Lecture 12

I. Quiz 4 CV physiology 8:20 next T < class→ Presentations. Q?
   For Quiz, 10 am section go to 112 WIL with Kelsey @ ~ 8:15!

II. Endocrinology Overview [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
- Recombinant DNA

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

**Steroid**

**Thyroid**
Steroid Hormone Structure: Cholesterol Backbone

- **Cortisol**
- **Aldosterone**
- **Testosterone**
- **Estradiol**
ANP = Atrial Natriuretic Polypeptide

Vasodilation

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

Krieger & Hughes 1980
Hypothalamus – Posterior Pituitary Nervous Connection

ADH/VP

Supraoptic nucleus

Optic chiasm

Paraventricular nucleus

Hypothalamic-hypophysial tract

Mammillary body

Anterior pituitary

Posterior pituitary

Contraction of sexual smooth m

H₂O retention by kidneys

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

Median eminence

Primary capillary plexus

Hypothalamic-hypophysial portal vessels

Posterior pituitary

Anterior pituitary

Artery

Mammillary body

Sinuses

1 of 6 Trophic/Nourishing Hormones

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

Pituitary removed!
### Table 74-1: Endocrine Glands, Hormones, and Their Functions and Structure

<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>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 (thryoxine 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
- Corticotropin
- Follicle stimulating
- Luteinizing
- Prolactin

Thyroid gland

Increases blood glucose level

Promotes secretion of insulin

Adrenal cortex

Pancreas

Ovary

Mammary gland

G&H 2016 fig 76-2
G&H 2011 fig 75-2
Paraventricular nucleus
Supraoptic nucleus
Median eminence
Portal system
Infundibulum

Hypothalamus

Anterior Pituitary

TSH

Prolactin

Thyroid

ACTH

Adrenal cortex

Growth hormone

Gonadotropins

FSH

LH

Ovary

Testis

Bone

Muscle

Adipose tissue
**GH, a Protein Hormone (191 AA)**

**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)

0 10 20 30

0800 1200 1600 2400 0400 0800

Time of day

ng/ml = nanograms per milliliter

cf: G&H 2016 fig 76-6
G&H 2011 fig 75-6
Questions + Discussion
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 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!!
Female Reproductive System

- Uterine tube
- Ovary
- Uterus
- Cervix
- Urinary bladder
- Vagina
- Urethra
- Clitoris
- Labium minora
- Labium majora
- Rectum
- Anus

G&H 2016 fig 82-1
G&H 2011 fig 81-1
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/Estrogen (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 ~ 0.5 °F
Stigma ≡ Sheath or case
≡ Sac or cavity
≡ Grain or seed

Egg ≡ Yellow body
Ovary 1.5-3.0 cm
Ovum ~100 μ

Granulosa cells
Preovulatory (mature) follicle

Degenerating corpus luteum
Corpus luteum

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

Graffian Follicle with developing ovum/egg

Ovum

Follicle undergoing atresia

Ovary cross section
Proposed Ovulation Mechanism

Luteinizing hormone

Follicular steroid hormones (progesterone)

Proteolytic enzymes (collagenase)

Weakened follicle wall

Degeneration of stigma

Follicle rupture

Evagination of ovum

Follicular hyperemia and prostaglandin secretion

Plasma transudation into follicle

Follicle swelling

G&H 2016 fig 82-6
G&H 2011 fig 81-5
Estrogen Production: Theca & Granulosa Cell Interaction
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
- **Location**
  - Fertilization site (upper third of oviduct): 30-60 min after ejaculation, 0.001 percent of ejaculated sperm.
  - Uterus: 10-20 min, 0.1 percent.
  - Cervical canal: 1-3 min, 3 percent.
  - Vagina: 0 min, 100 percent.

*Based on data from animals. Sperm and ovum enlarged.

**FIGURE 20-20**
Ovum and sperm transport to the site of fertilization

- 180 million sperm deposited
- 180,000 sperm in uterine cavity
- 5.4 million sperm in ampulla of oviduct
- 1800 sperm in oviduct's optimal site of fertilization

LS1 2004, LS2 2012
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**
- Spermatozoon
- Ovum (cross section)
- Fertilization

**Day 4-5**
- Blastocyst (cross section)
- Morula
- Cleavage
- Trophoblast

**Day 5-7**
- Inner cell mass
  - Destined to become fetus
- Trophoblast
  - Accomplishes implantation and develops into fetal portions of placenta

**Blastocoele**
- Becomes amniotic sac

**Implantation**
- Endometrium of uterus

**Ovary**
- Ovulation

**Actual size**

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>

Yikes! 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
- Prepuce
- Glans penis
- Testis
- Scrotum
- Vas deferens
- Epididymis
Figure 80-4 Structure of the human spermatozoon.
Figure 80-5 Abnormal infertile sperm, compared with a normal sperm on the right.