I. Paper Draft Due (step > outline) Next Tues Discussion!
Focus: help especially those presenting on February 18th.

II. Endocrinology Overview G&H ch 75, 76, 77, 78, 79; LS, Fox…
A. Endocrine vignette: Cushing’s Syndrome LS
B. What’s an endocrine? Hormone criteria & classifications?
C. Mechanisms of hormonal action G&H fig 75-6, 75-7...
D. Endocrinology focuses on the relationship between the Hypothalamus - Controller ➔ Pituitary - Subcontroller
E. Endocrine organ, hormonal overview G&H fig 76-1, tab 76-1
F. Hypothalamus-Post & Ant Pituitary G&H fig 76-9, 76-4, 76-2
G. Anterior pituitary hormone functions G&H tab 75-1, Fox, LS
H. Negative feedback loops G&H p 929-30, LS
I. Growth Hormone (GH/STH) G&H fig 76-5, 76-6, tab 76-3
   Body builder’s dream or fountain of youth? Neither!

III. Peripheral Endocrine Organs G&H ch 77, 78, 79
A. Pancreas: insulin vs. glucagon, diabetes, G&H ch 79 + Fox
B. Thyroid: T3 & T4 G&H fig 77-2 thru fig 77-9 + DC
C. Adrenal cortices G&H fig 78-1 & 78-2 + DC
Cushing’s Syndrome = Hypersecretion of Cortisol: Hypothalamic (CRH), Pituitary (ACTH), or Adrenal (Cortisol)

T = 0, near normal

T = 4 months later
Endocrine or Hormone?

1. **Made by gland?**
2. **Secreted into blood?**
3. **Acts on target?**
Endocrine or Hormone Classifications

**Exogenous**
- Porcine
- Thyroid
- Recombinant DNA

**Endogenous**
- Amino Acid, PP or Protein
- Steroid
Steroid Hormone Structure: Cholesterol Backbone

- Cortisol
- Aldosterone
- Testosterone
- Estradiol

G&H 2016 fig 75-3, G&H 2011 fig 74-3
Lipophilic (Steroid+Thyroid) Hormone Mechanisms

G&H 2016 fig 75-6
G&H 2011 fig 74-6
Common Hydrophilic (AA, PP, Pro) Mechanism

Extracellular fluid

Hormone

Cytoplasm

GTP

Adenylyl cyclase

cAMP

ATP

Active cAMP-dependent protein kinase

Inactive cAMP-dependent protein kinase

Protein – PO4 + ADP

Protein + ATP

Cell’s response

G&H 2016 fig 75-7
G&H 2011 fig 74-7
<table>
<thead>
<tr>
<th>Hormone</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenocorticotropic hormone (ACTH)</td>
<td>G&amp;H 2016 tab 75-3, G&amp;H 2011 tab 74-2</td>
</tr>
<tr>
<td>Angiotensin II (ANG II, epithelial cells)</td>
<td></td>
</tr>
<tr>
<td>Calcitonin</td>
<td></td>
</tr>
<tr>
<td>Catecholamines (β receptors)</td>
<td></td>
</tr>
<tr>
<td>Corticotropin-releasing hormone (CRH)</td>
<td></td>
</tr>
<tr>
<td>Follicle-stimulating hormone (FSH)</td>
<td></td>
</tr>
<tr>
<td>Glucagon</td>
<td></td>
</tr>
<tr>
<td>Human chorionic gonadotropin (hCG)</td>
<td></td>
</tr>
<tr>
<td>Luteinizing hormone (LH)</td>
<td></td>
</tr>
<tr>
<td>Parathyroid hormone (PTH)</td>
<td></td>
</tr>
<tr>
<td>Secretin</td>
<td></td>
</tr>
<tr>
<td>Somatostatin (SS, GH RIH)</td>
<td></td>
</tr>
<tr>
<td>Thyroid-stimulating hormone (TSH)</td>
<td></td>
</tr>
<tr>
<td>Vasopressin (ADH, VP, V2 receptor, epithelial cells)</td>
<td></td>
</tr>
</tbody>
</table>
G-Protein Coupled Receptor (blue) sits within lipid bilayer (green) to respond to hormone (yellow)

Robert Lefkowitz, MD
Duke University Cardiologist
2012 Nobel Prize in Chemistry

http://www.hhmi.org/bulletin/winter2013/features/index.html
Image by Wayne Decatur
ANP = Atrial Natriuretic Polypeptide

Figure 74-1 Anatomical loci of the principal endocrine glands and tissues of the body.

