Endocrinology

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• Course website: rci.rutgers.edu/~advis
• Lectures, tests, grades, office hours, textbook, extra books, recitations / study groups, instructor, graduate and undergraduate TAs availability
• Material to be covered in the course:
  • overview of the endocrine system as a communication system ----> (e.g., extracellular signal, receptor, intracellular links, mechanisms of hormonal action, physiological effect)
  • provide a “glance” on how information is obtained through endocrine research----> (e.g., experimental and clinical approaches, ablation and replacement therapies, DNA / RNA - related molecular approaches, signal transduction pathways)
  • relate basic endocrine communication to issues available to the general population -----> (e.g. endocrine pathologies, anabolic steroids, bST use, stress, control of appetite, obesity)

Endocrinology Course
(an overview)

<table>
<thead>
<tr>
<th>Meeting #</th>
<th>Description for the Endocrinology Course</th>
<th>Goodman’s textbook</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 - 17</td>
<td>An overview of the main controllers of the endocrine “play field” Introduction to the lecture and the recitation sections of this four - credit endocrinology course. Mechanisms of Action of Lipo-soluble (steroid, thyroid) and Water-soluble Hormones (all others). The Hypothalamic – Pituitary Unit (Hypothalamus and the Anterior and Posterior Pituitary Glands) Thyroid and Calcium Regulating Hormones, their Function, Mechanisms of Action and Control</td>
<td>1 – 4, 10</td>
</tr>
<tr>
<td>18 - 29</td>
<td>An overview of the main “players” of the endocrine game Endocrinology of the ANS, of the GI Systems, of the Endocrine Pancreas and of Diabetes Mellitus Endocrinology of the Adrenal Gland, its Glucocorticoid Hormones and the Intermediate Metabolism Endocrinology of Growth, of the main Growth – Related Hormones and of the main Growth Factors Endocrinology of the Adrenal Gland, its Mineralocorticoids, RAS and the Blood Pressure Control</td>
<td>1 – 11</td>
</tr>
<tr>
<td>30 – 39</td>
<td>An overview of “games” playing simultaneously in the endocrine play field Overview of Hormonal Integration and of the Homeostatic Control of the Endocrine System Integration of Sex Development, Reproductive Cycles and of the Neural Control of Reproduction Integration of Food Intake and of the Neuroendocrine Control of Appetite and Ingestive Behaviors Integration of Biological Rhythms, Immunity, Aging and the Endocrine Control of Homeostasis Integration and examples of the use of Human - related Case Studies as an Integration Tool</td>
<td>1 – 14</td>
</tr>
<tr>
<td>01 – 40</td>
<td>A recitation “reinforce” each week material by using editable essay questions Students must submit a draft answer for each weekly question BEFORE a recitation, in order to receive personal suggestions on how to edit them. Answers might be edited multiple times. EXAM #4 (25%) mean edited answers of all weekly recitation questions submitted on 12/01/2010</td>
<td>1 – 14</td>
</tr>
</tbody>
</table>
About the lecture slides

- There are not intended to be the sole source for studying the course material !!!!!!!!!!!!!!!!
- Slides are good to review the course material after you have study your book
- Slides are a good indicator of the relative importance of lecture topics
- Group slides by titles when using them to review the course material

A student e-mail after test #2

Hi,

Today after I had handed in my exam, I noticed something that really frustrated me and another student, who was walking out at about the same time as me. There was a student who had a pile of notes on the ground and was paging through them looking for answers for the exam. I don’t want to be considered as someone to rat one out, but I studied a lot for this exam and I am sure everyone would have liked to have their notes with them. Sorry but this got me really upset and just wanted to touch base with you on the matter.
The endocrine system is a communication system involved in the homeostatic control of life. It acts through its hormones which control four basic physiological processes: reproduction, growth and development, energy production, utilization & storage, and maintenance of the internal environment.

