**Exercise Physiology: Endocrine System**

**Key Terms**

**Adrenaline:** epinephrine; a hormone secreted by the adrenal glands, especially in conditions of stress, increasing rates of blood circulation, breathing, and carbohydrate metabolism and preparing muscles for exertion.

**Antidiuretic Hormone (ADH):** vasopressin; A small (peptide) molecule released by the pituitary gland after being made in the hypothalamus; has antidiuretic action that prevents production of dilute urine; regulates and balances the amount of water in your blood.

**Catecholamines:** any of a group of chemically related neurotransmitters, as epinephrine and dopamine, that have similar effects on the sympathetic nervous system.

**Downregulation:** A decrease in the number of receptors on the surface of target cells, making the cells less sensitive to a hormone or another agent.

**Glucagon:** a hormone secreted by the pancreas that acts in opposition to insulin in the regulation of blood glucose levels; raises concentration of glucose in the bloodstream in response to low blood glucose levels by:

- Stimulating the liver to break down glycogen to be released into the blood as glucose
- Activating **glycogenolysis**, conversion of glycogen into glucose
- Breaking down stored fat (triglycerides) into fatty acids for use as fuel by cells

**Hemoconcentration:** Decrease in the volume of plasma in relation to the number of red blood cells; increase in the concentration of red blood cells in the circulating blood.

**Hemodilution:** decreased concentration of cells and solids in the blood resulting from gain of fluid.

**Hyperglycemia:** high blood glucose as a result of too little insulin.

**Hypoglycemia:** low blood glucose (low blood sugar); symptoms include being tired, disoriented, hungry, having a headache, and in severe cases, convulsions.

**Insulin:** promotes the storage of glucose and the uptake of amino acids, increases protein and lipid synthesis, and inhibits lipolysis and gluconeogenesis.

- A rise in plasma glucose (increase in blood glucose) releases insulin, which increases glucose uptake by cells (to reduce the concentration of glucose in the blood).
- Specific target tissues are muscle, fat, and liver.
- Increases the number of glucose receptors in the membrane; muscle and fat cells contain a type of insulin-sensitive glucose transporter protein called GLUT-4.
Exercise physiology involves the mobilization of glucose transporters of muscle cells. Increased muscle activity during exercise promotes the formation of new GLUT-4 glucose transporters, thus increasing the ability of muscle cells to take up plasma glucose.

**Renin**: enzyme synthesized, stored, and secreted by the kidneys; catalyzes the conversion of angiotensinogen to angiotensin I, which is then converted to angiotensin II, leading to widespread vasoconstriction and elevation of blood pressure and aldosterone release.

**Second Messenger**: a chemical substance inside a cell that carries information farther along the signal pathway from the internal part of a membrane-spanning receptor embedded in the cell membrane.

**Thyrotropin (TSH)**: an anterior pituitary hormone that regulates the activity of the thyroid gland (considered a tropic hormone); promotes the secretion of thyroxine.

**Upregulation**: cell temporarily increases the number of receptors available to bind to the hormone (thereby increasing the probability of the formation of a hormone-receptor complex) and increases the cell's sensitivity to the hormone.

**Aldosterone**: hormone secreted by the adrenal cortex involved in regulation of plasma salts (Na⁺ and K⁺), blood pressure, and blood volume.

- Regulates plasma salts by acting on kidney tubules, stimulating the tubules to synthesize new protein molecules which enhance reabsorption of Na⁺ from kidney tubules for use in plasma.
- Aldosterone action on Na⁺ indirectly decreases plasma K⁺ levels by promoting K⁺ secretion into the kidney tubules (decreases K⁺ levels in plasma by increasing secretion of this ion in urine).
- A decrease in Na⁺ and increase in K⁺ in plasma → Aldosterone release.
- Aldosterone works to maintain Na⁺ levels in plasma as Na⁺ is important for the excitability of nerves and muscles, and it regulates plasma and extracellular water volume for blood pressure.

**Cortisol**: hormone from the adrenal cortex that promotes gluconeogenesis and lipolysis to increase blood glucose.

**Epinephrine**: adrenaline; hormone produced by the adrenal medulla in response to “fight or flight” and it increases blood pressure, increases heart rate and cardiac output, increases glycogenolysis (glycogen → glucose) and the release of glucose from the liver; acts mainly on the heart.

- Norepinephrine acts on the arterioles in the visceral organs to cause their vasoconstriction (shunts blood to exercising muscles and heart).

**Glucocorticoids**: cortisol and other similar hormones produced by the adrenal cortex. The glucocorticoids suppress inflammation and convert amino acids from protein breakdown into glucose (gluconeogenesis), thus raising the blood sugar levels. Their effect is antagonistic to that of insulin.

**Mineralcorticoids**: aldosterone and other similar hormones produced by the adrenal cortex that regulate the balance of water and electrolytes in the body (Na⁺ and K⁺ balance).
**Angiotensin-Converting Enzyme (ACE):** Angiotensin I $\rightarrow$ Angiotensin II; ACE released from lungs

**Renin-Angiotensin-Aldosterone Mechanism:** Renin, a hormone protein, splits angiotensinogen $\rightarrow$ angiotensin I $\rightarrow$ angiotensin II $\rightarrow$ releases aldosterone

- A decrease in blood pressure (caused by decreased sodium intake or blood loss) is detected by the kidneys which stimulate the release of renin
- Angiotensin increases blood pressure by causing vasoconstriction

**Renin-angiotensin system**

[Diagram of the renin-angiotensin system showing the pathways and interactions involved in the renin-angiotensin-aldosterone system.

**Steroid Hormone:** lipid soluble, most are formed from cholesterol, bind to intracellular receptors

**Nonsteroid Hormone:** proteins, amino acids, peptides that bind to a membrane bound receptor which initiates a secondary messenger to amplify the signal

**Thyroxine (T4):** hormone of the thyroid gland that influences metabolic rate; growth and development; metabolism of carbohydrates, fats, proteins, electrolytes, and water

- Increases metabolic rate by increasing the rate of oxygen consumption and heat production in body tissues including the heart, muscles, and visceral tissues
- T4 is converted to T3 (Triiodothyronine) in target cells as T3 is the active hormone
Cyclic Adenosine Monophosphate (cAMP): a cyclic nucleotide involved in the action of many hormones, including catecholamines, ACTH, and vasopressin. The hormone binds to a specific receptor on the cell membrane of target cells. This activates an enzyme, adenylate cyclase, which produces cyclic AMP from ATP. Cyclic AMP acts as a second messenger activating other enzymes within the cell.

Direct Gene Activation: used by steroid hormones to cause protein synthesis; hormone-receptor complex binds directly to DNA.

Growth Hormone (GH): any of several related polypeptide hormones secreted by the anterior lobe of the pituitary gland that directly influence protein, carbohydrate, and lipid metabolism and control the rate of skeletal and visceral growth; their secretion is in part controlled by the hypothalamus.

Hormone: chemical messengers that are manufactured by the endocrine glands, travel through the bloodstream, and affect other tissues.

Inhibiting Factors/Hormones: hormones that control other hormones by inhibiting their release. Examples include certain tropic hormones and hypothalamic hormones.

Releasing Factors/Hormones: hormones that control other hormones by stimulating their release.

- Ex) hypothalamus uses thyrotropin-releasing hormone (TRH) to tell the pituitary to release more thyrotropin, which regulates thyroxine.

Target Cells: any cell having a specific receptor that reacts with a specific hormone.
Study Questions

1. What is an endocrine gland? What are the functions of hormones?

   - **Endocrine Gland**: A group of cells or an organ that secretes hormones directly into the blood where they act as chemical signals throughout the body
   - **Hormones**: Chemical messengers that are manufactured by the endocrine glands, travel through the bloodstream, and affect other tissues; regulate cell/organ activity

2. Explain the difference between steroid hormones and nonsteroid hormones in terms of their actions at target cells.

   - **Steroid hormones** can pass through cell membranes and bind to receptors inside the cell, they use a mechanism called direct gene activation (hormone receptor binds to DNA) to initiate protein synthesis. Intracellular receptors are located within the nucleus and are considered inactive when not bound with ligand (hormone).
   - **Nonsteroid hormones** are proteins and cannot diffuse through the cellular membrane, so they bind to membrane-bound receptors. These receptors are located on the target cells’ plasmalemma and are linked to a second messenger (carry out hormone effects, intensify strength of hormone signal). The cellular response is ‘turned on’ when the hormone binds to the membrane-bound receptor, which initiates a second messenger via pre-existing signal transduction pathways within the cell.

   - **Cascade of events that result in actions of steroid hormones at target cells**
     - 1. Entrance of hormone into cell via simple diffusion
     - 2. Formation of hormone-receptor complex
     - 3. Hormone-Receptor complex attaches to a gene in the nucleus and stimulates protein synthesis
     - * Since the mechanisms of action of intracellular endocrine receptors involves the management of protein production, the biological activities stimulated by steroid hormones are typically slow to occur and are long lasting (actions of target cell by steroid hormones are slow to occur but last long bc of the use/influence of proteins)

   - **Nonsteroid hormones** are proteins and cannot diffuse through the cellular membrane, so they bind to membrane-bound receptors. These receptors are located on the target cells’ plasmalemma and are linked to a second messenger (carry out hormone effects, intensify strength of hormone signal). The cellular response is ‘turned on’ when the hormone binds to the membrane-bound receptor, which initiates a second messenger via pre-existing signal transduction pathways within the cell.
     - 1. Hormone binds to a membrane receptor
     - 2. The Hormone-Receptor complex activates adenylate cyclase
     - 3. Adenylate Cyclase activates cAMP
     - 4. cAMP activates protein kinase, which leads to a response
     - Hormone → Hormone-receptor complex → Adenylate Cyclase → active cAMP → protein kinase → response
     - Ex) hormone Epinephrine binds to receptor on the surface of a heart cell → hormone-receptor complex activates adenylate cyclase → activates cAMP → protein kinase → response (increases heart rate and contractility)
3. **How can hormones have very specific functions when they reach nearly all parts of the body through blood?**

- Even though endocrine glands may release hormones into the bloodstream where they come into contact with all tissues of the body, the hormone will only act on those cells that have receptors specific to that hormone.
- Each receptor has a 3D structure complimentary to the structure of a specific hormone, allowing the hormone and receptor to recognize each other due to their complimentary chemical structures (specificity).
  - 2 hormones with similar chemical structures can cross-react with each other’s receptors, though cross-reactivity is minimal and resultant cellular activity is negligible due to its low affinity binding.
- **Affinity**: strength of the bond formed between hormone and its receptor; determines how easily the bond may be broken.
  - High affinity requires more disturbance to break the bonds.
- **Saturation**: fraction of target cell’s receptors that are bound to hormone, depends on concentration of unbound circulating hormone – the greater the amount of hormone available to the target, the greater the probability that receptor sites will be occupied by hormone.
  - Affinity of receptors for that hormone.
- Not all of the cell’s receptors for that hormone are bound at maximal biological response:
  - 100% occupancy of receptors is NOT necessary to elicit maximal biological response.
  - “Overexpression” of receptors, or spare receptors, are necessary as the formation of hormone receptor complexes are dependent on the probability of the two bonding.
  - **No forces of attraction that bring complimentary hormones and receptors together; affinity sustains the bonds once formed**.
- **Redundancy**: same cell may respond to more than one hormone which affects the same biological process within the cell.
- Target cells express receptors for a host of different hormones so that various cellular functions regulated by the endocrine system can occur.

4. **How are the plasma concentrations of specific hormones controlled? (Regulation of Hormones)**

- **Self-Regulatory**: blood hormone level and the physiological parameter regulated by it interact automatically to maintain hormone secretion within predetermined and set limits.
  - Feedback control: output exerts control over the input
    - **Negative Feedback**: relationship between the output and input is inverse; ensures equilibrium and aims to maintain the system at a desired set point.
    - **Positive Feedback**: relationships between output and input are direct; creates disequilibrium and a vicious cycle.
- **Simple Hormonal Regulation**: secretion of hormone from endocrine gland is controlled directly (through negative feedback) by plasma concentration of the physiological variable the hormone is regulating
  - Endocrine gland cell $\rightarrow$ hormone $\rightarrow$ target cells $\rightarrow$ effect of hormone

- **Complex Hormonal Regulation**: activity of one endocrine gland is controlled by hormones of another gland; typically the pituitary gland controls other glands through tropic hormones
  - Pituitary effects conveyed by **tropic hormones** $\rightarrow$ stimulate target glands to secret own hormones and exert negative feedback on pituitary to inhibit the secretion of their respective tropic hormones
  - Pituitary $\rightarrow$ tropic hormone $\rightarrow$ endocrine gland $\rightarrow$ hormone $\rightarrow$ hormonal effects

