Lecture 13

I. Quiz 4 Covering CV physiology. Q?

II. Endocrinology Connections from Lecture 10

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

IV. Reproductive Physiology Primer ch 81 + 80 G&H + LS +…

A. Female reproductive system fig 81-1, 81-2
B. Ovarian hormones +FB: estrogen & progesterone pp 991-4
C. Follicle growth & ovulation mechanism fig 81-4, 81-5
D. Plasma gonadotropin & ovarian hormone [ ] in female sexual cycle fig 81-3
E. Female sexual cycle, menstruation fig 81-3, 81-8
F. Estrogen [ ] throughout lifespan, menopause fig 81-12
G. Birth control techniques L Sherwood + G&H
H. Male reproductive system fig 80-1 A & B
  I. Sperm & development fig 80-2, 80-7, 80-3, 80-4, 80-5
J. Feedback regulation in males fig 80-10
K. Plasma testosterone [ ] throughout lifespan fig 80-9
Hypothalamus – Anterior Pituitary Vascular Connection

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

Optic chiasm

Hypothalamus

Mammillary body

Median eminence

Primary capillary plexus

Hypothalamic-hypophysial portal vessels

Anterior pituitary

Posterior pituitary

Sinuses

1 of 6 Trophic/Nourishing Hormones
Capillary-Venule-Capillary Circulation

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

Anterior Pituitary

Krieger & Hughes 1980
Long hypophyseal-portal veins

Infundibulum/stalk

Pituitary removed!
Anterior Pituitary Metabolic Functions

- Thyrotropin
- Growth hormone
- Corticotropin
- Follicle stimulating
- Luteinizing
- Prolactin

Thyroid gland

Increases blood glucose level

Promotes secretion of insulin

Pancreas

Adrenal cortex

Ovary

Mammary gland
Hypothalamus → Hormone 1 → Anterior pituitary → Hormone 2 → Target endocrine gland → Hormone 3 → Target cells

Negative feedback
Comparison of weight gain of a rat injected daily with growth hormone with that of a normal littermate.
Progression & Development of Acromegaly
Growth Hormone ≡ Somatotrophin 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!!

[Graph showing growth hormone levels over time with peaks during sleep and exercise]

Growth hormone (ng/ml plasma)

0800 1200 1600 2400 0400 0800

Time of day

Strenuous exercise

Sleep

ng/ml = nanograms per milliliter

cf: G&H 2011 fig 75-6
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.
Times of Plenty!!

**NB:** Diabetics have problems either here or here.

-- Fox 1987

Cellular uptake and utilization of glucose

Store!
Glucose: Sugar in Blood

Normal: 70-99
Pre-Diabetes: 100-125
Diabetes: ≥ 126 mg/dL
\[ I_2 + HO-\text{CH}_2-\text{CHNH}_2-\text{COOH} \rightarrow \text{Peroxidase} \]

Tyrosine

\[ \text{HO-CH}_2-\text{CHNH}_2-\text{COOH} + \]

Monoiodotyrosine

\[ \text{HO-CH}_2-\text{CHNH}_2-\text{COOH} \]

Diiodotyrosine

\[ \text{Monoiodotyrosine + Diiodotyrosine} \rightarrow \]

\[ \text{HO-CH}_2-\text{CHNH}_2-\text{COOH} \]

\[ 3,5,3'-\text{Triiodothyronine (T}_3) \]

\[ \text{Diiodotyrosine + Diiodotyrosine} \rightarrow \]

\[ \text{HO-CH}_2-\text{CHNH}_2-\text{COOH} \]

\[ 3,3',5'-\text{Triiodothyronine (RT}_3) \]

\[ \text{Diiodotyrosine + Diiodotyrosine} \rightarrow \]

\[ \text{HO-CH}_2-\text{CHNH}_2-\text{COOH} \]

Thyroxine (T_4)

G&H 2011 fig 76-3
Inadequate Iodine Promotes Goiter!

Figure 76-7  Regulation of thyroid secretion.
Near absence of thyroid-hormone function + myxedema

Figure 76-8. Patient with myxedema. (Courtesy of Dr. Herbert Langford.)
Scoop of ice cream on North pole!

FIGURE 13-12
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.
Adrenal Cortex Zones

- Zona glomerulosa: aldosterone
- Zona fasciculata: Cortisol and androgens
- Zona reticularis

Epi + NE during fight/flight
Stress -> Hypothalamus

CRH = ACTH-RH

Anterior Pituitary

Corticotropin = ACTH

Adrenal Cortices

Cortisol

Glucose, Amino Acids, Fatty Acids

SOURCE: Modified after D Chiras 2003
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 ANNAALS 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
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-ß Estradiol)

- Ovary– Corpus Luteum
  - PRG/Progesterone
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
Primary Oocytes

Follicle undergoing atresia

Graffian Follicle with developing ovum/egg

Ovary cross section
**Proposed Ovulation Mechanism**

1. Luteinizing hormone
2. Follicular steroid hormones (progesterone)
   - Proteolytic enzymes (collagenase)
   - Follicular hyperemia and prostaglandin secretion
3. Weakened follicle wall
   - Degeneration of stigma
   - Follicle swelling
   - Follicle rupture
4. Evagination of ovum

*G&H 2011 fig 81-5*
Antrum

Thecal cells

Ovum (primary oocyte)

Granulosa cells
Estrogen Production: Theca & Granulosa Cell Interaction

LH → Theca cell
- Cholesterol → cAMP → Pregnenolone → Progesterone → Androgens
- LDL

LH → Granulosa cell
- Cholesterol → Pregnenolone → Progesterone → Androgens
- LDL
- FSH → Aromatase → Estrogens
- ATP + cAMP

Capillaries/Extracellular fluid

G&H 2011 fig 81-7
Days of female sexual cycle

FSH and LH (ng/mL)

Menstruation

LH

Ovulation

FSH

Progesterone

Estradiol

G&H 2011 fig 81-3
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
<table>
<thead>
<tr>
<th>Location</th>
<th>Time of appearance (min after ejaculation)</th>
<th>Percent of ejaculated sperm*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fertilization site (upper third of oviduct)</td>
<td>30–60</td>
<td>0.001</td>
</tr>
<tr>
<td>Uterus</td>
<td>10–20</td>
<td>0.1</td>
</tr>
<tr>
<td>Cervical canal</td>
<td>1–3</td>
<td>3</td>
</tr>
<tr>
<td>Vagina</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

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

**FIGURE 20-20**

Ovum and sperm transport to the 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.
### 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

• 6.4 Million pregnancies, ½ unwanted in US/yr
• 1.6 Million end in abortion
• 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/
http://www.kinseyinstitute.org/research/index.html
http://www.kinseyinstitute.org/resources/FAQ.html
Male Reproductive System

- Urinary bladder
- Ampulla
- Seminal vesicle
- Ejaculatory duct
- Bulbourethral gland
- Vas deferens
- Prostate gland
- Urethra
- Erectile tissue
- Prepuce
- Glans penis
- Testis
- Scrotum
- Epididymis
Testis cross section

Spermatogonia

Interstitial/ Leydig Cells

Seminiferous tubules

Testosterone

Tails of developing sperm

Testis cross section

H Howard 1984
Figure 80-4 Structure of the human spermatozoon.

G&H 2011
Figure 80-5 Abnormal infertile sperm, compared with a normal sperm on the right.
Feedback regulation in males

Behavioral effects

Hypothalamus

GnRH

Anterior pituitary

LH

FSH

Testis

Leydig cell

Sertoli cell

Testosterone

Inhibin

Androgenic effects

Spermatogenesis

G&H 2011 fig 80-10
Feedback regulation in males
G&H 2011 fig 80-9

The graph illustrates the changes in plasma testosterone (ng/ml) and sperm production (as a percentage of maximal) across different life stages:

- **Fetal**
  - Plasma testosterone levels increase sharply in the 3rd trimester.
  - Sperm production is low.

- **Neonatal**
  - Plasma testosterone levels decrease after birth.
  - Sperm production increases but is still low.

- **Pubertal**
  - Plasma testosterone levels rise sharply as puberty begins.
  - Sperm production increases significantly.

- **Adult**
  - Plasma testosterone levels remain high throughout adulthood.
  - Sperm production peaks and then declines.

- **Old age**
  - Plasma testosterone levels decrease gradually.
  - Sperm production continues to decline.

The graph uses different colors to distinguish between plasma testosterone (red) and sperm production (blue) across the life stages.