Vasodilation

BP
Lateral View Showing Relationship of the Pituitary Gland to the Hypothalamus

- Third Ventricle
- Pineal Body
- Hypothalamus
- Anterior Commissure
- Mamillary Body
- Optic Chiasm
- Median Eminence Area

Krieger & Hughes 1980
Hypothalamus – Posterior Pituitary Nervous Connection

ADH/VP

Supraoptic nucleus

Optic chiasm

Hypothalamic-hypophysial tract

Anterior pituitary

Posterior pituitary

H₂O retention by kidneys

Contraction of sexual smooth m

OXY

G&H 2016 fig 76-9
G&H 2011 fig 75-9
Hypothalamus – Anterior Pituitary Vascular Connection

Releasing (RH)/Release-Inhibiting (RIH) Hormones

1 of 6 Trophic/Nourishing Hormones

G&H 2016 fig 76-4
G&H 2011 fig 75-4
Capillary-Venule-Capillary Circulation

NB: Ensures RH/RIH super-concentrated upon arrival @ anterior pituitary!
Pituitary removed!

Long hypophyseal-portal veins

Infinidibulum/stalk

Krieger & Hughes 1980
# Endocrine Glands, Hormones, Structures & Functions

<table>
<thead>
<tr>
<th>Gland/Tissue</th>
<th>Hormones</th>
<th>Major Functions</th>
<th>Chemical Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothalamus (Chapter 75)</td>
<td>Thyrotropin-releasing hormone (TRH)</td>
<td>Stimulates secretion of thyroid-stimulating hormone (TSH) and prolactin</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>Corticotropin-releasing hormone (CRH)</td>
<td>Causes release of adrenocorticotropic hormone (ACTH)</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>Growth hormone–releasing hormone (GHRH)</td>
<td>Causes release of growth hormone</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>Growth hormone inhibitory hormone (GHIH)</td>
<td>Inhibits release of growth hormone</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>(somatostatin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gonadotropin-releasing hormone (GnRH)</td>
<td>Causes release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH)</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>Dopamine or prolactin-inhibiting factor (PIF)</td>
<td>Inhibits release of prolactin</td>
<td>Amine</td>
</tr>
<tr>
<td>Anterior pituitary (Chapter 75)</td>
<td>Growth hormone</td>
<td>Stimulates protein synthesis and overall growth of most cells and tissues</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>TSH</td>
<td>Stimulates synthesis and secretion of thyroid hormones (thyroxine and triiodothyronine)</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>ACTH</td>
<td>Stimulates synthesis and secretion of adrenocortical hormones (cortisol, androgens, and aldosterone)</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>Prolactin</td>
<td>Promotes development of the female breasts and secretion of milk</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>FSH</td>
<td>Causes growth of follicles in the ovaries and sperm maturation in Sertoli cells of testes</td>
<td>Peptide</td>
</tr>
<tr>
<td></td>
<td>LH</td>
<td>Stimulates testosterone synthesis in Leydig cells of testes; stimulates ovulation, formation of corpus luteum, and estrogen and progesterone synthesis in ovaries</td>
<td>Peptide</td>
</tr>
</tbody>
</table>
Anterior Pituitary Metabolic Functions

- Thyrotropin
- Growth hormone
- Thyroid gland
- Increases blood glucose level
- Promotes secretion of insulin
- Pancreas
- Corticotropin
- Adrenal cortex
- Follicle stimulating
- Ovary
- Luteinizing
- Mammary gland
- Prolactin

G&H 2011 fig 75-2
G&H 2016 fig 76-2
Hypothalamus

Hormone 1

Anterior pituitary

Hormone 2

Target endocrine gland

Hormone 3

Target cells

Negative feedback
Growth Hormone/GH/Somatotrophic Hormone/STH Protein Hormone (191 AA) & Rat Growth

Injected daily with growth hormone

Body weight (grams)

Days

G&H 2016 fig 76-5
G&H 2011 fig 75-5
Progression & Development of Acromegaly

Age 13

Age 21

Age 35
Growth Hormone ≡ Somatotrophic Hormone

Body Builder’s Dream?
GH/STH Effects: Insulin Resistance/Type II Diabetes?

↑ Amino Acid uptake & Protein synthesis

↑ Lipolysis & Fatty Acid mobilization

↓ Glucose uptake
  (skeletal muscle & adipocytes)

↑ Glucose production
  (liver glycogenolysis)

↑ Insulin secretion

Mismatch!!
Increase GH naturally with exercise & sleep!!

Growth hormone (ng/ml plasma)

Time of day

ng/ml = nanograms per milliliter

cf: G&H 2016 fig 76-6
G&H 2011 fig 75-6
Growth Hormone & Protein Deficiency

![Bar graph showing plasma growth hormone levels in different conditions.]

- **Protein deficiency (kwashiorkor)**
- **Carbohydrate treatment (3 days)**
- **Protein treatment (3 days)**
- **Protein treatment (25 days)**

G&H 2016 fig 76-7
G&H 2011 fig 75-7
Questions + Discussion
Endocrine Pancreas: Insulin (I) & Glucagon (G) See-Saw Hormones in Regulating Blood Glucose

LS 2007
NB: Diabetics have problems either here or here.

Cellular uptake and utilization of glucose

Fox 1987

Times of Plenty!!

Fox 1987
Insulin Stores Sugar, Glucagon Mobilizes Sugar!

- High blood sugar promotes insulin release
- Low blood sugar stimulates glucagon uptake from blood

Peripheral Endocrine & Digestive Organ

Glucagon mobilizes sugar
Insulin stores sugar

- Liver
  - Glycogen breakdown: Stimulates glycogen breakdown
  - Glycogen formation: Stimulates glycogen formation
  - Lowers blood sugar
  - Tissue cells: Stimulates glucose uptake from blood

- Pancreas
- 4-6 hr of stored glucose
Proinsulin with C-Connecting Peptide

Fig. 10-4. Amino acid sequence of a mammalian proinsulin molecule. Note how the insulin molecule can be formed by cleaving this polypeptide chain at two locations to liberate the C peptide.
Diabetic & Normal Response to Glucose Load

Ingest Glucola or eat meal
Glucose: Sugar in Blood

Normal: 70-99
Pre-Diabetes: 100-125
Diabetes: ≥ 126 mg/dL
1994 Diabetes Prevalence in the US by State

Key:
- <4.5%
- 4.5%-5.9%
- 6.0%-7.4%
- 7.5%-8.9%
- ≥9%

Source: Centers for Disease Control, Division of Diabetes Translation, [http://www.cdc.gov/diabetes/statistics](http://www.cdc.gov/diabetes/statistics), S&W 2014 fig 4-15 p139A.
2010 Diabetes Prevalence in the US by State

Source: Centers for Disease Control, Division of Diabetes Translation, [http://www.cdc.gov/diabetes/statistics](http://www.cdc.gov/diabetes/statistics), S&W 2014 fig 4-15 p139B.
Table 4–9

Warning Signs of Diabetes

These signs appear reliably in type 1 diabetes and, often, in the later stages of type 2 diabetes.

- Excessive urination and thirst
- Glucose in the urine
- Weight loss with nausea, easy tiring, weakness, or irritability
- Cravings for food, especially for sweets
- Frequent infections of the skin, gums, vagina, or urinary tract
- Vision disturbances; blurred vision
- Pain in the legs, feet, or fingers
- Slow healing of cuts and bruises
- Itching
- Drowsiness
- Abnormally high glucose in the blood
Diabetics must constantly juggle diet, exercise & medication to control blood glucose!
Like others, diabetics benefit from whole grains, vegetables, fruits, legumes & non-/low-fat milk products!
Exercise is a must based on its insulin-like effect!
Inadequate Iodine Promotes Goiter!
Near absence of thyroid-hormone function + myxedema
Adrenal Gland

The adrenal glands sit atop the kidney and consist of an outer zone of cells, the adrenal cortex, which produces a variety of steroid hormones, and an inner zone, the adrenal medulla. The adrenal medulla produces adrenalin and noradrenalin.
Adrenals/Suprarenals

- Adrenal medulla
- Adrenal cortex
  - Mineralocorticoids (aldosterone)
  - Glucocorticoids (cortisol) and sex hormones (dehydroepiandrosterone)
  - Catecholamines (epinephrine and norepinephrine)

- Connective tissue capsule
- Zona glomerulosa
- Zona fasciculata
- Zona reticularis
- Medulla
Stress → Hypothalamus → Anterior Pituitary → Adrenal Cortices → Cortisol

CRH = ACTH-RH

Corticotropicin = ACTH

Metabolic Fuels, Building Blocks, Relieve Stress

Glucose, Amino Acids, Fatty Acids

SOURCE: Modified after D Chiras 2003
Adrenal Cortex Zones

- Zona glomerulosa
  - Aldosterone

- Zona fasciculata
  - Cortisol and androgens

- Zona reticularis

Medulla (catecholamines)

Cortex

Magnified section

Epinephrine 80% + Norepinephrine 20%

Fight/Flight Alarm Reaction

G&H 2016 fig 78-1
G&H 2011 fig 77-1
Questions + Discussion