- Nervous system can override the self-regulatory system to initiate new hormonal responses or set new baselines for hormonal secretion
  - Hypothalamus exerts direct effects on secretion of some endocrine glands by modifying activity of sympathetic and parasympathetic nerves (which innervate these glands)

5. **Define the terms upregulation and downregulation. How do target cells become more or less sensitive to hormones?**

- **Upregulation**: the cell temporarily increases the number of receptors available to bind to the hormone (thereby increasing the probability of the formation of a hormone-receptor complex) and increases the cell’s sensitivity to the hormone

- **Downregulation**: the cell temporarily decreases the number of receptors available to bind to hormone (this decreases the probability of a hormone-receptor complex forming) and dampens the cell’s sensitivity to the hormone thereby maintaining its own homeostasis
  - Allows the target cell to respond in a way beneficial to its needs

- Target cells become less sensitive to hormones when an increased volume of a specific hormone decreases the number of cell receptors available to it; with fewer receptors there are fewer hormone molecules that can bind

- Target cells become more sensitive to hormones when there is a prolonged presence of large amounts of a hormone or the number of available receptors increases

6. **What are secondary messengers and what role do they play in hormonal control of cell function?**

- Secondary messengers are signal relaying molecules that help intensify the strength of the signal and can trigger numerous cellular processes. The first messenger is the hormone itself, which binds to its receptor.
7. **Briefly outline the major endocrine glands, their hormones, and the specific action of these hormones.**

- Hypothalamus: releases hormones/factors that simulates pituitary to release its hormones
- Pituitary
  - Antidiuretic Hormone (ADH): redirects water from the kidneys to the blood to increase the concentration of water in the blood; conservation of water
- Thyroid
  - Thyroxin (T4): hormone of the thyroid gland that influences metabolic rate and is regulated by thyrotropin
- Adrenals
  - Outer Adrenal Cortex
    - Aldosterone: regulates plasma salts, especially for reabsorption of Na\(^+\) into plasma from kidneys
    - Cortisol: steroid hormone secreted in response to stress, as it promotes gluconeogenesis (catabolizes proteins \(\rightarrow\) amino acids \(\rightarrow\) glucose) and increases blood glucose
  - Inner Adrenal Medulla: part of the sympathetic NS
    - Sympathetic stimulation increases secretion of epinephrine and norepinephrine (hormones that prepare the body for stressful situations, though exercise can bring about similar responses)
      - Increased heart activity and blood pressure (need for O\(_2\) and nutrients)
      - Bronchiolar dilation, vasodilation of blood vessels to heart and exercising muscles, and shunting of blood in inactive muscles
- Pancreas
  - Insulin: Decreases blood sugar; glucose \(\rightarrow\) glycogen; cellular up-take of glucose; conversion of excess glucose to fat
  - Glucagon: Increase blood sugar; glycogenolysis (glycogen \(\rightarrow\) glucose)