The endocrine system interacts with the nervous system to fulfill most of its homeostatic goals. It also interacts with the immune system.
Endocrine Physiology
(or what does the endocrine system do and how do we know it)

Fig 1: Look for PDFs attached to lecture #1 in the website (extra files)
Endocrine Physiology
(or what does the endocrine system do and how do we know it)

Chemical communication between cells. A: Local. Secretors product, shown as red dots, reaches nearby target cell by diffusion through extracellular fluid (paracrine or autocrine communication). Juxtacrine. Communication by physical contact via signaling molecules in the membrane of one cell activating membrane receptor molecules in an adjacent cell. B: Endocrine. Secretory product released from terminals of long cell processes reaches target cells distant from the nerve cell body by diffusion across the synaptic cleft.
Endocrine Physiology
(or what does the endocrine system do and how do we know it)

levels of organization

MOLECULAR LEVEL
Regulation of:
- Gene transcription
- Protein synthesis and degradation
- Enzyme activity
- Protein conformation and protein-protein interactions

hormone actions

CELLULAR LEVEL
Regulation of:
- Cell division
- Differentiation
- Death (apoptosis)
- Malignancy
- Secretion
- Nutrient uptake

Endocrine Physiology
(or what does the endocrine system do and how do we know it)

structure - function

Chemical Nature of the Classic Hormones

<table>
<thead>
<tr>
<th>Tyrosine derivatives</th>
<th>Steroids</th>
<th>Peptides (&gt;20 amino acids)</th>
<th>Proteins (&gt;20 amino acids)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>T3/T4</td>
<td>Oxytocin</td>
<td>Insulin</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>Estradiol</td>
<td>Vasopressin</td>
<td>Glucagon</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Progesterone</td>
<td>Angiotensin</td>
<td>Adrenocorticotropic hormone</td>
</tr>
<tr>
<td>Triiodothyronine</td>
<td>Cortisol</td>
<td>Melanocyte-stimulating hormone</td>
<td>Thyroid-stimulating hormone</td>
</tr>
<tr>
<td>Thyroxine</td>
<td>Aldosterone</td>
<td>Somatostatin</td>
<td>Thyrotrypsin-releasing hormone</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Somatostatin</td>
<td>Somatotropin</td>
<td>Follitropin-stimulating hormone</td>
</tr>
</tbody>
</table>

The classical hormones fall into 3 categories:
1- derivatives of the amino acid tyrosine
2- steroids, which are derived from cholesterol
3- peptides/proteins, which comprise the largest and most diverse class of hormones.
Endocrine Physiology
(or what does the endocrine system do and how do we know it)

I suggest you put this information into a table YOU design !!!
Main Communication Systems
(overview of what will be stressed in this endocrinology course)

1: levels of organization
2: structure - function
3: homeostatic regulation

An Important Concept
(chemical structures are linked to the mechanism of action)

The ligands you are studying are watersoluble or liposoluble ??
An Important Concept
(chemical structures are linked to the mechanism of action)

<table>
<thead>
<tr>
<th>Precursor</th>
<th>Type of compound</th>
<th>Example of hormone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>Protein</td>
<td>Growth hormone</td>
</tr>
<tr>
<td>Peptide</td>
<td>ACTH</td>
<td></td>
</tr>
<tr>
<td>Thryonine</td>
<td>Thyroxine</td>
<td></td>
</tr>
<tr>
<td>Steroid</td>
<td>Cortisol</td>
<td></td>
</tr>
<tr>
<td>Steroid</td>
<td>1,25 OH-D$_3$</td>
<td></td>
</tr>
<tr>
<td>Amino acid</td>
<td>Modified amino acid</td>
<td>Eglinphrine</td>
</tr>
<tr>
<td>Tripeptide</td>
<td>TRH</td>
<td></td>
</tr>
<tr>
<td>Fatty acid</td>
<td>Retinoid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Retinoic acid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eicosanoid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prostaglandin E$_1$</td>
<td></td>
</tr>
</tbody>
</table>

The ligands you are studying are watersoluble or liposoluble???

