Lecture 12

I. Quiz 4 CV physiology 8:15 next T < class → Presentations. Q?
   For Quiz, 12 n section go to 112 WIL with Nelson @ ~ 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)
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**

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.

G&H 2016 fig 75-1
G&H 2011 fig 74-1
Lateral View Showing Relationship of the Pituitary Gland to the Hypothalamus

Hypothalamus

Anterior Commissure

Optic Chiasm

Pituitary

Third Ventricle

Pineal Body

Mamillary Body

Median Eminence Area

Krieger & Hughes 1980
Hypothalamus – Posterior Pituitary Nervous Connection

ADH/VP

Supraoptic nucleus

Optic chiasm

Paraventricular nucleus

Mammillary body

Hypothalamic-hypophysial tract

Anterior pituitary

Posterior pituitary

H₂O retention by kidneys

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

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

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

Krieger & Hughes 1980
### 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</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>Peptide</td>
</tr>
<tr>
<td></td>
<td>Dopamine or prolactin-inhibiting factor (PIF)</td>
<td></td>
<td>Amine</td>
</tr>
<tr>
<td>Anterior pituitary</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
- Adrenal cortex
- Ovary
- Mammary gland
- Corticotropin
- Follicle stimulating
- Luteinizing
- Prolactin

G&H 2016 fig 76-2
G&H 2011 fig 75-2
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)

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.

Semen? G&H 2016 p 1024
G&H 2011 p 976
~60% seminal vesicle fluid - mucoid, PGE₂, fructose, fibrinogen
~30% prostatic fluid - NaHCO₃, clotting enzyme, Ca²⁺, profibrinolysin
~10% sperm + vas deferens fluid
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

- 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
   - **Anterior Pituitary**
     - Gonadotropes/Basophilic Cells
     - **FSH/Follicle Stimulating Hormone**
     - **LH/Luteinizing Hormone**
     - **Target Organs – Ovaries**
8. **Ovary – Follicles (~8-14)**
   - **E/Estrogen (17-β 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
- Ovarian follicles
- Corpus luteum
- Broad ligament of uterus
- Uterine cavity
- Endometrium
- Myometrium
- Uterosacral ligament
- Cervical canal
- Vagina
- Vaginal rugae
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
Ovulation

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

Graffian Follicle with developing ovum/egg

Ovary cross section

Follicle undergoing atresia

Ovum
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
4. Follicle rupture
5. Evagination of ovum
Estrogen Production: Theca & Granulosa Cell Interaction

Theca cell
- Cholesterol
  - cAMP
  - Pregnenolone
  - Progesterone
  - Androgens

Granulosa cell
- Cholesterol
  - Pregnenolone
  - Progesterone
  - Androgens
  - Estrogens

LDL
ATP
FSH
Capillaries/Extracellular fluid
Aromatase

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.

G&H 2016 fig 82-9
G&H 2011 fig 81-8
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

<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.
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.
~ 30 mm

~ 56 days
### 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, 20</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
- 638,169 legal abortions reported in 2015
- 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
https://www.cdc.gov/mmwr/volumes/67/ss/ss6713a1.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
- Vas deferens
- Prostate gland
- Urethra
- Erectile tissue
- Prepuce
- Glans penis
- Testis
- Scrotum

G&H 2016 fig 81-1 A
G&H 2011 fig 80-1 A
Figure 80-4 Structure of the human spermatozoon.
Figure 80-5  Abnormal infertile sperm, compared with a normal sperm on the right.

G&H 2016 fig 81-5
G&H 2011 fig 80-5
Male Feedback Regulation

Behavioral effects

GnRH

Anterior pituitary

LH

FSH

Testis

Leydig cell

Sertoli cell

Testosterone

Inhibin

Androgenic effects

Spermatogenesis