Endocrine & Reproductive Physiology
Chapters 15 & 16

15th & 16th Lectures
Wed & Fri
18th & 20th Feb 2009
Vertebrate Physiology
ECOL 437 (MCB/VetSci 437)
Univ. of Arizona, spring 2009
Kevin Bonine & Kevin Oh

Housekeeping, Wed 18 February 2009

Readings
Today: finish Ch 14
begin Ch 15
LAB Wed 18 Feb: Three Endocrine Readings
Fri 20 Feb: Ch 15 & 16

Lab discussion leaders: 25 Feb
Lab discussion leaders: 18 Feb
1pm - Jesse, Hang
1pm - Maggie, Shandy
3pm - Alex, Max
3pm - Shawn, Kendall

Endocrine System

- Hormone action often amplified by second-messenger cascade
- Hormones often released in very low concentrations Made them difficult to study!

Glycogenolysis Example:
(glycogen -> glucose)
- Epi (muscle)
- Glucagon (liver)

Goal is to increase blood [glucose]

Feedback...

Feedback

Negative Feedback

Short loop

Long loop

No Feedback

Open loop
Endocrine and Nervous Systems Have Similarities

Categories of cellular secretions:
- **Autocrine** - affect the secreting cell directly
- **Paracrine** - affect neighboring cells
e.g., histamine and inflammation
- **Endocrine** - release into bloodstream
- **Exocrine** - release onto epithelial surface
e.g., sweat onto skin, bile into digestive system

- **Pheromone** - exocrine secretion to signal other individuals
- **Neuroendocrine** - secretion from axon terminal into blood stream

Neurosecretory cells and Neurohormones control much of the endocrine system

Three Hormone Classes

1. **Amines** - small
   (e.g., epinephrine, norepi, thyroid, melatonin)

2. **Steroid Hormones** from cholesterol
   (e.g., testosterone, estrogen)

3. **Peptide Hormones** - common, large, complex
   (e.g., insulin, ADH, GH)

Endocrine System - Glands & Hormones

Secretions with consequences
All cells secrete, but
Specialized secretory cells grouped into glands
Secrete same specialized substance (e.g., hormone)

Nervous System neurotransmitter acts near and fast
Other secretions, such as hormones, may act more distantly and over a longer time period

Neuroendocrine Systems

Neurosecretory cells secrete neurohormones
Axon terminates into neurohemal organ
Neurohormones often affect other glands/hormones

<table>
<thead>
<tr>
<th>TABLE 16.2 Peptides, steroids, and axon hormones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Property</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Type of secretion</td>
</tr>
<tr>
<td>Structure</td>
</tr>
<tr>
<td>Solubility</td>
</tr>
<tr>
<td>Stability</td>
</tr>
<tr>
<td>Transport</td>
</tr>
<tr>
<td>Metabolism</td>
</tr>
<tr>
<td>Location of synthesis</td>
</tr>
<tr>
<td>Magnitude of effect</td>
</tr>
</tbody>
</table>

Hill et al. 2004
Amines – small
(e.g., epi, norepi, thyroid)

Modified Amino Acids
1. catecholamines (epi, norepi, dopamine; tyrosine)
2. thyroid (lipid soluble; tyrosine)
3. melatonin (tryptophan)

Glandular Secretion
Response to stimulus
Hormone
Neurotransmitter
Action Potential
etc. (e.g., osmolarity and ADH)

Storage before Secretion
Large molecules easily stored because can’t leave readily
Small molecules often stored bound to accessory proteins
Some molecules actively/continuously taken into vesicles
Steroid hormones (lipid soluble) tend to leak out soon
Hydrophobic steroid and thyroid hormones move in blood, bound to carrier proteins

Table 15.1 in Hill et al. 2008 p.393

<table>
<thead>
<tr>
<th>Endocrine Tissue</th>
<th>Hormone</th>
<th>Class of molecule</th>
<th>Main functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal cortex</td>
<td>Aldosterone (mineralocorticoids)</td>
<td>Steroids</td>
<td>Stimulates renal sodium and water reabsorption and K secretion in kidney</td>
</tr>
<tr>
<td></td>
<td>Androgens</td>
<td>Steroids</td>
<td>Action to increase growth spurt in puberty, increase sex drive, or induce behavior or action in brain</td>
</tr>
<tr>
<td></td>
<td>Glucocorticoids</td>
<td>Steroids</td>
<td>Part of stress response affect metabolism of many tissues to increase blood glucose and cause protein synthesis/catabolism</td>
</tr>
<tr>
<td>Adrenal medulla</td>
<td>Epinephrine and norepinephrine</td>
<td>Catecholamines</td>
<td>Part of stress response influence cardiovascular function and other metabolic functions of many tissues</td>
</tr>
</tbody>
</table>


Hormone ACTION!
Where are the receptors?

1. Lipid Soluble
   - Steroid and Thyroid Hormones (~long-lived)
   - Through Membrane
   - Bind cytoplasmic receptors, then to Nucleus
   - Directly affect transcription (therefore long-term)

2. Lipid Insoluble
   - Bind cell-surface receptors
   - Often one or more 2nd messengers
   - Amplification
   ~ Rapid, short-duration responses
Hormone ACTION (receptors etc.)

2. Lipid Insoluble Hormones and Intracellular Signaling

- A few receptors with direct catalytic activity, but most via 2nd messengers:
- Possible 2nd messengers:
  1. cAMP, cGMP (cyclic nucleotide monophosphates)
  2. IP3, DAG (diacylglycerol; inositol phospholipids)
  3. Ca²⁺ ions

General Model of Hormone Binding and Intracellular Signaling:

<table>
<thead>
<tr>
<th>Signal</th>
<th>Tissue</th>
<th>Cellular response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulatory Epinephrine (β-receptor)</td>
<td>Skeletal muscle</td>
<td>Breakdown of glycogen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased breakdown of lipids</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Heart: Increased heart rate and force of contraction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intestinal: Fluid secretion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Smooth muscle: Relaxation</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone (TSH)</td>
<td>Thyroid gland</td>
<td>Thyroxine secretion</td>
</tr>
<tr>
<td>ADH (vasopressin)</td>
<td>Kidney</td>
<td>Reabsorption of water</td>
</tr>
<tr>
<td>Glucagon</td>
<td>Liver</td>
<td>Breakdown of glycogen</td>
</tr>
<tr>
<td>Serotonin</td>
<td>Intestinal and gland (bile)</td>
<td>Fluid secretion</td>
</tr>
<tr>
<td>Prostaglandin E1</td>
<td>Blood platelets</td>
<td>Inhibition of aggregation and secretion</td>
</tr>
<tr>
<td>Inhibitory Epinephrine (α-receptor)</td>
<td>Blood platelets</td>
<td>Stimulation of aggregation and secretion</td>
</tr>
<tr>
<td></td>
<td>Fat cells</td>
<td>Decreased lipid breakdown</td>
</tr>
<tr>
<td></td>
<td>Adrenocorticotrophic hormone</td>
<td>Fat cells</td>
</tr>
</tbody>
</table>

Source: Berend, 1985

**Glandular Secretion**

**Secretory Vesicles**

- Exocytosis - common release mechanism
- Regulation via Calcium - free cytosolic calcium concentration is correlated with exocytosis (including of NT, hormones, etc.)

**Ca²⁺ ions**

- Intracellular stores (ER)
- Influx from extracellular fluid
1. binds and activates Troponin C in skeletal muscle
2. binds and activates Calmodulin also

**Multiple Cleavage Events to Make Active Hormone**

- proinsulin
- insulin
Major Endocrine Players

Hypothalamus
- (~7 neurohormones)
- mostly peptides

Pituitary (9 hormones)
1. Anterior (~nonneuronal)
2. Posterior (~neuronal control)

Posterior Pituitary

Similar, highly conserved peptide hormones

Anterior Pituitary

Tropic hormones = act on other endocrine tissues (e.g., adrenal cortex, thyroid, gonads)

Tropic Hormones of Anterior Pituitary

**Hormone** | **Structure** | **Negative Feedback** | **Regulation**
--- | --- | --- | ---
ACTH | Peptide | Adrenal cortex | Cortisol releasing hormones
FSH | Glycoprotein | Ovarian follicles | Inhibin, estradiol, inhibin
FSH | Glycoprotein | Ovarian follicles | Inhibin, estradiol, inhibin
LH | Glycoprotein | Ovarian follicles | Inhibin, estradiol, inhibin
TSH | Glycoprotein | Thyroid gland | TRH induces secretion
In response to cold, fright, pain etc...

