Reproductive System

In the beginning…

Fertilized egg
(undifferentiated gonad)

Genetic sex

XY
XX
In the beginning...

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

- **Genetic sex**
  - XY (Week 7)
  - XX (Week 9)

- **Gonadal sex**
  - Testes
  - Ovaries

**Fertilized egg**
(undifferentiated gonad)

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

- **Testes Determining Factor**
  (coded for by SRY gene)

  - Testes Medullary region of undifferentiated gonad develops
  - Ovary Cortical region of undifferentiated gonad develops
Reproductive System

In the beginning...

Fertilized egg
(undiﬀerentiated gonad)

- XY
  - Testes
    - Germ cells (spermatogonia)
      - Sertoli cells
      - Leydig cells
      - Antimüllarian hormone
      - Testosterone
    - Male phenotypic sex
- XX
  - Ovaries
    - Germ cells (oogonia)
      - Thecal cells
      - Granulosa cells
      - Antimüllarian hormone
      - Testosterone
    - Female phenotypic sex

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

Genetic sex

(XY) (Week 7) (XX) (Week 9)

Gonadal sex

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 Müllarian ducts (♀) present in undifferentiated embryo

- Testosterone
  - Antimüllarian hormone
  - Epididymis
  - Testis
  - Vas Deferens
  - Seminal Vesicle
  - Prostate
  - Wolﬀian duct differentiation:
    - Epididymis
    - Vas deferens
    - Seminal vesicles
  - Antimüllarian hormone inhibits development of Mullarian ducts
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 atrophication
- NO antimüllerian 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

Developmental window: 6 – 12 weeks
Take Home Message:

“Males are merely females who are ‘hopped up’ on testosterone”

Phenotypic Sex:

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

Syndrome of 5α-reductase deficiency
Puberty:

- Gonadal function driven by hypothalamic-pituitary axis:

  Genetic component to onset of maturational process

  A) Missing Link Hypothesis: Components of brain missing / non-functional during pre-pubescence
  B) Critical Weight Hypothesis: Critical amount of fat relative to lean body mass necessary

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

Puberty:

- Pulsatility of GnRH required for normal reproductive function:

  Boys:
  - Increasing LH & FSH trigger testosterone production
  - Leydig cells proliferate
  - Testicular growth (semiferous tubules)
  - Accessory gland growth (e.g., prostate)
  - Initiation of spermatogenesis

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

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

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

Semen = spermatozoa (20 – 100 million) + seminal fluids (2 – 5 ml)
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
1) Scrotum (two separate chambers)
2) Countercurrent exchange

Spermatogenic system
- Ductus deferens
- Blood vessels
- Nerves
- Lymphatic vessels

Countercurrent exchange
1 - 2°C below body temperature

Seminiferous tubules:
- Slender, tightly coiled tubules
  (sperm production)

Rete testis:
- Passageways collecting sperm from seminiferous tubules

Rete testis
- Seminiferous tubule
  (~ 0.5 miles / testis)

Tunica vaginalis
- Two-layered; derived from peritoneum

Tunica albuginea
- Divides testis into lobules

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 27.2 / 27.21

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 27.3
Testes - Histology:

- **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 - Spermatogenesis:

- **Spermatogonia** (stem cell)
  - (diploid)
  - Mitosis
- **Spermatocytes** (diploid)
  - Meiosis (crossing over)
- **Spermatids** (haploid)
- **Spermatozoa** (haploid)
  - ~ 14 yrs. of age
  - 9 week process
  - 128 million / day

Reproductive System
Testes - Spermatogenesis:

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

Testes - Testosterone Synthesis:

Reminder:

Cholesterol → Pregnenolone → 17-hydroxy pregnenolone → Dehydroepiandrosterone → Androstenedione

Adrenal glands (zona reticularis)

Blood proteins function as a reservoir for circulating hormones

98% of T bound in blood:
   - 40% = sex steroid-binding protein
   - 60% = albumin / other proteins
**Testes - Regulation of Activity:**

Luteinizing hormone (LH):
(Target = Leydig cells)
- