecretion	Impaired glucose tolerance Diabetes mellitus
Prolactin hypersecretion	Prolactinoma – higher FPG in small studies Physiological hyperprolactinaemia – insulin resistance?
TSH hypersecretion	Insulin resistance, worsening of diabetes
Anterior pituitary hyposecretory conditions	
Panhypopituitarism	Hypoglycaemia
GH deficiency	Children – insulin sensitivity, fasting hypoglycaemia Adults – insulin resistance
Functional hypogonadotropic hypogonadism	Insulin resistance, impaired glucose tolerance, higher visceral adipose tissue, adverse cardiovascular outcome

Figure 2: Anterior Pituitary Disorder (Source: touchEndocrinology Bhattacharya et al.)

4.2 Posterior Pituitary Gland

The posterior lobe of the pituitary gland (**neurohypophysis**) is responsible for the release of two major hormones: **antidiuretic hormone** (**ADH** or **vasopressin**) and **oxytocin** (**OXT**). It contains the axons of the supraoptic and paraventricular nuclei, which manufacture ADH and oxytocin. These hormones travel along the axons into the posterior lobe, where they enter into capillaries.

- **ADH** is a peptide hormone, tending to act on the kidney, where it facilitates the reabsorption of water into the blood. ADH also plays a role in **vasoconstriction** (narrowing of blood vessels).
  - It is secreted in response to increases in solute concentration in the blood or decreases in blood volume or blood pressure.
  - Specialized neurons, **osmoreceptors**, respond to changes in osmotic concentration of fluids and thus signal neurosecretory cells to release ADH when solute concentrations rise.

- **Oxytocin** is a peptide hormone that has numerous functions. In women, it stimulates smooth muscle contraction of the uterus wall, promoting labor. After birth, it also plays a role in triggering milk ejection. The relationship between oxytocin release and milk ejection is known as the **milk let-down reflex**.

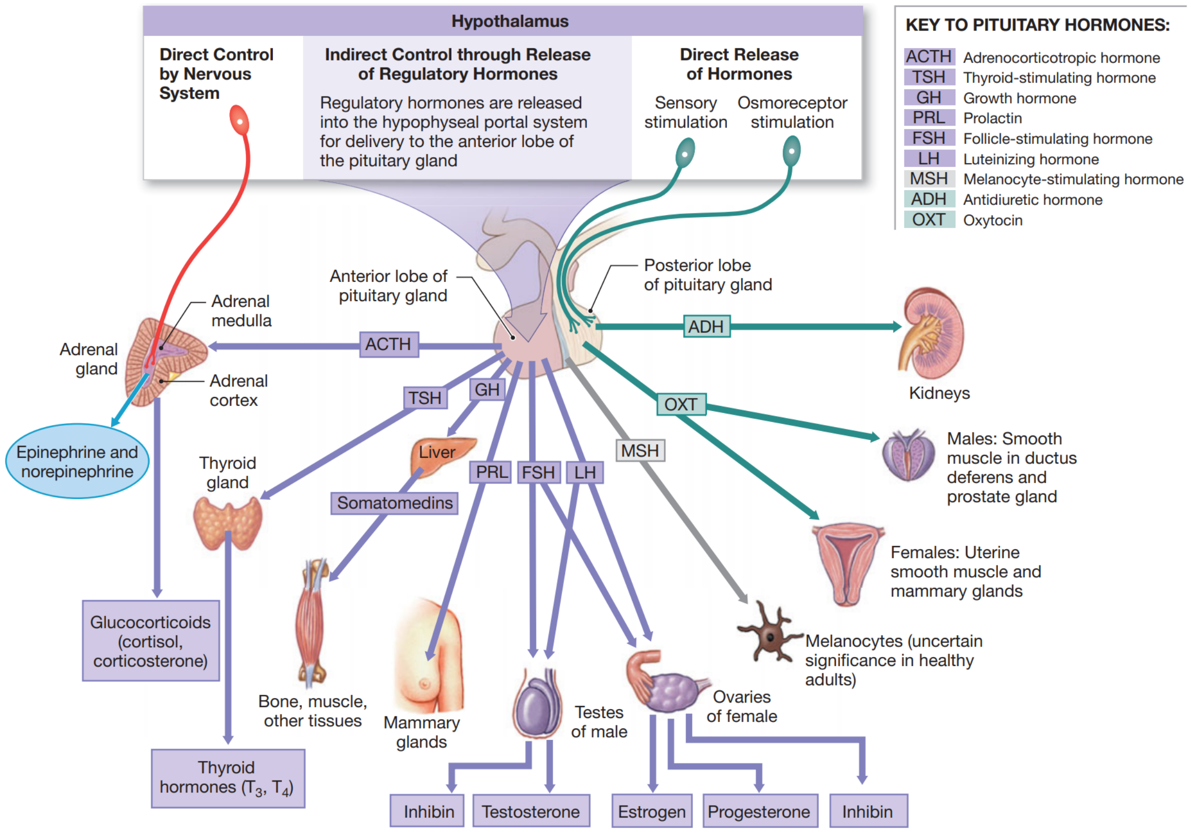

Figure 3: Pituitary Hormones (Source: Frederic Martini Fundamentals of Anat. and Phys.)

Example 4.1 (USABO Semifinals Exam 2011) A patient is diagnosed with a disorder in which the pituitary gland overproduces anti-diuretic hormone (ADH). Which of the following combinations of symptoms would you expect to be associated with this disorder?

A. Reduced urine volume and low blood osmolarity
B. Reduced urine volume and high blood osmolarity
C. Increased urine volume and low blood osmolarity
D. Increased urine volume and high blood osmolarity
E. Increased urine volume with no change in blood osmolarity

Solution: ADH is responsible for the control of water reabsorption. Therefore, overproduction of ADH would cause highly reduced urine volume, as more water is being reabsorbed into the blood. Osmolarity indicates the amount of solute in the water. Since ADH reduces solute concentration, osmolarity would decrease. **The correct answer is A**.

5 Hormones of the Adrenal Gland

The **adrenal gland** plays a major role in the **stress response**. It is situated atop the kidneys and is composed of two endocrine glands, the adrenal cortex and the adrenal medulla. The cortex is the outer portion and the medulla is the inner portion. The medulla consists of neurosecretory cells, whereas the cortex consists of endocrine cells. This forms a network of neuroendocrine and endocrine pathways.

5.1 Adrenal Medulla

The medulla is responsible for the release of two different hormones, which coordinate the "fight or flight response": epinephrine and norepinephrine. The stimulus of a stressor causes the hypothalamus to signal to the adrenal medulla synaptically.

- Epinephrine and norepinephrine fall under the category of catecholamines, which are a subclass of amino acid-derived hormones.
- Catecholamines have a wide-ranging effect on the body. This is made possible by the different types of adrenergic receptors, all of which use G protein-coupled receptors (GPCRs).
  - The adrenergic receptors can be divided into 2 distinct types: alpha and beta receptors.
  - Alpha-1 receptors are generally located on the tunica media of blood vessels and sphincters. Upon binding a catecholamine, they trigger vasoconstriction and smooth muscle contraction. However, it's worth noting that epinephrine tends to have a higher binding affinity to these receptors.
    * The Gq alpha subunit activates phospholipase C, which splits phosphatidylinositol (3,4,5)-trisphosphate (PIP3) into inositol triphosphate (IP3) and diacylglycerol (DAG). This increases intracellular calcium concentration, causing contraction and constriction.
  - Alpha-2 receptors are located on neurons, where they act to inhibit neurotransmitter release. In the pancreas, they inhibit insulin release and cause smooth muscle contraction.
    * The Gi alpha subunit inhibits adenylyl cyclase (AC) and aids in this process. Other Gi subunits open K^+ channels, allowing for hyperpolarization, which helps inhibit neurotransmitter release.
  - Beta-1 receptors are situated on the cells of heart nodes and kidney juxtaglomerular (JG) cells. In the heart nodes, they increase action potential propagation and contractility, thus increasing heart rate. In the kidneys, they increase renin secretion.
  - Beta-2 receptors are located on vascular smooth muscle tissue, skeletal muscles, bronchioles, and the liver. They cause vasodilation (relaxation of blood vessel smooth muscle), bronchodilation (relaxation of bronchiole smooth muscle), and inhibition of insulin secretion, which causes glycogen breakdown and gluconeogenesis.
  - Beta-3 receptors are generally located on adipose tissue, where they act to induce lipolysis.

Receptor Type	Tissue Distribution	Mechanism of Action	Agonist Potency	Physiological Effects	Agonist	Antagonist
α1	Vascular Smooth Muscles, Visceral smooth Muscles	Gq-protein coupled activates Phospholipase C, IP3+DAG	Epi ≥ NE >> Iso	Smooth muscle contractions, Gluconeogenesis, Vasoconstriction	Norepinephrine, Phenylephrine, Methoxamine	Doxazosin, Phentolamine, Prazosin
α2	Pre-synaptic terminals, pancreas, platelets, Ciliary epithelium, Salivary Glands	Gi-protein coupled inhibits Adenyl cyclase	Epi ≥ NE >>Iso	Inhibits release of Neurotransmitter	Clonidine, Monoxidine	Yohimbine, Idazoxan, Tolazoline
β1	Heart, Kidney, some pre-synaptic terminals	Gs-protein coupled activates Adenyl cyclase +PKA	Iso > Epi ≥ NE	Increase heart rate and Renin secretion	Isoproterenol, Norepinephrine, Dobutamine	Propranolol, Metoprolol, Atenolol
β2	Visceral smooth muscles, Bronchioles, Liver, Skeletal Muscles	Gs-protein coupled activates Adenyl cyclase +PKA, Ca-channels	Iso > Epi >> NE	Vasodilation, Bronchodilation, Inhibits insulin secretion	Isoproterenol, Salbutamol, Salmeterol, Albuterol, Formoterol, Terbutaline, Levalbuterol	Propranolol, ICI-118,551, Nadolol, Butoxamine
β3	Adipose Tissue	Gs-protein coupled activates Adenyl cyclase +PKA	Iso = NE > Epi	Increase lipolysis	Isoproterenol, Amibegron, Solabegron	SR59230A

NE: Norepinephrine, **Epi:** Epinephrine and **Iso:** Isoproterenol

Figure 4: Adergenic Receptors. (Source: Sharma et al.)

5.2 Adrenal Cortex

The adrenal cortex responds to stresses that correlate to low blood sugar, decreased blood volume, and decreased blood pressure.

- Once ACTH reaches the adrenal cortex via blood vessels, it stimulates the synthesis and secretion of steroid hormones called corticosteroids.
- Corticosteroids can be further divided into glucocorticoids and mineralocorticoids.
- Glucocorticoids, such as cortisol (e.g., hydrocortisone), make glucose more available by promoting gluconeogenesis in the liver.
- In the skeletal muscles, they prevent glucose uptake by antagonizing insulin release and promoting the breakdown of proteins into amino acids.
- These amino acids are transported to the liver, where glucose is produced.
- When blood sugar levels are in equilibrium, glucocorticoids can suppress the immune system and therefore serves as a functional anti-inflammatory agent.
- Mineralocorticoids maintain salt and water balance. Aldosterone (ALD) maintains ion and water balance within the blood by increasing Na^+ reabsorption and K^+ excretion in the kidney.
- A rise in K^+ levels is very effective in stimulating aldosterone release. In addition, angiotensin II can trigger aldosterone release.

Hormone	Primary Target	Hormonal Effect	Regulatory Control
Mineralocorticoids (primarily aldosterone)	Kidneys	Increase renal reabsorption of Na^+ and water (especially in the presence of ADH) and accelerate urinary loss of K^+	Stimulated by angiotensin II, elevated plasma K^+ or a fall in plasma Na^+; inhibited by ANP and BNP
Glucocorticoids (cortisol [hydrocortisone], corticosterone)	Most cells	Release of amino acids from skeletal muscles and lipids from adipose tissues; promote liver formation of glucose and glycogen; promote peripheral utilization of lipids; anti-inflammatory effects	Stimulated by ACTH from the anterior lobe of the pituitary gland

Figure 5: Cortex Hormones. (Source Martini Fundamentals of Anat. and Phys.)

6 Hormones of the Thyroid and Parathyroid

Below we will discuss the thyroid and parathyroid.

6.1 Thyroid

The thyroid is situated just under the larynx and can be split into three general areas: the isthmus (the bridge between the two lobes), the left lobe, and the right lobe. The thyroid's main function is the regulation of metabolism.

- The thyroid has special endocrine cells called follicle cells.
- In follicle cells, thyroglobulin is synthesized from the amino acid tyrosine and released into storage units known as thyroid follicles.
- TSH stimulates the funneling of I^- into the follicle cells.
- Here, I^- is attached to thyroglobulin. These iodide-attached thyroglobulins are paired to form the thyroid hormones T4 (tetraiodothyronine) and T3 (triiodothyronine).
- T4 and T3 are released into the circulatory system while bound to a variety of carrier proteins. They then act on their target cells to regulate metabolism and bioenergetics.
- They do this by binding to cytoplasmic receptors, increasing ATP synthesis. In addition, they can bind to nuclear receptors, where they alter genetic material to increase the production of enzymes.
- Another hormone secreted by the thyroid is calcitonin, which is carried out by parafollicular (C) cells.
- Calcitonin regulates Ca^{2+} concentration by inhibiting osteoclasts, which slows the release of Ca^{2+} from bones, and by signaling the kidney to release Ca^{2+} from the body.

6.2 Parathyroid

The parathyroid glands are situated on the posterior side of the thyroid gland and are integral in Ca^{2+} regulation. Ca^{2+} regulation is important, as high amounts in the blood can cause organ damage, while low amounts can lead to uncontrollable contraction of skeletal muscle.

- When blood Ca^{2+} levels are low (below 10mg/dL), the parathyroid gland releases parathyroid hormone (PTH).
- In the bones, PTH stimulates the breakdown of the mineralized matrix, releasing Ca^{2+} and phosphate ions.
- In the kidney, PTH stimulates the reabsorption of Ca^{2+} through the renal tubules.
  - It also reduces reabsorption of phosphate to allow for larger amounts of excretion to offset the release when breaking down mineralized matrix.
- In addition, PTH increases calcitriol (vitamin D) synthesis, which increases the absorption of Ca^{2+} in the intestine.
  - Vitamin D synthesis occurs in the skin when UV rays form vitamin D3 from a cholesterol derivative.
  - You can also ingest a form of vitamin D called vitamin D2 from plants.
  - Regardless of the source vitamin D is activated by hydroxylation in the liver by 25 hydroxylase enzyme and then in the liver by 1 hydroxylase to form 1,25dihydroxyvitaminD.
    * In this form vitamin D can stimulate absorption of calcium and phosphate in the liver.

6.3 Metabolic Bone Diseases

- **Rickets** in children or **Osteomalacia** in adults occurs when the bone is insufficiently mineralized, resulting in soft and easily fractured bones. This can occur due to a deficiency in vitamin D.
- **Osteoporosis** occurs during an imbalance of bone secretion to bone absorption due to hormonal levels or more commonly aging. It is more common in women and can be treated with **SERMs**, osteoclast inhibitors like **bisphosphonates**, and estrogen analogs. SERMs interact with estrogen receptors while estrogen analogs act like estrogen. (Read the reproduction handout to understand the effect of estrogen on bones).
- **Hypercalcemia** (high calcium) can be caused by tumor of the parathyroid glands or by **humoral hypercalcemia of malignancy** in which certain cancer cells (like breast cells) release PTH related peptide which is so similar to PTH it acts just like it; in this scenario PTH levels are actually low due to negative feedback. The treatment in this case is to remove the tumor. Lethargy, nausea and vomiting are caused in hypercalcemia because calcium lowers neuron excitability.

- **Hypocalcemia** (low calcium) can be caused by low PTH (as occurs when thyroid removed) and thus low vitamin D too. It can also be caused by PTH resistance in target tissues which is known as **pseudohypoparathyroidism**. **Secondary hyperparathyroidism** occurs when vitamin D fails to be absorbed from the small intestine leading to hypocalcemia and hyperparathyroidism that can result in bone degeneration.
  - Hypocalcemia leads to increased neuron excitability (normal calcium levels stabilize sodium channels, low calcium results in more activation of sodium channels) which can lead to seizures.

Table 18–4 Hormones of the Thyroid Gland and Parathyroid Glands

Gland/Cells	Hormone	Target	Hormonal Effect	Regulatory Control
THYROID GLAND				
Follicular epithelium	Thyroxine (T_4) Triiodothyronine (T_3)	Most cells	Increases energy utilization, oxygen consumption, growth, and development	Stimulated by TSH from the anterior lobe of the pituitary gland
C cells	Calcitonin (CT)	Bone, kidneys	Decreases Ca^{2+} concentrations in body fluids	Stimulated by elevated blood Ca^{2+} levels; actions opposed by PTH
PARATHYROID GLANDS				
Parathyroid (chief) cells	Parathyroid hormone (PTH)	Bone, kidneys	Increases Ca^{2+} concentrations in body fluids	Stimulated by low blood Ca^{2+} levels; PTH effects enhanced by calcitriol and opposed by calcitonin

Figure 6: Thyroid and Parathyroid Hormones. (Source: Martini Fundamentals of Anat. and Phys.)

Example 6.1 (USABO Semifinals Exam 2017) A patient exhibits excessive irritability of the muscles and nerves; even minor stimuli result in tremors, cramps, and convulsions. Blood tests show an abnormally elevated concentration of phosphate and an abnormally low concentration of calcium. These are symptoms of

A. Hyperadrenocorticalism
B. Hyperparathyroidism
C. Hyperthyroidism
D. Hypoparathyroidism
E. Hypothyroidism

Solution: The parathyroid gland is responsible for the regulation of Ca^{2+} concentration. Hypo- indicates a decrease, and parathyroidism indicates a disorder of the parathyroid gland. We can deduce that PTH levels must be decreased and blood Ca^{2+} levels must be low. This would cause uncontrollable muscle contraction explaining the irritability, cramps, and tremors. As a result, **the correct answer is D**.

7 Hormones of the Pineal Gland

- The pineal gland contains specialized cells called pinealocytes. Using serotonin, a neurotransmitter, the pinealocytes synthesize melatonin, which is derived from tryptophan.

- Melatonin is responsible for the regulation of circadian rhythms, inhibition of different reproductive processes, and protection of neurons from free radicals.
- Melatonin levels are generally at their lowest in daylight and increase during nighttime.

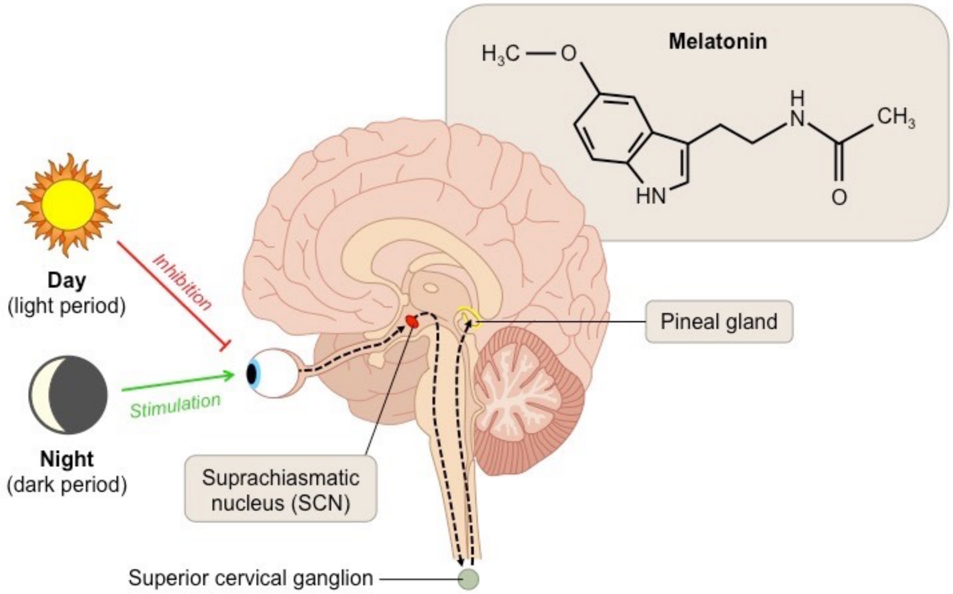

Figure 7: Pineal Physiology (Source: BioNinja)

Example 7.1 (USABO Opens Exam 2017) In order to study the effects of certain hormone deficiencies, you inject a mouse with a tyrosine hydroxylase inhibitor. Since tyrosine hydroxylase catalyzes the rate-limiting step in the synthesis of catecholamines, which one of the following hormones do you expect to NOT be affected:

A. Serotonin
B. Epinephrine
C. Dopamine
D. Norepinephrine
E. None of the above

Solution: If you recall from earlier, epinephrine and norepinephrine are both catecholamines, meaning they can be eliminated as possible answer choices. Dopamine is an amino-acid-derived hormone that is formed from tyrosine. Serotonin is derived from tryptophan and therefore does not utilize tyrosine hydroxylase. Therefore, **the correct answer is A**.

8 Hormones of the Pancreas

The pancreas, which is primarily an exocrine gland, contains clusters of cells known as the islets of Langerhans. They have specialized endocrine cells responsible for releasing distinct hormones. Below, we will focus on insulin and glucagon, as well as the cells that secrete them.

- The pancreas contains many different types of specialized cells.

- Beta cells release insulin and amylin.
- Alpha cells are responsible for glucagon secretion.
- Delta cells secrete somatostatin (this was covered earlier).
- Gamma cells secrete pancreatic polypeptide, which works to reduce appetite.

- Insulin is a peptide hormone responsible for the regulation of circulating blood glucose levels. The hormone acts by binding to transmembrane insulin receptors.
- Beta cells have channels that act as glucose detectors. When circulating blood-glucose levels are elevated (greater than 70-110 mg/dL), insulin is secreted.
- In the skeletal muscles, insulin increases glucose uptake and conversion into glycogen.
- It acts similarly in the liver, but it also inhibits enzymes responsible for glycogen breakdown and inhibits gluconeogenesis (proteins/fats $\rightarrow$ glucose).
- In adipose tissue (fat cells), insulin calls for the uptake of glucose for lipogenesis (fat synthesis).
- It also allows for the uptake of amino acids for conversion into proteins.
- Glucagon is a peptide hormone that plays a role in increasing blood glucose levels.
- It acts on the liver and skeletal muscles, where it promotes the breakdown of glycogen into glucose.
- It also promotes lipolysis (fat breakdown)

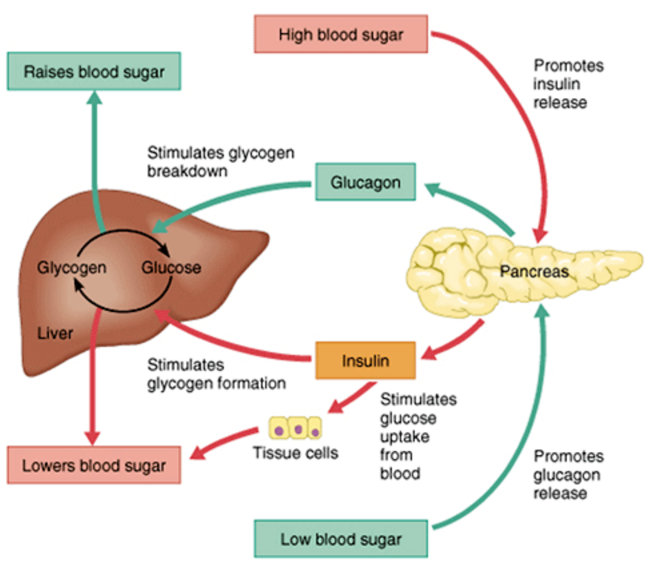

Figure 8: Insulin/Glucagon and Homeostasis (Source: ATrain Education)

9 Hormones of the Gonads

The gonads (testes in males and ovaries in females) are responsible for the growth and development of sexual characteristics, maintenance of reproductive cycles, and coordination of sexual behavior. They produce and secrete androgens, estrogens, and progesterone.

9.1 Testes

- The testes primarily produce and release androgens, the main one being testosterone. In developing males, it functions to promote the development of male reproductive structures.
- It also helps the development of CNS structures, particularly the hypothalamic nuclei, which are involved in sexual behaviors.
- The testes contain specialized cells called nurse cells that are responsible for many things.
- Under FSH stimulation, these cells secrete inhibin, which inhibits GnRH and FSH secretion.
- In puberty, androgens are responsible for the development of secondary sex characteristics. High androgen concentrations can cause lengthening and thickening of vocal cords, increases in hair growth, and increases in muscle and bone mass.

9.2 Ovaries

- Estrogens, the most important being estradiol, are responsible for the maintenance of the female reproductive system. It is generally produced by the ovaries through LH and FSH stimulation.
- Inhibin is also produced by the ovaries and functions similarly to the male inhibin system.
- Progesterone and other progestins are involved in maintaining tissues of the mammalian uterus while also supporting the growth and development of embryos.
- They are stimulated by LH, which is secreted by the anterior pituitary gland.

Structure/Cells	Hormone	Primary Target	Hormonal Effect	Regulatory Control
TESTES				
Interstitial cells	Androgens	Most cells	Support functional maturation of sperm, protein synthesis in skeletal muscles, male secondary sex characteristics, and associated behaviors	Stimulated by LH from the anterior lobe of the pituitary gland
Nurse cells	Inhibin	Pituitary gland	Inhibits secretion of FSH	Stimulated by FSH from the anterior lobe
OVARIES				
Follicular cells	Estrogens	Most cells	Support follicle maturation, female secondary sex characteristics, and associated behaviors	Stimulated by FSH and LH from the anterior lobe of the pituitary gland
	Inhibin	Pituitary gland	Inhibits secretion of FSH	Stimulated by FSH from anterior lobe
Corpus luteum	Progestins	Uterus, mammary glands	Prepare uterus for implantation; prepare mammary glands for secretory activity	Stimulated by LH from the anterior lobe of the pituitary gland

Figure 9: Gonad Hormones (Source: Martini Fundamentals of Anat. and Phys.)

10 Neuroendocrine Coordination in Invertebrates

- Within invertebrates, molting is carried out by a common neuroendocrine pathway.
- Neurosecretory cells within the brain produce a peptide hormone known as prothoracicotropic hormone (PTTH), which is transported through body fluids.

- PTTH signals for the prothoracic gland to secrete another hormone, ecdysteroid.
- Bursts of this hormone stimulate each successive molt. However, ecdysteroid also controls metamorphosis.
- Due to the dual functionality of ecdysteroids, another signaling hormone plays a role in the control of metamorphosis, juvenile hormone (JH).
- JH is secreted by a pair of endocrine glands situated on the posterior side of the invertebrate brain.
- JH levels regulate the activity of ecdysteroids. For instance, when JH levels are high, ecdysteroids trigger molting. However, when JH levels are low, it induces pupa formation and thus metamorphosis.

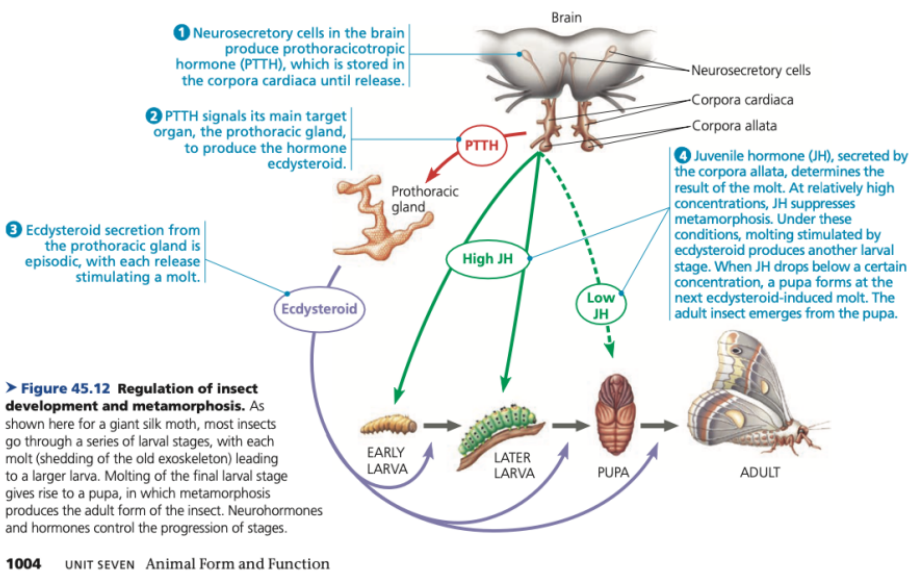

Figure 10: Invertebrate Neuroendocrine Pathway (Source: Campbell Biology)

11 Conclusion

Understanding how the endocrine system functions and contributes to homeostasis is crucial to establishing a fundamental understanding of many of the other organ systems. All of these hormones are quite difficult to memorize, so I recommend using Quizlet or Anki to help. I hope you enjoyed reading this handout and I wish you the best of luck on the USABO exams (if you're taking them).

- **Rithik Sogal**