**Hypothalamus**
- corticotropin-releasing hormone (CRH)
  - Portal vessel

**Anterior Pituitary**
- Adrenocorticotropic (ACTH)
  - Blood Stream

**Adrenal Cortex**
- (corticosterone; stress hormones)

**H-P-A axis**
(stress response)
1. **Hypothalamus**
   - (~7 neurohormones)
   - mostly peptides
2. **Pituitary**
   - (9 hormones)
   1. Anterior (~nonneuronal)
   2. Posterior (~neuronal control)
3. **Adrenal**
   - (Portal Vessels)

**Adrenal Gland(s)**

**Catecholamines**
(from medulla)

**Glucocorticoids**
(from cortex)

**Glucocorticoids**
(from adrenal cortex)
Includes 'Stress Hormones'
- Cortisol, cortisone, corticosterone

Released in response to ACTH (Adrenocorticotropic) from Anterior Pituitary

Steroid hormones (lipid soluble) derived from cholesterol
(mobilize a.a.s and glucose, suppress immune system etc.)
Water and Electrolyte Balance

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Tissue of origin</th>
<th>Structure</th>
<th>Target Tissue</th>
<th>Principal action</th>
<th>Regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidiuretic hormone</td>
<td>Tubular epithelium</td>
<td>Neuronal</td>
<td>Kidney</td>
<td>Increases arginine vasopressin</td>
<td>Stimulates thirst, ADH pathway</td>
</tr>
<tr>
<td>PTH</td>
<td>Parathyroid gland</td>
<td>Neuronal</td>
<td>Kidney, bones, parathyroid</td>
<td>Increases calcium, decreases phosphate</td>
<td>Paracrine through PTH receptors</td>
</tr>
</tbody>
</table>

Calcitonin decreases Ca++ in blood; PTH increases Ca++ in blood.

Catecholamines

- Fight/flight, exertion
- Catecholamines (adrenal medulla)
  - Epi, Norepi

Secretion regulated by sympathetic preganglionic cholinergic neurons

Catecholamine receptors are Alpha and Beta adrenoreceptors

Alpha - smooth muscle contraction
Beta1 - cardiac muscle stimulant
Beta2 - broncho/vaso dilation

Thyroid Hormone

(aka Thyroxine)

- T3 and T4 (# of iodines)
- Lipid soluble
  - Development, maturation, protein synthesis, metabolism
- Being cold can stimulate
  - Thyroid energy
  - Increased oxygen consumption and heat production

Insulin and Glucagon

Classic NEGATIVE FEEDBACK

Hypothyroid Goiter

(e.g. not enough iodine in diet)

Hyperthyroid Goiter

(e.g. 1. thyroid hormone receptors on hypothalamus or anterior pituitary don't work, or 2. receptor for thyroid stimulating hormone is activated by autoimmune antibody.)
Insulin and Glucagon Regulate blood [glucose]
- Insulin in response to high [glu]
- Glucagon in response to low [glu]
Both from pancreatic gland:
Insulin from beta cells
Glucagon from alpha cells

Leads to glucose uptake into tissues ETC.
Causes glycogenolysis and glucose release from tissues (liver, muscles)

Type 1 Diabetes
- when beta cells decrease insulin production
Type 2 Diabetes
- when insulin receptor-signal pathway defective

Growth Hormone
Metabolic and developmental effects
From Anterior Pituitary
Often has opposite effect of insulin
Stimulates gluconeogenesis
Reserves glucose for NS
Promotes use of fatty acids as fuel
Works with Thyroid hormone in growth and development

Gigantism / Acromegaly
Gigantism
-Acromegaly
Dwarfism

Vertebrate Reproduction
Asexual Parthenogenetic Whiptail Lizards

Reproductive Hormones
Steroid Hormones from Adrenal cortex and Gonads
Hypothalamus
GnRH
Anterior Pituitary
FSH, LH
Gonads, Adrenal Cortex

9-39 Randall et al. 2002
See Fig 14.1, Hill et al. 2004
Steroid Hormones from Adrenal cortex and Gonads
Male Sex Hormones

Testosterone and other androgens

Released from Leydig Cells in response to LH, FSH

FSH binding to Sertoli cells stimulates spermatogenesis

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Steroid Abuse

Homeostasis & Negative Feedback

What happens if you take too much exogenous testosterone?

