Section 04: The Endocrine System

Chapter 20 – The Endocrine System: Organization and Acute and Chronic Responses to Exercise

HPHE 6710 Exercise Physiology II
Dr. Cheatham

Chapter 20

The Endocrine System: Organization and Acute and Chronic Responses to Exercise
**Chapter Objectives**

- Understand the general mechanisms of action for hormones
- Understand the functions and control of the major hormones
- Understand the hormonal responses to acute exercise
- Understand the effects of exercise (endurance and resistance) on hormone levels

**Endocrine System Overview**

- Glands
  - Pituitary
  - Thyroid
  - Parathyroid
  - Adrenal
  - Pineal
  - Thymus
- Also areas of the
  - Pancreas
  - Gonads
  - Hypothalamus
Endocrine System Organization

- Endocrine system consists of:
  1. Host organ (gland)
  2. Chemical messenger (hormone)
  3. Target organ

- Endocrine (hormone secreting) gland
  - Possess no ducts
  - Hormone is secreted directly into the extracellular space around the gland, diffuses into blood, and is transported to target organ

- Exocrine
  - Contain secretory ducts that carry substances directly to a specific compartment or surface
Endocrine System Organization

• Types of hormones
  – Steroid-derived hormones
  – Amino acid–synthesized hormones
    – Amine
    – Polypeptide
  • Soluble in blood (i.e. water soluble)

  • Half-Life
    • Time required to reduce a hormone’s blood concentration by half

Endocrine System Organization

Table 20.1

<table>
<thead>
<tr>
<th>Peptide Hormones</th>
<th>Steroid Hormones</th>
<th>Catecholamines</th>
<th>Thyroid Hormones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Examples</td>
<td>Androgens, OHE,</td>
<td>Epinephrine,</td>
<td>Thyroxine (I)</td>
</tr>
<tr>
<td></td>
<td>protein, ACTH</td>
<td>norepinephrine</td>
<td></td>
</tr>
<tr>
<td>Synthesis and</td>
<td>Made in advance;</td>
<td>Made in advance;</td>
<td></td>
</tr>
<tr>
<td>Storage</td>
<td>stored in secretory vesicles</td>
<td>stored in secretory vesicles</td>
<td></td>
</tr>
<tr>
<td>Release from</td>
<td>Simple diffusion</td>
<td>Exocytosis</td>
<td>Simple diffusion</td>
</tr>
<tr>
<td>Parent Cell</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transport Medium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifespan</td>
<td>Short</td>
<td>Long</td>
<td>Short</td>
</tr>
<tr>
<td>(half-life)*</td>
<td>Dissolved in plasma</td>
<td>Bound to carrier proteins</td>
<td>Dissolved in plasma</td>
</tr>
<tr>
<td>Receptor Location</td>
<td>On cell membrane</td>
<td>Cytosol or nucleus; some have membrane receptors</td>
<td>On cell membrane</td>
</tr>
<tr>
<td>Response to</td>
<td>Activation of second messenger system; may activate genes</td>
<td>Activation of second messenger systems</td>
<td>Activation of second messenger systems</td>
</tr>
<tr>
<td>Receptor-Ligand</td>
<td></td>
<td></td>
<td>Activation of second messenger systems; may activate genes</td>
</tr>
<tr>
<td>Binding*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Target</td>
<td>Modification of existing proteins and induction of new protein synthesis</td>
<td>Induction of new protein synthesis</td>
<td>Induction of new protein synthesis</td>
</tr>
<tr>
<td>Response</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Process in which intracellular vesicles fuse with the cell membrane and release their contents into the extracellular fluid.

*Half-life is the time required to reduce hormone concentration by one half.

*Sign that binds to receptors; may activate genes or trigger intracellular signaling pathways.

Copyright © 2007 Lippincott Williams & Wilkins.
Endocrine System Organization

Endocrine System Organization

**Hormone-Target Cell Specificity**

- Hormones alter cellular reactions of specific target cells by
  - Stimulating DNA to alter rate of protein synthesis
  - Altering rate of enzyme activity
  - Altering plasma membrane transport via second messengers
  - Inducing secretory activity
Endocrine System Organization

• Hormone-Target Cell Specificity
  – Hormone-Receptor Binding
    • The first step in initiating hormone action
    • Target cells activation by a hormone is dependent on:
      – Hormone concentration in blood
      – Sensitivity of receptor for the hormone
        » Upregulation
          • Target cells form more receptors in response to increasing hormone levels
        » Downregulation
          • Loss of receptors (i.e. sensitivity) due to prolonged exposure to high hormone concentrations
      – Number of target cell receptors

Endocrine System Organization

• Hormone-Target Cell Specificity (cont’d)
  – Hormone-Receptor Binding
    • Cyclic AMP: Intracellular Messenger
      – Binding of amine-based hormones to receptor sites may activate the enzyme adenylate cyclase.
      – Adenylate cyclase catalyzes the degradation of ATP to cyclic 3'5' adenosine monophosphate (cyclic AMP).
      – Cyclic AMP then acts to activate protein kinases that alter cellular activity.

[Image of cyclic AMP pathway]
Hormone-Target Cell Specificity (cont’d)

- Effects on Enzymes
  - Enzyme activity may be altered in one of three ways.
    - Stimulate enzyme production
    - Allosteric modulation
    - Activating inactive forms of the enzyme

Factors that Determine Hormone Levels

- Quantity synthesized in the host gland
- Rate of catabolism or secretion into blood
- Quantity of transport proteins present (for some but not all hormones)
- Changes in plasma volume

- Secreted amount:
  - Refers to the plasma concentration of a hormone
  - Is a function of “Addition” and “Removal”
Endocrine System Organization

- Patterns of Hormone Release
Anterior Pituitary Hormones

- Used to be termed the “Master Gland”
- Now we know that the hypothalamus actually controls anterior pituitary activity

- Releasing Factors

**Growth Hormone (GH)** (somatotropin)

- Direct actions (growth stimulation)
- Indirect actions (growth stimulation)
- Liver and cellular effects
- Somatomedins
- Causes secretion of insulin and glucagon
- Increases synthesis of protein and new cell growth
Resting and Exercise-Induced Endocrine Secretions

Anterior Pituitary Hormones

• Growth Hormone (cont’d)
  – Response to Acute Exercise
    • Acute PA causes an increase in GH
  – Response to Chronic Exercise (Training)
    • Trained vs. Sedentary show similar increases in GH during exercise to exhaustion
    • At a given submaximal workload, sedentary have higher GH levels
      – GH more related to relative intensity (%VO₂max) of exercise

• Insulin-Like Growth Factors (IGF)
  – Synthesized by liver
  – Mediate many of GH effects
  – Travel in blood attached to binding proteins

• Thyrotropin (TSH)
  – Controls hormone secretion by the thyroid gland
    • Thyroid hormones help to regulate overall body metabolism
  – Response to Exercise
    • It would be expected that TSH would increase during exercise but this is not consistently observed
**Adrenocorticotropic Hormone (ACTH)**

- Functions:
  - Regulates adrenal cortex release of hormones
    - Part of Hypothalamic-pituitary-adrenal axis
  - Acts directly to increase FA mobilization, increase gluconeogenesis, stimulate protein catabolism
- Control:
  - CRH from hypothalamus (diurnal)
  - AVP inhibits ACTH
- Exercise:
  - May increase proportionally with exercise intensity if intensity exceeds 25% VO\(_{2\text{max}}\)

**Prolactin (PRL)**

- Functions:
  - Initiates and supports milk secretion
  - Female sexual functions
- Exercise:
  - Increase with high intensity exercise and return to baseline within 45 minutes of recovery
  - Increases in men following maximal exercise - ??
Resting and Exercise-Induced Endocrine Secretions

Anterior Pituitary Hormones

• Gonadotropic Hormones
  – Follicle Stimulating Hormone (FSH)
    • Initiates follicle growth in ovaries
    • Stimulates sperm production
    • Stimulates estrogen production
  – Luteinizing Hormone (LH)
    • Estrogen secretion, rupture of follicle
    • Stimulates secretion of testosterone
  – Exercise
    • Response is unclear
    • LH levels are thought to increase before exercise

Resting and Exercise-Induced Endocrine Secretions

• Posterior Pituitary Hormones
  • Outgrowth of the hypothalamus (resembles true neural tissue)
  • Does not “produce” hormones, but rather stores hormones that are produced by the hypothalamus
  – Oxytocin
    • Initiates muscle contraction in the uterus and milk ejection
Resting and Exercise-Induced Endocrine Secretions

Posterior Pituitary Hormones

- Anti-Diuretic Hormone (ADH) (Arginine Vasopressin (AVP))
  - Functions:
    • Increases water reabsorption by the collecting ducts of the kidneys
    • May also increase sodium reabsorption by kidneys
  - Control:
    • Responds to dehydration (increase in plasma osmolality)
    • Responds to blood pressure
    • Probably stimulated by AGII
  - Exercise:
    • Increases with exercise and exercise intensity

Figure 2.14: The mechanism by which antidiuretic hormone (ADH) conserves body water.
Thyroid Hormones
- Thyroxine (T₄) and triiodothyronine (T₃)
  - Major Functions:
    - Regulators of metabolism
    - Tissue growth and development
    - Maintaining blood pressure
  - Control:
    - TSH (hypothalamus), thyrotropin (AP)
  - Exercise:
    - Increases ~ 35% (T₄)
    - Role (unclear)

Parathyroid Hormones
- Low blood calcium concentration
- PTH release from parathyroid gland
- Activates osteoclasts; calcium and phosphorus released to blood
- Vitamin D activation
- Increased calcium uptake by intestinal mucosa
- Rise in blood calcium concentration
- Thyroid gland (anterior view)
- Parathyroid glands
- Thyroid gland (posterior view)
- Larynx (anterior view)
- Esophagus
- Trachea
Adrenal Hormones

- Medulla (inner portion)
- Cortex (outer portion)
- Considered distinct glands

Adrenal Medulla Hormones

- Norepinephrine
  - SNS neurotransmitter
  - Also hormone (20% of medulla secretions)

- Epinephrine
  - 80% of medulla secretions
  - Stimulated by neural impulses from hypothalamus

- Functions:
  - CV system
  - Glycogenolysis (mostly EPI), lipolysis
Resting and Exercise-Induced Endocrine Secretions

![Diagram showing the relationship between blood concentrations of norepinephrine and epinephrine with exercise intensity.](image-url)

- Blood concentrations (ng/mL⁻¹)
  - Rest: 0.5
  - 50%: 1.0
  - 75%: 1.5
  - 100%: 2.0

Exercise intensity (% VO₂max)

Copyright © 2007. All rights reserved. Williams & Wilkins.
**Adrenal Hormones**

- **Adrenocorticol Hormones**
  - Mineralcorticoids
  - Glucocorticoids
  - Androgens
- **Aldosterone (mineralcorticoid)**
  - Function:
    - Stimulates sodium reabsorption and extracellular fluid volume
  - Control:
    - CRH, ACTH, blood pressure, AGII
  - Exercise:
    - Increases take approximately 45 minutes. So, role is more evident during prolonged exercise and recovery
Resting and Exercise-Induced Endocrine Secretions

Renin-angiotensin-aldosterone system

1. Sweating reduces plasma volume and blood flow to the kidneys.
2. Angiotensin II stimulates aldosterone release from the zona glomerulosa of the adrenal gland, which increases blood pressure.
3. Reduced renal blood flow stimulates renin release from the kidneys. Renin acts on the formation of angiotensin I, which is converted to angiotensin II.
4. Angiotensin II stimulates the release of aldosterone from the zona glomerulosa.
5. Aldosterone increases Na⁺ and H₂O reabsorption from the distal tubules.
6. Plasma volume increases; plasma osmolality decreases after several days of exercise.