8. **Which of the hormones outlined in question 7 are of major significance during exercise?**
<table>
<thead>
<tr>
<th>Gland/Hormone</th>
<th>General</th>
<th>Exercise</th>
<th>Carb Metabolism</th>
</tr>
</thead>
</table>
| Thyroid T3 and T4   | ▪ Increases rate of metabolism  
▪ Increases rate and contractility of heart | Increases with increased rates of work         |                                                                                  |
| Adrenal Medulla     | ▪ Stimulates breakdown of glycogen in liver and muscle  
▪ Stimulates lipolysis in adipose tissue and muscle  
▪ Increases skeletal muscle bloodflow  
▪ Increases heart rate and contractility  
▪ Increases oxygen consumption | Increases with increased rates of work starting at about 70% VO2 max | ▪ Liver releases more glucose than is being taken up by muscles  
▪ Muscle uses its glycogen stores before using plasma glucose |
| Epinephrine         | ▪ Constricts arterioles and venules  
▪ Stimulates lipolysis in adipose tissue and muscle to a lesser extent than E | Increases with increased rates of work starting at about 50% VO2 max | Shunting of blood (increases flow of blood to working muscles by decreasing blood to inactive muscles) |
| Adrenal Medulla     | ▪ Constricts arterioles and venules  
▪ Stimulates lipolysis in adipose tissue and muscle to a lesser extent than E | Increases with increased rates of work starting at about 50% VO2 max | Shunting of blood (increases flow of blood to working muscles by decreasing blood to inactive muscles) |
| Norepinephrine      | ▪ Constricts arterioles and venules  
▪ Stimulates lipolysis in adipose tissue and muscle to a lesser extent than E | Increases with increased rates of work starting at about 50% VO2 max | Shunting of blood (increases flow of blood to working muscles by decreasing blood to inactive muscles) |
| Pancreas Insulin    | ▪ Lowers blood glucose  
▪ Increases use of glucose and synthesis of fat | Decreases with increased rates of work  
▪ Muscle cell’s sensitivity to insulin increases (upregulation) | Slight increase in plasma glucose |
| Pancreas Glucagon   | ▪ Increases blood glucose  
▪ Stimulates breakdown of protein and fat | Increases with increased rates of work  
▪ Increases significantly after 15-20 min of exercise |                                                                                  |
| (target organ = liver) |                                                                                  |                                                                                  |                                                                                  |
| Adrenal Cortex      | ▪ Controls metabolism of carbs, fats, and proteins  
▪ Anti-inflammatory | Increases only at high rates of work and long duration  
▪ Increases at 30 min until around 2 hours of exercise |                                                                                  |
| Cortisol            |                                                                                  |                                                                                  |                                                                                  |
| Growth Hormone      | ▪ Increases rate of protein synthesis | Increases with increasing work rate | Decreases rate of carb use as for long duration |
9. What hormones are involved in regulation of metabolism during exercise? How do they influence the availability of carbohydrates and fats for energy during exercise lasting for hours?

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Intensity (high) &gt; 70% VO2 Max</th>
<th>Duration (several hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Decrease or stay the same</td>
<td>Decrease or stay the same</td>
</tr>
<tr>
<td>Glucagon</td>
<td>Increase bc the body needs glucose (glycogen → glucose)</td>
<td>Increase but at less of a rate as secretion of this hormone will begin to plateau</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Increase bc body needs glucose; fast energy (glycogen → glucose)</td>
<td>Increase but at less of a rate (begin to plateau)</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>Increase bc it increases blood glucose and bc it increases blood flow to working muscle</td>
<td>Increase but at less of a rate (begin to plateau)</td>
</tr>
<tr>
<td>Cortisol</td>
<td>Increase if duration is long enough as it increases blood glucose by gluconeogenesis (amino acids + fats → glucose)</td>
<td>Increase with greater than 30 minutes of exercise (don't need it prior to 30 min bc the other hormones meet initial energy needs)</td>
</tr>
</tbody>
</table>

10. Describe the hormonal regulation of fluid balance during exercise.

- **ADH**: regulates plasma water (water in the blood) as well as blood volume and pressure
  - Released/secreted when the blood has an increase in the concentration of plasma sodium ions (more “solids” in blood than water)
    - secreted by the posterior pituitary (extension of the hypothalamus) which mainly consists of nerve fibers; nervous stimulation causes the release of ADH – an example of how the nervous system regulates/influences the endocrine system
  - Increases the permeability of kidney collecting ducts to water (increases water channels in kidneys; aquaporins) so that water moves by osmosis from kidney ducts into the plasma, which increases the amount of water in the blood
  - ADH redirects water from the kidneys to the blood to increase the concentration of water in the blood, activated in response to decreased water in the blood due to activities such as sweating; water retention to prevent dehydration
- **Aldosterone**: regulates plasma salts by acting on kidney tubules, stimulating the tubules to synthesize new protein molecules which enhance reabsorption of Na⁺ from kidney tubules for use in plasma. As Na⁺ goes to the blood, water follows, thus aldosterone increases blood volume.

**The Hormones During Exercise**

![Graph showing hormone levels during exercise](image)

**Sources**

- [https://www.premedhq.com/major-endocrine-glands](https://www.premedhq.com/major-endocrine-glands)
- [http://www.diabetes.co.uk/body/glucagon.html](http://www.diabetes.co.uk/body/glucagon.html)
- Medical Dictionary