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Female Sex Hormones

Estrogens

Ova created and stored before birth (mammals and birds)

Repro cycle in 2 phases:
- Follicular and Luteal

FSH stimulates beginning of follicular phase → development of ovarian follicles

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Luteal Phase

7. FSH, LH ∪
   Estrogen ∪

8. LH changes ruptured follicle into corpus luteum

9. corpus luteum secretes estrogen and progesterone which inhibit FSH, LH release from anterior pituitary by slowing GnRH

10. progesterone leads to richer endometrium

11. without fert. degenerates and cycle begins again

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Luteal Phase

12. with fert. Chorionic gonadotropin maintains CL, maintaining high levels of estrogen and progesterone; maintaining endometrium; follicular development inhibited

13. Placenta takes over hormone production

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Dear Cecil:
I just hit 40 and still have an unanswered question from my teens that has always bothered me. Aerosmith in "Sweet Emotion" sings about being accused of impregnating a girl. At the end of the verse they sing, "can't catch me 'cause the rabbit done died," referring to a pregnancy test. Arguments start over just what this test entails. Most say the bunny will die, but can't agree as to why. Some say the rabbit will always die because they kill it before they take its blood (which seems pretty dumb). Some say they inject it with some fluid taken from the woman and it dies a horrible, convulsive death. And some say they have to dissect the rabbit after it has been injected. This was before those home test kits, but wasn't there a better way? --Joe Shredl, Colonial Heights, Virginia

**Birth Control Pills?**

- **Progesterone and Estradiol** - mimic early pregnancy and inhibit ovulation

**Parturition (Birth)**
- Oxytocin released in response to cervical stretch
- Oxytocin causes uterine smooth muscle contractions

**Positive Feedback Loop**

**Lactation**
- Decreased progesterone levels and presence of prolactin (milk production) and oxytocin (milk ejection) and other hormones

- **Antibodies**
- **Vitamins**
- **Mechanosensory feedback**
- **Dopamine** inhibits prolactin secretion

**Randall et al. 2002**

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Time of action</th>
<th>Source</th>
<th>Target tissue</th>
<th>Primary action</th>
<th>Regulation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary sex hormones</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estrogen (E₃)</td>
<td>Ovary</td>
<td>Early pregnancy</td>
<td>Uterus, adrenals, skin cells</td>
<td>Increases DNA and LH levels estrogen secretion</td>
<td></td>
</tr>
<tr>
<td>Testosterone (T)</td>
<td>Testes</td>
<td>Male sex traits</td>
<td>Skin cells, hair follicles, bone</td>
<td>Increases FSH and LH levels testosterone secretion</td>
<td></td>
</tr>
<tr>
<td><strong>Progestogens</strong></td>
<td>Corpus luteum, adrenal cortex</td>
<td>Early pregnancy</td>
<td>Uterus, adrenals, skin cells</td>
<td>Increases progestins levels estrogen secretion</td>
<td></td>
</tr>
<tr>
<td>Progesterone (P)</td>
<td>Corpus luteum, adrenal cortex</td>
<td>Early pregnancy</td>
<td>Uterus, adrenals, skin cells</td>
<td>Increases progestins levels estrogen secretion</td>
<td></td>
</tr>
<tr>
<td><strong>Other Hormones</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Prolactin (PRL)</td>
<td>Mammary gland</td>
<td>Pregnancy</td>
<td>Uterus, adrenals, skin cells</td>
<td>Increases prolactin levels estrogen secretion</td>
<td></td>
</tr>
<tr>
<td><strong>Negative feedback</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisol</td>
<td>Adrenal cortex</td>
<td>Stress response</td>
<td>Skin cells, hair follicles, bone</td>
<td>Increases cortisol levels stress response</td>
<td></td>
</tr>
<tr>
<td>Dopamine</td>
<td>Hypothalamus</td>
<td>Stress response</td>
<td>Adrenal cortex, skin cells, hair follicles</td>
<td>Decreases prolactin levels stress response</td>
<td></td>
</tr>
</tbody>
</table>

**Charionic gonadotropin** (hCG)

**eCG**