Lecture 12

I. **Quiz 4** on CV physiology next T in class → Presentations. Q?
   For Quiz, 10 am section go to 112 WIL with Stacy just < 8:30!

II. **Endocrinology Overview** from Lecture 10 G&H ch 75, 76

III. **Med Physiol News** Sex Allergy? Mom’s eggs execute dad’s mitochondria? *Science News*

IV. **Reproductive Physiology Primer** G&H ch 82, 81 +L Sherwood…
   A. Female reproductive system fig 82-1, 82-2
   B. Ovarian hormones +FB: estrogen, progesterone pp 1042-7
   C. Follicle growth & ovulation mechanism fig 82-5, 82-3
   D. Plasma gonadotropin & ovarian hormone [ ] in female sexual cycle fig 82-4
   E. Female sexual cycle, menstruation fig 82-4, 82-9
   F. Estrogen [ ] throughout lifespan, menopause fig 82-12
   G. Birth control techniques L Sherwood + G&H
   H. Male reproductive system fig 81-1 A & B
      I. Sperm & development fig 81-2, 81-7, 81-3, 81-4, 81-5
   J. Feedback regulation in males fig 81-10
   K. Plasma testosterone [ ] throughout lifespan fig 81-9
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
- Bovine
- Recombinant DNA

**Endogenous**
- Amino Acid, PP or Protein
- Steroid

- Thyroid
Steroid Hormone Structure: Cholesterol Backbone

Cortisol

Aldosterone

Testosterone

Estradiol

G&H 2016 fig 75-3, G&H 2011 fig 74-3
ANP = Atrial Natriuretic Polypeptide

Figure 74-1 Anatomical loci of the principal endocrine glands and tissues of the body.
Lateral View Showing Relationship of the Pituitary Gland to the Hypothalamus

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

Krieger & Hughes 1980
Hypothalamus – Posterior Pituitary Nervous Connection

ADH/VP → Supraoptic nucleus → Optic chiasm → Paraventricular nucleus

H₂O retention by kidneys

OXY

Contraction of sexual smooth m

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

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

- **Optic chiasm**

- **Anterior pituitary**

- **Mammillary body**

- **Median eminence**

- **Primary capillary plexus**

- **Hypothalamic-hypophysial portal vessels**

- **Posterior pituitary**

- **Sinuses**

G&H 2016 fig 76-4
G&H 2011 fig 75-4
NB: Ensures RH/RIH super-concentrated upon arrival @ anterior pituitary!
Long hypophyseal-portal veins

Infinibulum/stalk

Pituitary removed!

Krieger & Hughes
1980
<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) (somatostatin)</td>
<td>Inhibits release of growth hormone</td>
<td>Peptide</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>Amine</td>
</tr>
<tr>
<td></td>
<td>Dopamine or prolactin-inhibiting factor (PIF)</td>
<td></td>
<td></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

Anterior pituitary gland

Corticotropin

Adrenal cortex

Follicle stimulating

Ovary

Luteinizing

Prolactin

Mammary gland

G&H 2016 fig 76-2
G&H 2011 fig 75-2
**Figure 75-5**

Comparison of weight gain of a rat injected daily with growth hormone with that of a normal littermate.
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
Increase GH naturally with exercise & sleep!!

Growth hormone (ng/ml plasma)

- Strenuous exercise

Sleep

Time of day

0800 1200 1600 2400 0400 0800

ng/ml = nanograms per milliliter

cf: G&H 2016 fig 76-6
G&H 2011 fig 75-6
Sex allergy: No laughing matter

The phrase “Not tonight, dear” may be a deadly serious matter for women who suffer from an allergy to their husband’s seminal fluid, the liquid that carries sperm. In rare cases, such an allergic response can cause death.

The first case of an allergy to human seminal fluid was documented in 1958. Since then, the disorder has been diagnosed in a small number of cases. However, allergists believe the disorder is not readily recognized by gynecologists.

Some women with this condition report a dramatic, whole-body reaction to seminal fluid. Their symptoms include wheezing, vomiting, diarrhea, unconsciousness, or complete circulatory collapse. Other women experience a localized reaction, such as vaginal burning or swelling.

Researcher Jonathan A. Bernstein of the University of Cincinnati College of Medicine and his colleagues decided to study the prevalence of the disorder. They administered a questionnaire to 1,073 women who had reported symptoms consistent with the allergy.

Bernstein’s team found that 12 percent of the women they studied met the diagnostic criteria for an allergy to seminal fluid. This result indicates that the disorder is much more common than previously suspected. The team reports its findings in the January ANNALS OF ALLERGY, ASTHMA, & IMMUNOLOGY.

Allergists can treat the condition, the researchers point out. Regular injections of purified seminal proteins can prevent the relationship-stopping symptoms, says Bernstein. — K.F.
Mom’s eggs execute Dad’s mitochondria

In “Hamlet,” Rosencrantz and Guildenstern deliver a letter to the rulers of England that carries the ill-fated duo’s own death sentence. Perhaps Shakespeare knew a bit about reproductive biology.

