Lecture 13

I. **Announcements** Quiz today covers CV physiology. Q?

II. **Endocrinology Connections** from Lecture 12

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
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!!

Strenuous exercise

Sleep

Growth hormone (ng/ml plasma)

Time of day

0800 1200 1600 2400 0400 0800

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
Diabetic & Normal Response to Glucose Load

Blood glucose level (mg/100 ml)

Hours

G&H 2000 cf: G&H 2011 fig 78-12
Glucose: Sugar in Blood

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

\text{Tyrosine}

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

\text{Diiodotyrosine}

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

\text{HO}\text{-}\text{O}\text{-}\text{CH}_2\text{-}\text{CHNH}_2\text{-}\text{COOH} \rightarrow \text{3,5,3\textsuperscript{-}Triiodothyronine (T₃)}

\text{Diiodotyrosine} + \text{Diiodotyrosine}

\text{HO}\text{-}\text{O}\text{-}\text{CH}_2\text{-}\text{CHNH}_2\text{-}\text{COOH} \rightarrow \text{3,3\textsuperscript{'}\text{,5-Triiodothyronine (RT₃)}}

\text{Diiodotyrosine} + \text{Diiodotyrosine}

\text{HO}\text{-}\text{O}\text{-}\text{CH}_2\text{-}\text{CHNH}_2\text{-}\text{COOH} \rightarrow \text{Thyroxine (T₄)}

\text{G\&H 2011 fig 76-3}
Basal metabolic rate vs. Days

Thyroxine injected
Inadequate Iodine Promotes Goiter!

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

Figure 76-8. Patient with myxedema. (Courtesy of Dr. Herbert Langford.)
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**

- **Medulla**
  - (catecholamines)

- **Cortex**

Epi + NE during fight/flight

Magnified section

G&H 2011 fig 77-1
Stress $\rightarrow$ Hypothalamus $\rightarrow$ Diurnal Rhythm

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 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...
Female Reproductive System
Gonadotropes/Basophilic Cells
LH/Luteinizing Hormone
FSH/Follicle Stimulating Hormone
Ovary– Corpus Luteum
PRG/Progesterone

10 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-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
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
- Ovarian follicles
- Endometrium
- Uterine cavity
- Myometrium
- Uterosacral ligament
- Cervical canal
- Vagina
- Vaginal rugae
- Cervix
Stigma ≡ Sheath or case
≡ Sac or cavity
≡ Grain or seed

Ovary 1.5-3.0 cm
Ovum ~100 μ
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

Evagation of ovum

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

Relative blood levels

Months after beginning of last menstrual period

Fertilization

Delivery
G&H 2011 fig 81-11

![Graph showing changes in total urinary gonadotropins with age for males and females.](image-url)

- **Female**
  - Increase in gonadotropins during puberty
  - Peak around menopause

- **Male**
  - Generally lower levels of gonadotropins
  - Steady increase with age

**Axes:**
- **Y-axis:** Total urinary gonadotropins (units/24 hr)
- **X-axis:** Age (yr)
<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.
<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>
**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

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

G&H 2011 fig 80-1 A
Figure 80-7 Interstitial cells of Leydig, the cells that secrete testosterone, located in the interstices between the seminiferous tubules.
Testis cross section

- Spermatogonia
- Seminiferous tubules
- Interstitial/ Leydig Cells
- Tails of developing sperm
- Testosterone
- Testis cross section

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