Figure 3.17. The influence of water loss, fluid intake during exercise, and post-exercise restitution on plasma volume and osmolality.
Resting and Exercise-Induced Endocrine Secretions

- Adrenocorticol Hormones (cont’d)
  - Cortisol (Hydrocortisone) (Glucocorticoid)
    - Functions:
      - Promotes protein breakdown to amino acids
      - Blunts the effects of insulin
      - Increases lipolysis
      - Increases gluconeogenesis
      - Net effect = mobilization of fuel
    - Control:
      - CRH, ACTH, stress, blood glucose concentration
    - Exercise:
      - Increases with exercise intensity

Figure 2.18 Changes in plasma volume and aldosterone concentrations during 2 h of cycling exercise. Note that plasma volume declines rapidly during the first few minutes of exercise and then shows a smaller rate of decline despite large sweat losses. Plasma aldosterone concentration, on the other hand, increases rather steadily throughout the exercise.
Resting and Exercise-Induced Endocrine Secretions

- Gonadocorticoids
  - Produced in adrenal cortex
  - Similar actions to sex steroids
    - Dehydroepiandrosterone (DHEA)
      - Exerts effects similar to testosterone.
Resting and Exercise-Induced Endocrine Secretions

- Gonadal Hormones
  - Testosterone
  - Estrogen
  - Progesterone

- Exercise:
  - Exercise increases free testosterone after 15-20 minutes of exercise
  - Estrogen and progesterone increase with exercise

Figure 20.16 Pattern of plasma cortisol and testosterone concentrations measured at three time intervals (4 h before swimming, immediately after multiple sprint swims, and after 1-h recovery) over a 26-week swim-training season. Bar graphs on right show values for swim volume, time-trial performance, and blood lactate during the four 6-week training periods. (Modified from Bonifant M, et al. Blood levels of exercise during the training season. In: Miyashita M, et al., ed. Medicine and science in aquatic sports. Basel: Karger, 1984.)
Resting and Exercise-Induced Endocrine Secretions

- Pancreatic Hormones
  - Insulin
    - Mediates glucose metabolism
    - Affects fat synthesis
    - Facilitates protein synthesis
    - Stimulates glucose transporters (GLUTs)
Resting and Exercise-Induced Endocrine Secretions

- Increased for Insulin Secretion
  - Most tissues
  - Adipose tissue
  - Liver and muscle
  - Liver

- Glucose uptake
- Brain, liver, skeletal muscle
- Fats and triglyceride synthesis
- Glucose synthesis
- Fatty acid and triglyceride breakdown

- Protein synthesis
- Protein breakdown

---

Resting and Exercise-Induced Endocrine Secretions

- Insulin and GLUT-4
- Exercise and GLUT-4
Figure 2.15 Changes in plasma concentrations of glucose and insulin during prolonged cycling at 65% to 70% of \( VO_{2\max} \). Note the gradual decline in insulin throughout the exercise, suggesting an increased sensitivity to insulin during prolonged effort.
Resting and Exercise-Induced Endocrine Secretions

• Diabetes
  – Type 1 diabetes
    • Typically occurs in younger individuals
    • 5 – 10% of all cases
    • Exercise has greater metabolic effects.
  – Type 2 diabetes
    • Tends to occur after 40
    • Often produces reduced exercise tolerance

