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
Capillary-Venule-Capillary Circulation

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

Anterior Pituitary
Long hypophyseal-portal veins

Infindibulum/stalk

Pituitary removed!

Krieger & Hughes
1980
Anterior Pituitary Metabolic Functions

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

- Thyroid gland
- Adrenal cortex
- Ovary
- Mammary gland

- Increases blood glucose level
- Promotes secretion of insulin

G&H 2011 fig 75-2
A flowchart showing a hormonal regulatory system:

1. Hypothalamus
2. Hormone 1
3. Anterior pituitary
4. Hormone 2
5. Target endocrine gland
6. Hormone 3
7. Target cells

The flowchart includes a feedback loop from the target endocrine gland to the anterior pituitary, indicating negative feedback. The arrows show the direction of hormone action or feedback.
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)

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
Glucose: Sugar in Blood

Normal: 70-99
Pre-Diabetes: 100-125
Diabetes: ≥ 126 mg/dL
I₂ + HO-\(\text{CH}_2\text{CHNH}_2\text{-COOH}\) → Peroxidase

Tyrosine

HO-\(\text{CH}_2\text{CHNH}_2\text{-COOH}\) + Monoiodotyrosine

Diiodotyrosine
Monoiodotyrosine + Diiodotyrosine →

3,5,3'-Triiodothyronine (T₃)
Diiodotyrosine + Diiodotyrosine

3,3',5-Triiodothyronine (RT₃)
Diiodotyrosine + Diiodotyrosine

Thyroxine (T₄)
G&H 2011 fig 76-4

Basal metabolic rate

+10

+5

Thyroxine injected

Days

0 10 20 30 40

G&H 2011 fig 76-4
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.)
**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.

**FIGURE 13-12**

Scoop of ice cream on North pole!
Adrenal Cortex Zones

- Zona glomerulosa
  - aldosterone

- Zona fasciculata
  - Cortisol
  - androgens

- Zona reticularis

- Medulla
  - (catecholamines)

Epi + NE during fight/flight

Magnified section

G&H 2011 fig 77-1
Stress → Hypothalamus → CRH = ACTH-RH

CRH = ACTH-RH → Anterior Pituitary

Anterior Pituitary → Corticotropin = ACTH

Corticotropin = ACTH → Adrenal Cortices

Adrenal Cortices → Cortisol

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 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.
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—are 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!!
Female Reproductive System
1. Hypothalamus

2. Anterior Pituitary
   Gonadotropes/Basophilic Cells

3. Target Organs – Ovaries
   Ovary– Follicles (~8-14)
   E/Estrogen (17-β Estradiol)

4. Ovary– Corpus Luteum
   PRG/Progesterone

10 Female Hormones

GnRH

LH/Luteinizing Hormone

FSH/Follicle Stimulating Hormone

PRG/Progesterone

E/Estrogen (17-β Estradiol)
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 $\Delta$ during last $\frac{1}{2}$ of monthly cycle

2. **Breasts**:
   $\uparrow$ lobules & alveoli

3. **Uterus**: smooth muscle
   $\downarrow$ excitability & motility

4. **Hypothalamus**:
   $\uparrow$ body temp $\sim 0.5 \degree F$
Uterus, Ovary & Uterine/Fallopian Tube

Perimetrium

Isthmus of uterine tube

Ovarian ligament

Ovarian stroma

Ampullae of uterine tube

Mucosal folds of uterine tube

Fimbriae

Ovarian vessels

Corpus luteum

Broad ligament of uterus

Uterine cavity

Endometrium

Myometrium

Uterosacral ligament

Cervical canal

Vagina

Vaginal rugae

Isthmus of uterus

Cervix

Ovarian follicles
G&H 2011 fig 81-4

Stigma $\equiv$ Sheath or case

Sac or cavity $\equiv$ Grains or seed

Ovary 1.5-3.0 cm
Ovum $\sim$ 100 $\mu$

Yellow body $\equiv$ Corpus luteum

Egg $\equiv$ Ovum

Corona radiata

G&H 2011 fig 81-4
Primary Oocytes

Follicle undergoing atresia

Graffian Follicle with developing ovum/egg

Ovum

Ovary cross section

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 2011 fig 81-5
Estrogen Production: Theca & Granulosa Cell Interaction

Theca cell

- Cholesterol
- cAMP
- Progesterone
- Androgens

Granulosa cell

- Cholesterol
- Progesterone
- Androgens

Capillaries/Extracellular fluid

Aromatase + cAMP

Estrogens

G&H 2011 fig 81-7
Diagram showing the fluctuation of hormones during the female sexual cycle.

- Estradiol (red line) and Progesterone (blue line) levels are graphed against days of the cycle.
- FSH and LH (FSH: red, LH: blue) levels are also shown.

Key events:
- Menstruation
- Ovulation

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.

- **Day 1**: Spermatozoa fertilize the ovum (cross section).
- **Day 4-5**: Blastocyst (cross section) begins to develop, blastocyst becomes amniotic sac.
- **Day 5-7**: Trophoblast develops, inner cell mass differentiates into trophoblast that will later form the placenta. Ovulation occurs.

**Implantation**: Blastocyst begins to implant into the endometrium of 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>
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<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
Figure 80-4 Structure of the human spermatozoon.
Figure 80-5 Abnormal infertile sperm, compared with a normal sperm on the right.
Behavioral effects

Hypothalamus

GnRH

Anterior pituitary

LH

FSH

Testis

Leydig cell

Sertoli cell

Testosterone

Inhibin

Androgenic effects

Spermatogenesis

Feedback regulation in males

G&H 2011 fig 80-10
The diagram illustrates the changes in plasma testosterone (ng/ml) and sperm production (% of maximal) across different life stages:

- **Fetal**: Low levels of plasma testosterone and sperm production.
- **Neonatal**: Slight increase in plasma testosterone and sperm production.
- **Pubertal**: Significant increase in plasma testosterone and sperm production.
- **Adult**: Peak levels of plasma testosterone and sperm production.
- **Old age**: Decline in plasma testosterone and sperm production.

**Trimester gestation**
- 1st trimester: Low levels of plasma testosterone and sperm production.
- 2nd trimester: Increase in plasma testosterone and sperm production.
- 3rd trimester: Peak levels of plasma testosterone and sperm production.

**Birth**
- Birth: Shift from fetal to neonatal stages.

**Years**
- Year 17: Pubertal phase.
- Year 40: Adult phase.
- Year 60: Decline in sperm production.
- Year 80: Aging phase.