Scientists have now found that during a sperm’s creation, its *mitochondria*—energy-producing units that power all cells—*acquire molecular tags that mark them for destruction* once the sperm fertilizes an egg. This death sentence, a protein called *ubiquitin*, may explain why mammals inherit the DNA within mitochondria only from their mothers, a biological curiosity geneticists have used to trace human evolution (SN: 2/6/99, p. 88). The finding may also have implications for species mitochondrial inheritance. Sperm mitochondria sometimes avoid destruction when two different species of mice mate, and Schatten’s team has shown this also holds true in cattle. It’s hard to understand how an egg distinguishes between paternal mitochondria of closely related species, says Schon.

When paternal mitochondria escape destruction in normal mating, the resulting embryo may suffer. Schatten notes that a colleague has found sperm mitochondria in some defective embryos from infertility clinics.

The success of cloning may depend on an egg’s ability to destroy foreign mitochondria. In the technique used to create

May Day! May Day! We’re doomed!!
**1° Female Hormones**

1. **Hypothalamus**
   - GnRH

2. **Anterior Pituitary**
   - Gonadotropes/Basophilic Cells
     - FSH/Follicle Stimulating Hormone
     - LH/Luteinizing Hormone

3. **Target Organs – Ovaries**
   - Ovary– Follicles (~8-14)
     - E/Estradiol (17-β Estradiol)
   - Ovary– Corpus Luteum
     - PRG/Progesterone

Ah Ha! Stain purple!
What Do Estrogen & Progesterone Do?

**Estrogen – E**

Growth & Development of:

1. **Ovaries, fallopian tubes, uterus, vagina, external genitalia**
2. **Breasts** stroma, ductile systems, adipocytes
3. **Skeleton** → osteoblastic activity

**Progesterone – PRG**

Promotes Progestation!

1. **Uterus:** endometrium
   - Secretory Δ during last ½ of monthly cycle
2. **Breasts:**
   - ↑ lobules & alveoli
3. **Uterus:** smooth muscle
   - ↓ excitability & motility
4. **Hypothalamus:**
   - ↑ body temp \(\sim 0.5 \, ^\circ F\)
Stigma
≡ Sheath or case
≡ Sac or cavity
≡ Grain or seed

Ovary 1.5-3.0 cm
Ovum ~100 μ

G&H 2016 fig 82-5
G&H 2011 fig 81-4
Primary Oocytes

Follicle undergoing atresia

Ovary cross section

Graffian Follicle with developing ovum/egg

Ovum

H Howard 1984
Proposed Ovulation Mechanism

Luteinizing hormone

Follicular steroid hormones (progesterone)

Proteolytic enzymes (collagenase)

Follicular hyperemia and prostaglandin secretion

Weakened follicle wall

Plasma transudation into follicle

Degeneration of stigma

Follicle swelling

Follicle rupture

Evagination of ovum

G&H 2016 fig 82-6
G&H 2011 fig 81-5
Estrogen Production: Theca & Granulosa Cell Interaction

G&H 2016 fig 82-8

G&H 2011 fig 81-7
Figure 81-8 Phases of endometrial growth and menstruation during each monthly female sexual cycle.
Home-pregnancy test + "morning" sickness?

Basis of birth control pills = false luteal phase
**FIGURE 20-20**
Ovum and sperm transport to the site of fertilization

*Based on data from animals. Sperm and ovum enlarged.*
Early stages of development from fertilization to implantation

Note that the fertilized ovum progressively divides and differentiates into a blastocyst as it moves from the site of fertilization in the upper oviduct to the site of implantation in the uterus.

Day 1

Day 4-5

Day 5-7

Structures not drawn to scale.
### Average Failure Rate of Various Contraceptive Techniques

<table>
<thead>
<tr>
<th>Contraceptive Method</th>
<th>Average Failure Rate (annual pregnancies/100 women)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>90</td>
</tr>
<tr>
<td>Natural (rhythm) methods</td>
<td>20–30</td>
</tr>
<tr>
<td>Coitus interruptus</td>
<td>23</td>
</tr>
<tr>
<td>Chemical contraceptives</td>
<td>20</td>
</tr>
<tr>
<td>Barrier methods</td>
<td>10–15</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>2–2.5</td>
</tr>
<tr>
<td>Implanted contraceptives</td>
<td>1</td>
</tr>
<tr>
<td>Intrauterine device</td>
<td>4</td>
</tr>
</tbody>
</table>

*Abstinence works best!*
Important Facts

- 4 Million births in the US per yr
- 200 abortions per 1000 live births
- 664,000 legal abortions reported in 2013
- Sperm survive for 48 hr to 5 d in female reproductive tract
- Eggs start to disintegrate 12-24 hr > ovulation
- Ovulation varies & may be tough to predict...

http://www.cdc.gov/nchs/fastats/births.htm
http://www.who.int/reproductivehealth/en/
https://kinseyinstitute.org/research/index.php
Male Reproductive System

- Urinary bladder
- Ampulla
- Seminal vesicle
- Ejaculatory duct
- Bulbourethral gland
- Prostate gland
- Urethra
- Erectile tissue
- Vas deferens
- Prepuce
- Glans penis
- Epididymis
- Testis
- Scrotum
Figure 80-4  Structure of the human spermatozoon.
Figure 80-5 Abnormal infertile sperm, compared with a normal sperm on the right.
Behavioral effects

Male Feedback Regulation

Hypothalamus

GnRH

Anterior pituitary

LH

FSH

Testis

Leydig cell

Sertoli cell

Inhibin

Testosterone

Androgenic effects

Spermatogenesis