Reproductive System

In the beginning...
Fertilized egg (undifferentiated gonad)

Genetic sex
XY  XX

Gonads:
Endocrine glands specialized to support development and maturation of germ cells

Sex-Chromosomes

XY  XX

Gonadal sex
(Testes)  (Ovaries)

(Week 7)  (Week 9)

Undifferentiated gonad

Cortical region of undifferentiated gonad develops

(SRY gene)

Formation of testes

Medullary region of undifferentiated gonad develops

Testes

Sertoli cells
Leydig cells

Ovaries

Granulosa cells
Thecal cells

Male phenotype

Female phenotype

Phenotypic Sex:

The physical characteristics of the internal genital tract and the external genitalia

Differentiation of internal genital tracts:

Wolffian ducts (♂) and Müllerian ducts (♀) present in undifferentiated embryo

Testosterone

Anti-Müllerian hormone

Phenotypic sex

Male

Female
Reproductive System

Phenotypic Sex:
- The physical characteristics of the internal genital tract and the external genitalia

Differentiation of internal genital tracts:
- Wolffian ducts (♂) and Müllerian ducts (♀) present in undifferentiated embryo

Anterior Pituitary

NO antimüllarian hormone triggers Mullarian duct differentiation:
- Fallopian tubes
- Uterus
- Vagina

NO testosterone triggers Wolffian duct atrophication

Testosterone

Antimüllarian hormone

Female external genitalia develops in absence of Y chromosome:
- Clitoris
- Labia

Male external genitalia depends on production of dihydrotestosterone (DHT)
- Penis
- Scrotum

Take Home Message:
“Males are merely females who are ‘hopped up’ on testosterone”

Pathophysiology:

True hermaphrodite:
Both ovarian and testicular tissue present in an individual
- Fusion of zygotes
- Mutation in the SRY gene

Pseudohermaphrodite:
Individuals have gonads of one sex and external genitalia of opposite sex
- Male pseudohermaphrodite gonads = ♂; genitalia = ♀
  - Lack of testosterone
  - Receptor defect / absence
  - Pathway defect

Costanzo (Physiology, 4th ed.) – Figure 10.2

Puberty:
- Gonadal function driven by hypothalamic-pituitary axis:
  - Gonadotropins (LH & FSH) trigger gonadal function

Costanzo (Physiology, 4th ed.) – Figure 10.3

Boys:
- Testosterone production
- Initiation of spermatogenesis

Girls:
- Estrogen production
- Initiation of oogenesis

Events of Puberty

Males:
- Pubarche
- Penis growth
- Growth spurt

Females:
- Menarche
- Breast development
- Growth spurt

Costanzo (Physiology, 4th ed.) – Figure 10.3
Male Reproductive System

- **Reproductive System**
  - **Testes** (spermatozoa production)
  - **Duct system** (spermatozoa transport)
  - **Accessory glands** (seminal fluids)

**Semen** = spermatozoa (20 – 100 million) + seminal fluids (2 – 5 ml)

- **Cryptorchidism** ("hidden testis")
  - Undescended testis(es)
  - ~3% full-term (~30% premature)
  - Undescended = sterility

**Reproductive System**

- **Semen** = spermatozoa (20 – 100 million) + seminal fluids (2 – 5 ml)

- **Seminal vesicles**
  - Produce seminal fluid

- **Ejaculatory ducts**
  - Blend with seminal fluid

- **Prostate gland**
  - Secretes prostate fluid

- **Spermatic cord**
  - Ductus deferens
  - Blood vessels
  - Nerves
  - Lymphatic vessels

- **Spermatic cord** passes through inguinal canal (weak point – inguinal hernia)

**Spermatogenesis** requires 35 – 36°C temperatures

1) **Scrotum** (two separate chambers)
   - **Cremaster muscle**
   - **Countercurrent exchange**

2) **Countercurrent exchange**

**Spermatogenesis**

- **Sertoli cells** (sustentacular cells)
  - Provide nourishment to developing sperm
  - Form tight junctions; 'blood–testis barrier'
  - Secrete fluids to assist sperm transport

- **Leydig cells** (interstitial cells)
  - Produce testosterone

- **Spermatogonia** (stem cell)

- **Sertoli cells** (sustentacular cells)

- **Spermatids** (haploid)

- **Spermatozoa** (haploid)

**Spermatogenesis**

- ~14 yrs. of age
- 9 week process
- 128 million / day
Testes - Spermatogenesis:

1) Head:
   • Nucleus - contains DNA
   • Acrosomal cap
   • Hydrolases (enzymes)
   • Egg penetration

2) Midpiece:
   • Mitochondria; ATP synthesis

3) Tail:
   • Flagellum; movement
   - Lack most intracellular structures
   - Nutrients from environment

Testes - Regulation of Activity:

1) Testosterone Synthesis:
   - Cholesterol
   - Desmolase
   - Androstenedione
   - Dihydrotestosterone

2) Testosterone Action:
   - Stimulates growth of musculature
   - Hair growth (e.g., mobility)
   - Sebaceous gland activity

Testes - Accessory Glands:

- Seminal vesicles: 60% semen volume
- Bulbourethral glands: 5% semen volume
- Prostate: 30% semen volume
- Benign prostate hyperplasia

Testes - Other Characteristics:

- Thick, alkaline solution (buffer / lubricant)
- Antibiotic
- Promotes general body growth without masculinizing other regions

Testes - Embryonic Development:

- Differentiation of internal and external genitalia
- Stimulation of spermatogenesis
- Stimulation of secondary sexual characteristics
- Stimulation of growth of musculature

Endocrine System:

Testosterone binds to intracellular receptor (nuclear)
Female Reproductive System

Ovaries:
• Oogenesis
• Estrogen / Progesterone production

Ovarian follicle (functional unit):
• Provides nutrients for developing ovum
• Release ovum at proper time (ovulation)
• Prepare duct system for fertilization
• Prepare uterus for implantation
• Maintain fetus during opening weeks

Primordial Follicle:
- Primary Oocyte + Granulosa cells

Ovarian Cycle: (~ 28 days)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Primary Follicle</td>
<td>Granulosa cells enlarge / replicate</td>
</tr>
<tr>
<td>2) Secondary Follicle</td>
<td>Thecal cells develop; Oocyte increases in size; Open spaces develop</td>
</tr>
<tr>
<td>3) Tertiary Follicle</td>
<td>Thecal layer enlarges; Central chamber appears (antrum)</td>
</tr>
<tr>
<td>4) Ovulation</td>
<td>Primary oocyte matures to secondary ovum (1st polar body formed); Ovarian wall ruptures</td>
</tr>
<tr>
<td>5) Corpus albicans</td>
<td>Thecal / granulosa cells collapse; form endocrine structure</td>
</tr>
</tbody>
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Atresia: Degeneration of primary oocytes
Puberty: ~ 400,000 primary oocytes remaining
Menopause: ~ 0 primary oocytes remaining

Remember: ~ 500 eggs released / life

Oogenesis (ovum production 

Before Birth           At Puberty            After Fertilization

Corpus albicans: Scar in ovary remaining after the corpus luteum degenerates

Ovaral Cycle: (~ 28 days)
**Estrogen synthesized by granulosa & thecal cells**

**Ovary:**

- **Cholesterol** → **Pregnenolone** → **17α-hydroxypregnenolone** → **Dehydroepiandrosterone** → **Androstenedione**
- **Androstenedione** → **17α-hydroxylase** → **17,20-lyase** → **3β-hydroxysteroid dehydrogenase**

**Thecal cells**

**Granulosa cells**

**Progesterone synthesized by thecal cells**

**Ovary:**

- **Cholesterol** → **Pregnenolone** → **17α-hydroxypregnenolone** → **Dehydroepiandrosterone** → **Androstenedione**
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**Thecal cells**

**Granulosa cells**

**Estrogen / Progestone levels vary during female reproductive cycle**

- **Follicular Phase:**
  - **FSH**:
    - Stimulates growth of granulosa cells
    - Stimulates Estrogen synthesis
  - **LH** (Follicular phase)
  - Critical level of estrogen reached; estrogen triggers surge of LH / FSH

- **Midcycle:**
  - **FSH**:
    - High E2 levels upregulate GnRH receptors in gonadotrophs
  - **LH / FSH** trigger ovulation

- **Luteal Phase:**
  - Corpus luteum forms; begins synthesizing progesterone
  - Granulosa cells reduce / abolish aromatase activity

**Estrogen / Progestone levels regulated via positive & negative feedback**

- **FSH**:
  - High E2 levels upregulate GnRH receptors in gonadotrophs
  - LH / FSH trigger ovulation

- **Luteinizing hormone (LH):**
  - Stimulates Estrogen synthesis
  - Stimulates growth of granulosa cells
  - Stimulates Estrogen synthesis

**Birth Control Pill**
Endocrine System

Estrogen

- Ovary:
  - Estrogen binds to intracellular receptor (nuclear)
  - Differentiation of internal and external genitalia
    - Prepares reproductive tract for insemination
    - ↑ cell proliferation / cell growth / increased contractility in uterus
    - ↑ contractility / ciliary activity in fallopian tubes
    - stimulates cell proliferation and keratinization in vagina epithelium

- Stimulates secondary sexual characteristics
  - Pubertal growth spurt
  - Closure of epiphyseal plates of bones
  - Deposition pattern of subcutaneous fat
  - Growth of lobular ducts
  - Enlargement of areola
  - ↑ adipose tissue

- Stimulates breast development
  - ↑ secretory activity
  - ↑ cell proliferation / increased contractility in uterus and fallopian tubes
  - ↑ cell differentiation / inhibits cell proliferation in vagina

- Stimulation of breast development
  - ↑ cell differentiation / inhibits cell proliferation in vagina

- Mild thermogenic activity
  - "Rhythm" method of birth control

Progesterone

- Ovary:
  - Progesterone binds to intracellular receptor (nuclear)
  - Maintains reproductive tract for pregnancy
    - ↑ secretory activity / ↓ contractility in uterus and fallopian tubes

- Stimulation of breast development
  - ↑ cell differentiation / inhibits cell proliferation in vagina

- "Rhythm" method of birth control

Duct / Development System:

- Infundibulum: Expanded funnel
- Fimbriae: Finger-like projections (collect egg)
- Ampulla: Middle segment of tube
- Isthmus: Connection of tube to uterus wall

- Uterus layers: Endometrium / myometrium
  - Endometrium
    - 1) Menses: Endometrium sloughs off from uterine wall (~7 days)
    - 2) Proliferative Phase: Cells multiple across endometrium (~7 days)
      - ↑ connective tissue / extracellular collagen deposits (3–5 mm)
      - Thickened mucus provide access channels for sperm
    - 3) Secretory Phase: Endometrial glands enlarge / increase secretions (~14 days)
      - If no implantation, lymphocytes invade endometrium; sloughing begins due to loss of progesterone

- Uterus
  - 1) Mechanical protection
  - 2) Nutritional support
  - 3) Waste removal
  - 4) Ejection

- Trip takes 3–4 days
- Fertilization must occur within ~24 hours of release