Reproductive System

In the beginning...

Fertilized egg
(undifferentiated gonad)

Genetic sex

XY  XX

Reproductive System

Sex Chromosomes

Autosome
Reproductive System

In the beginning...

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

Fertilized egg (undifferentiated gonad)

Genetic sex
XY
XX

Gonadal sex
Testes
Ovaries

(Week 7)

(Week 9)

Sex-determining Region of Y chromosome (SRY gene) induces formation of testes

Undifferentiated gonad
(Cortical and medullary regions)

Testes
Mesodermal region of undifferentiated gonad develops

Ovary
Cortical region of undifferentiated gonad develops

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

Differentiation of internal genital tracts:

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

Testosterone

Antimüllarian hormone

Testosterone triggers Wolffian duct differentiation:
• Epididymis
• Vas deferens
• Seminal vesicles

Antimüllarian hormone inhibits development of Mullarian ducts

Phenotypic sex
Male phenotypic sex
Female phenotypic sex
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

- NO testosterone triggers Wolffian duct atrophy
- NO antimüllarian hormone triggers Müllerian duct differentiation:
  - Fallopian tubes
  - Uterus
  - Vagina

Differentiation of external genitalia:

- 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
• External genitalia often ambiguous
  Cause:
  • 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

Phenotypic Sex:
Reproductive System

Lynn Elizabeth Harris

Cause:
Lynn Edwards Harris

Pseudohermaphrodite:
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Puberty:
Reproductive System

Genetic component to onset of maturational process

Puberty:
• Gonadal function driven by hypothalamic-pituitary axis:

Boys:
Increasing LH & FSH trigger testosterone production
  • Leydig cell proliferation
  • Testicular growth (interstitial cells / tubules)
  • Accessory gland growth (e.g., prostate)
  • Initiation of spermatogenesis

Girls:
Increasing LH & FSH trigger estrogen production
  • Follicular cell development
  • Initiation of oogenesis

EVENTS OF PUBERTY

Male
  • Puberty
  • Male growth

Female
  • Puberty
  • Breast development
  • Menarche
  • Growth spurt

Costanzo (Physiology, 4th ed.) Figure 10.3
Costanzo (Physiology, 4th ed.) Figure 10.2

Women and pregnant women should wash or handle this product...
Male Reproductive System

- **Reproductive System**
  - Testes (spermatogenesis)
  - Duct system (spermatozoa transport)
  - Accessory glands (semen)

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

1. **Testes**
   - Descend from abdominal cavity at ~7 months in utero
   - Cryptorchidism (hidden testis)
     - Undescended testis(es)
     - ~3% full-term (~30% premies)
     - Undescended = sterility
   - Spermatogenesis requires 35 - 36°C temperatures

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

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

4. **Spermatogenesis requires 35 - 36°C temperatures**
   - 1. Scrotum (two separate chambers)
   - 2. Countercurrent exchange

5. **Countercurrent exchange**
   - 1 - 2°C below body temperature
Testes:
- Spermatogenesis
- Testosterone production

Spermatogenesis:
- Spermatogonia (stem cell)
- Mitosis
- Spermatocytes (diploid)
- Meiosis (crossing over)
- Spermatids (haploid)
- Spermiogenesis
- Spermatzoa (haploid)

Semeniferous tubules:
- Slender, tightly coiled tubules (sperm production)
- Rete testis: Passageways collecting sperm from seminiferous tubules

Semeniferous tubule
- ~ 0.5 miles / testis

Rete testis

Tunica vaginalis
- Two-layered, derived from peritoneum

Tunica albuginea
- Divides testis into lobules

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

Leydig Cells
- Interstitial cells
- Produce testosterone

Sertoli cells
- Sustentacular cells
- Provide nourishment to developing sperm
- Form tight junctions; ‘blood – testis barrier’
- Secrete fluids to assist sperm transport

Testes - Histology:

Reproductive System

Reproductive System
1) **Head:**
   - Nucleus - contains DNA
   - Acrosomal cap
   - Hydrolytic enzymes
   - Egg penetration

2) **Midpiece:**
   - Mitochondria; ATP synthesis

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

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**Testes - Spermatogenesis:**

- **Head**
  - Nucleus - contains DNA
  - Acrosomal cap
  - Hydrolytic enzymes
  - Egg penetration

- **Midpiece**
  - Mitochondria; ATP synthesis

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**Testes - Testosterone Synthesis:**

- **Reminder:**
  - Cholesterol
  - Pregnenolone
  - 17-hydroxyprogrenolone
  - Dehydroepiandrosterone
  - Androstenedione
  - Adrenal glands ( zona reticularis)

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**Testes - Regulation of Activity:**

- **Luteinizing hormone (LH):**
  - Stimulates testosterone synthesis
  - (Stimulates cholesterol desmolase activity)

- **Follicle stimulating hormone (FSH):**
  - Stimulates spermatogenesis
  - Stimulates Sertoli cell function

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Testosterone binds to intracellular receptor (nuclear)

- Differentiation of internal and external genitalia (works in conjunction with dihydrotestosterone)
- Stimulates spermatogenesis (paracrine activity)
- Stimulates secondary sexual characteristics
  - ↑ sex organ growth
  - ↑ sebaceous gland activity
  - ↑ hair growth (axillary / pubic)
  - Deepens voice
- Stimulates growth of musculature
- Acne

Anabolic steroids: Promote general body growth without masculinizing other regions

Reploglione: smooth muscle contraction

Fibrinogen: temporarily clot vagina

Buffers; neutralize acids

- ↑ (prostate) sperm activation
- Seminalplasmin; antibiotic
- Bulbs; neutralize acids

Benign prostate hyperplasia

- Thick, alkaline solution (buffer / lubricant)
Female Reproductive System:

- **Ovaries** (oocyte production)
- **Duct system** (oocyte transport)
- **Development system** (nourish fetus)

**Ovaries:**
- Oogenesis
- Estrogen / Progesterone production

**Ovarian follicle** (functional unit)
- Provides nutrients for developing oocyte
- Release oocyte at proper time (ovulation)
- Prepare duct system for fertilization
- Prepare uterus for implantation
- Maintain fetus during opening weeks
Oogenesis (ovum production – long process):

Atresia: Degeneration of primary oocytes

Puberty = < 400,000 primary oocytes remaining
Menopause = < 0 primary oocytes remaining

Remember: ~ 500 eggs released / life

Primary Oocytes (~ 2,000,000)

Mitosis

Secondary Oocyte

1st polar body

Mature Ovum

Oogenesis occurs within ovarian follicles

1) Primary Follicle
   - Granulosa cells enlarge / replicate
   - Zona Pellucida: Acellular matrix; Increases surface area around egg

2) Secondary Follicle
   - Thecal cells develop
   - Oocyte increases in size
   - Open spaces develop

3) Tertiary Follicle
   - Thecal layer enlarges
   - Central chamber appears (antrum)

4) Ovulation
   - Primary oocyte matures to secondary oocyte (1st polar body formed)
   - Ovarian wall ruptures

5) Corpus Luteum
   - Thecal / granulosa cells collapse; form endocrine structure
   - Pregnancy = CL remains
   - No Pregnancy = CL degenerates (14 days)
Estrogen synthesized by granulosa & thecal cells

Thecal cells
Granulosa cells

Progesterone synthesized by thecal cells

Thecal cells
Granulosa cells

Estrogen / Progesterone levels vary during female reproductive cycle

Predominately estradiol
Predominately progesterone

(Mensus)

 Corpora lutea
Ovulation

Basal lamina
**Reproductive System**

**Ovary:**

Estrogen / Progesterone levels regulated via positive & negative feedback

**Follicular Phase:**

- **Hypothalamus**
  - GnRH
    - **Gonadotroph-releasing hormone**
      - **Anterior Pituitary**
        - LH
          - (+)
          - **Arcuate nucleus**
            - Gonadotroph
            - releasing hormone
            - **Estrogen**
              - (+)
              - **FSH**
                - (<)
                - Estrogen
                - [low]

  - Luteinizing hormone (LH):
    - Stimulates Estrogen synthesis
    - (↑ cholesterol desmolase activity)
  - Follicle stimulating hormone (FSH):
    - Stimulates growth of granulosa cells
    - Stimulates Estrogen synthesis

**Midcycle:**

- Critical level of estrogen reached; estrogen triggers surge of LH / FSH
  - High E2 levels upregulate GnRH receptors on gonadotrophs
  - LH / FSH trigger ovulation

**Luteal Phase:**

- Corpus luteum forms; begins synthesizing progesterone
  - Granulosa cells reduce / abolish aromatase activity
  - Birth Control Pill

**Birth Control Pill**

- **Estrogen / Progesterone levels regulated via positive & negative feedback**

- **Luteal**
  - **Corpus luteum**
    - Begins synthesizing progesterone
    - Granulosa cells reduce / abolish aromatase activity
    - Birth Control Pill

- **Luteinizing hormone (LH):**
  - Stimulates Estrogen synthesis
  - (↑ cholesterol desmolase activity)
  - Follicle stimulating hormone (FSH):
    - Stimulates growth of granulosa cells
    - Stimulates Estrogen synthesis

- **FSH**
  - (<)
  - Estrogen
  - [low]

- **GnRH**
  - (+)
  - **Anterior Pituitary**
    - LH
      - (+)
      - **Arcuate nucleus**
        - Gonadotroph
        - releasing hormone
        - **Estrogen**
          - (+)
          - **FSH**
            - (<)
            - Estrogen
            - [low]
Estrogen binds to intracellular receptor (nuclear)

- Differentiation of internal and external genitalia
- Prepares reproductive tract for insemination
  - cell proliferation / increased contractility in uterus
  - cell differentiation / 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
- Stimulates breast development:
  - Growth of lobular ducts
  - Enlargement of areola
  - ↑ adipose tissue

Progesterone binds to intracellular receptor (nuclear)

- Maintains reproductive tract for pregnancy
  - ↑ secretory activity / ↓ contractility in uterus and fallopian tubes
  - ↑ cell differentiation / inhibits cell proliferation in vagina
- Stimulates breast development:
  - ↑ secretory activity
- Mild thermogenic activity
- "Rhythm" method of birth control

Duct / Development System:

- Infundibulum: Expanded funnel
- Fimbriae: Finger-like projections (collect egg)
- Isthmus: Connection of tube to uterus wall
- Trip takes 3 – 4 days
  - Fertilization must occur within ~ 24 hours of release
- 1) Mechanical protection
- 2) Nutritional support
- 3) Waste removal
- 4) Ejection
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Endocrine System

Duct / Development System:

Uterine Cycle: (28 days)

1) Menses: Endometrium sloughs off from uterine wall (~7 days)
   - Collagen deposits (3–5 mm)
   - Thickened mucus provide access channels for sperm.

2) Follicular Phase: Cells multiple across endometrium (~7 days)
   - Connective tissue / extracellular collagen deposits (3–5 mm)
   - If no implantation, lymphocytes invade endometrium; sloughing begins due to loss of progesterone

3) Secretory Phase: Endometrial glands enlarge / increase secretions (~14 days)
   - Endometrium sloughs off from uterine wall (~7 days)

Endometrium / myometrium

Uterus layers

Endometrium

Myometrium

Luteal Phase

Non-fertile Cycle