An Important Concept
(chemical structures are linked to the mechanism of action)

- watersoluble
- liposoluble

<table>
<thead>
<tr>
<th>Cellular response</th>
<th>mRNA</th>
<th>protein synthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na / K pump</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroid S + R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DNA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XX1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cAMP ---&gt; PKA ---&gt; channel / enzyme</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The ligands you are studying are watersoluble or liposoluble???
An Important Concept
(chemical structures are linked to the mechanism of action)

Steroid S + R ----> SR

extracellular receptor
activates enzyme
open/close channel

intracellular receptor
protein synthesis

DNA

Cellular response

AC

cAMP --> PKA --> channel / enzyme

extracellular receptor

liposoluble

Steroid S

R

watersoluble

An Important Concept
(chemical structures are linked to the mechanism of action)

liposoluble

Chemical structures are linked to the mechanism of action

Steroid S

R

watersoluble

An Important Concept
(chemical structures are linked to the mechanism of action)
Another Important Concept
(negative feedback is the most important regulatory control)

from communication links to negative feedbacks and to physiological integrators

Another Important Concept
(negative feedback is the most important regulatory control)

Visualize each arrow as a “story line”. Do you remember what a story line was?
Another Important Concept
(negative feedback is the most important regulatory control)

For each hormone, the student should know:
1. Its cell of origin
2. Its chemical nature, including:
   a. Distinctive features of its chemical composition
   b. Biosynthesis
   c. Whether it circulates free or bound to plasma proteins
   d. How it is degraded and removed from the body
3. Its principal physiological actions:
   a. At the whole body level
   b. At the tissue level
   c. At the cellular level
   d. At the molecular level
   e. Consequences of inadequate or excess secretion
4. What stimuli or perturbations in the internal or external environment evoke or suppress its secretion:
   a. How these signals are transmitted
   b. How that secretion is controlled
   c. What factors modulate the secretory response
   d. How rapidly the hormone acts
   e. How long it acts
   f. What factors modulate its action

I suggest you put this information into a table YOU design!!!

<table>
<thead>
<tr>
<th>Stimuli</th>
<th>Endo cell</th>
<th>Hormone</th>
<th>Receptor</th>
<th>Target cell</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>B cells in pancreas</td>
<td>Insulin</td>
<td>Tyrosine kinase</td>
<td>All cells</td>
<td>Anabolic Glut-4</td>
</tr>
</tbody>
</table>

Another Important Concept
(negative feedback is the most important regulatory control)

the need to use a basic “story line” table to learn endocrinology

stimulus ➔ A Chemical messenger ➔ B target cell

e.g. neuro / endo cell ➔ target cell

( expand each box content and / or add more boxes as the course progress)

However, a single story line by itself is not a regulated event, but if several ....
Another Important Concept
(negative feedback is the most important regulatory control)

... if story lines are linked through an integrator, then you have “control”...

Another Important Concept
(negative feedback is the most important regulatory control)

“control” through feedback as well as feedforward
Another Important Concept  
(negative feedback is the most important regulatory control)

“control” as that shown in the negative feedback regulatory diagram.

Another Important Concept  
(negative feedback is the most important regulatory control)

“control” as that shown for thyroid and growth axis.
Another Important Concept
(negative feedback is the most important regulatory control)

“control” as that shown for Ca metabolism, by PTH, Vit.D, and Calcitonin.

Another Important Concept
(negative feedback is the most important regulatory control)

When story lines are linked through an integrator then you have “control”.

What is the role of an integrator in a controlled system???
Putative Role for an Integrator
(a “reflex arc” that is the basis for a regulatory control model)

Feedback inputs

\[ \Sigma \]

Single / limited output

Set point

What is the role of an integrator in a controlled system???

A set point can be modulated by its own inputs. An integrator or “comparator”, compares what it should be (set point) against what actually is (the negative feedback signal).

Putative Role for an Integrator
(a “reflex arc” that is the basis for a regulatory control model)

Examples of brain integration centers

ARC-ME

Paraventricular nucleus of the hypothalamus

Arcuate median eminence

Region of the hypothalamus

What is the role of an integrator in a controlled system???
Putative Role for an Integrator
(a “reflex arc” that is the basis for a regulatory control model)

three physiological brain integration centers

what is the role of an integrator in a controlled system???

large # of neuropeptides

what is the role of an integrator in a controlled system??

large # of neuropeptides (chemical structure of some of them)
Endocrine Physiology
(or what does the endocrine system do and how do we know it)

Feedback mechanisms regulate endocrine homeostatic functions by controlling their “story lines”.

When story lines are linked through an integrator and there is a negative feedback involved then you have “control”.

For each hormone, the student should know
1. Its cell of origin
2. Its chemical nature, including
   a. Distinctive features of its chemical composition
   b. Biosynthesis
   c. Whether it circulates free or bound to plasma proteins
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   b. How that secretion is controlled
   c. What factors modulate the secretory response
   d. How rapidly the hormone acts
   e. How long it acts
   f. What factors modulate its action

I suggest you put this information into a table YOU design!!!

Examples of “story line” items
(hormones the communication signals of the endocrine system)

Examples of some “stuff” you will learn in the course linked to the “story line” idea and the need for you to start working on your table NOW:

- Sterling and secretin, hormones and neurohormones, Harris and portal vessels, Halaz and the hypothalamic hypophysiotropic area
- hormone biosynthesis: aminoacid derived hormones, protein and glycoprotein hormones, steroid hormones
- hormone release: static vs. pulsatile release, Circhoral, circadian and circannual release
- hormone transport: half-life, binding proteins, free versus bound circulating hormones
- hormone receptors as mediators of hormone action: signal transduction and genomic effects
- Some examples of physiological roles of hormones are found in the next slide .................>>>

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Examples of “story line” items
(hormones the communication signals of the endocrine system)

Examples of some “stuff” you will learn in the course linked to the “story line” idea and the need for you to start working on your table NOW:

- they affect synthesis and secretion of other hormones within other endocrine glands and in neurons.
- they affect anabolic and catabolic processes in most cells. In muscles they also affect contraction and relaxation.
- control reproduction, gonadal differentiation and gametogenesis. They stimulate / inhibit cellular proliferation, thus affecting growth.
- regulate excretion and reabsorption of inorganic cations and anions. Na, K, Ca, and P ions are particularly affected.
- some have a permissive action on the effects of other hormones. Their effectiveness is often enhanced and / or inhibited by the action of another hormone.
- they play important roles in animal behavior. Sexual & aggressive behaviors are affected by hormones, particularly during certain phases of the reproductive cycle. Maternal behavior is controlled by gonadal and pituitary hormones.

How do we know what we know
(a list of some methodological approaches)

Ablation / replacement therapy the classical experiment.
brain lesions and electrical stimulation as neuroendocrine approaches. MUA recording immunological approaches: ICC and RIA as anatomical and quantitative approaches molecular biological approaches: use of sense and antisense DNA probes, knock-out models pharmacological approaches: use of agonists, antagonists, and dose - response curves receptor assay as screening tools in pharmaceutical industry

**History, from endocrinology to neuroendocrinology**

- Berthold
- Sterling
- Banting & Best
- Loewi
- Cannon
- Scharrer
- Harris
- Halaz
- Schally
- Guilleman
- Yalow
- Sutherland (*)
How do we know what we know
(a list of some methodological approaches)

history, from endocrinology to pharmaceutical production

- Berthold
- Sterling
- Banting & Best
- Loewi
- Cannon
- Scharrer
- Harris
- Halaz
- Schally
- Guilleman
- Yalow
- Sutherland (*)

Endocrine Pathologies
(pushing feedback regulatory envelopes beyond homeostasis)

too much or too little hormone, from here or from there
Examples from our daily life
(a “reflex arc” that is the basis for a regulatory control model)

appetite, food intake, water metabolism and the stress response

sensor

integrator center

afferent “story line”

diagram for a control system as that present in a refrigerator

efferent “story line”

negative feedback “story line”

effector

When story lines are linked through an integrator then you have “control”.

Appetite, Food Intake, Obesity
(or additional endocrine examples from Time magazine)
Control of Water Metabolism
(or inputs and outputs of the PVN integration center)

Do you see the “circle” on your left, in the picture on top?

The Stress Response
(or a basic physiological background of a homeostatic event)

The gazelle and the lion, as an example of the stress response, or of a very stupid gazelle