AT RISK FOR TYPE 2 DIABETES

- Body mass exceeds 20% of ideal
- First-degree relative with diabetes (genetic influence)
- Member of a high-risk ethnic group (black, Hispanic, American, Pacific Islander, American Indian, Asian)
- Delivered a baby weighing more than 9 pounds or developed gestational diabetes
- Blood pressure at or above 140/90 mm Hg
- HDL cholesterol level of 35 mg·dL⁻¹ or below
  and/or a triacylglycerol level of 250 mg·dL⁻¹ or above
- Impaired fasting plasma glucose or impaired glucose tolerance on previous testing
Resting and Exercise-Induced Endocrine Secretions

- Metabolic Syndrome X
  - Insulin resistance
  - Hyperinsulinemia
  - Dyslipidemia
  - Hypertension

**METABOLIC SYNDROME X**

- Insulin resistance
- Glucose intolerance
- Dyslipidemia (high triacylglycerols, low HDL, high LDL)
- Stroke
- Upper-body obesity
- Type 2 diabetes mellitus
- Hypertension
- Coronary artery disease
- Reduced ability to dissolve blood clots
Resting and Exercise-Induced Endocrine Secretions

- Glucagon
  - Increases blood glucose
  - Increases glycogenolysis in the liver

![Glucagon diagram]

Exercise Training (Endurance) and Endocrine Function

<table>
<thead>
<tr>
<th>TABLE 20.5</th>
<th>HORMONES AND THEIR RESPONSES TO ENDURANCE TRAINING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hormone</strong></td>
<td><strong>Training Response</strong></td>
</tr>
<tr>
<td>Hypothalamus-pituitary hormones</td>
<td></td>
</tr>
<tr>
<td>Growth hormone</td>
<td>No effect on resting values; less dramatic rise during exercise</td>
</tr>
<tr>
<td>Thymosin</td>
<td>No known training effect.</td>
</tr>
<tr>
<td>ACTH</td>
<td>Increased exercise levels.</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Some evidence that training lowers resting values.</td>
</tr>
<tr>
<td>FSH, LH, and testosterone</td>
<td>Trained females have depressed values; reduced testosterone in males (testosterone levels may increase in males with long-term resistance training)</td>
</tr>
<tr>
<td>Posterior pituitary hormones</td>
<td></td>
</tr>
<tr>
<td>Vasopressin (ADH)</td>
<td>Slightly reduced ADH at a given workload.</td>
</tr>
<tr>
<td>Oxytocin</td>
<td>No research results available.</td>
</tr>
<tr>
<td>Thyroid hormones</td>
<td>Reduced concentration of total T₄ and increased free T₃ levels at rest</td>
</tr>
<tr>
<td>Triiodothyronine (T₃)</td>
<td>Increased turnover of T₄ and T₃ during exercise</td>
</tr>
<tr>
<td>Adrenal hormones</td>
<td>No training adaptation.</td>
</tr>
<tr>
<td>Aldosterone</td>
<td>Slight elevation during exercise.</td>
</tr>
<tr>
<td>Cortisol</td>
<td>Decreased secretion at rest and at the same absolute exercise intensity after training.</td>
</tr>
<tr>
<td>Epinephrine and norepinephrine</td>
<td></td>
</tr>
<tr>
<td>Pancreatic hormones</td>
<td>Increased sensitivity to insulin; normal decrease in insulin during exercise greatly reduced with training</td>
</tr>
<tr>
<td>Insulin</td>
<td>Smaller increase in glucose levels during exercise at absolute and relative workloads</td>
</tr>
<tr>
<td>Glucagon</td>
<td>No apparent training effect.</td>
</tr>
<tr>
<td>Kidney enzyme and hormone</td>
<td></td>
</tr>
<tr>
<td>Renin and angiotensin</td>
<td></td>
</tr>
</tbody>
</table>

Copyright © 2007 Lippincott Williams & Wilkins.
• Anterior Pituitary Hormones
  – Growth Hormone
    • ET individuals show less rise in GH at a given exercise intensity
      – Reduced exercise stress and training progresses and fitness improves

• ACTH
  – Training increases ACTH release during exercise
    • Increases FA mobilization for energy
    • Glycogen sparing

• Prolactin
  – Little information
  – Male runners appear to have lower resting values than sedentary males
Exercise Training (Endurance) and Endocrine Function

Anterior Pituitary Hormones

- FSH, LH, Testosterone
  - Regular exercise depresses reproductive hormone responses in men and women

![Graph showing testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) levels in controls and runners.]

Exercise Training (Endurance) and Endocrine Function

- Posterior Pituitary Hormones
  - ADH
    - At the same relative intensity (%VO_2max)
      - No difference between trained and untrained
    - At the same absolute submaximal workload
      - Lower with training
  - Oxytocin
    - ??
• Parathyroid Hormone
  – Endurance training enhances exercise-related increases in PTH

• Thyroid Hormones
  – Training results in an increase in thyroid hormone turnover
    – In women
      • Sedentary to 48 km/week
        – Decrease in T3 and T4
      • Doubling exercise
        – Increased levels (due to greater %Body Fat loss)

• Adrenal Hormones
  – Aldosterone
    • Training does not effect resting levels or normal increases observed with exercise
  – Cortisol
    • At given absolute submaximal exercise intensity
      – Less of an increase in trained vs. untrained
  – Epinephrine and Norepinephrine
    • At given absolute submaximal exercise intensity
      – Lower in trained than untrained
    • At a given relative exercise intensity
      – Higher in trained than untrained
        » Greater absolute demand for substrates
        » Increased CV response
        » Larger muscle mass activation
• Pancreatic Hormones
  – Endurance training maintains blood levels of insulin and glucagon during exercise closer to resting values
  – The “trained state” requires less insulin at any stage from rest through light to moderately intense exercise
Exercise Training (Endurance) and Endocrine Function

On your slide, the colors are reversed for insulin. For the bottom panel.
**Exercise Training (Resistance) and Endocrine Function**

- **Testosterone**
  - Single bout of resistance training elicits a short-term rise in testosterone and decrease in cortisol
  - Resistance training in men increases frequency and amplitude of testosterone and GH secretion
    - Large muscle groups (dead lifts, power cleans, squats)
    - High intensity (85-95% 1-RM) or large volume with limited rest periods
  - Long-term resistance training increases resting testosterone levels in men
    - Correlates with the pattern of strength improvements over time

---

**Exercise, Infectious Illness, Cancer, and Immune Response**

[Diagram showing the relationship between stress, exercise, immune system, and illness]
Exercise, Infectious Illness, Cancer, and Immune Response

Table 20.6: IMMUNE SYSTEM COMPONENTS THAT EXHIBIT CHANGE FOLLOWING PROLONGED, INTENSE EXERCISE

- High neutrophil and low lymphocyte blood counts, induced by high concentrations of plasma cortisol.
- Increase in blood granulocyte and monocyte phagocytosis (engulfing of infectious agents) and of breakdown products of muscle fibers, decrease in nasal neutrophil phagocytosis.
- Decrease in granulocyte oxidative burst activity (killing activity).
- Decrease in nasal mucociliary clearance (swinging movement of cilia).
- Decrease in NK cell cytotoxic activity (the ability to kill infected cells or cancer cells).
- Decrease in mitogen-induced lymphocyte proliferation (a measure of T-cell function).
- Decrease in the delayed-type hypersensitivity skin response (the ability of the immune system to produce hives/red taps after the skin is pricked with antigens).
- Increase in plasma concentrations of pro- and antiinflammatory cytokines (e.g., interleukin-6 and interleukin-1 receptor antagonist).
- Decrease in ex vivo production of cytokines (interferon-β, interleukin-1, and interleukin-6) to mitogens and endotoxin.
- Decrease in nasal and salivary lysozyme concentration (an important antibody).
- Marked expression of major histocompatibility complex (MHC) II in macrophages (an important step in recognition of foreign agents by the immune system).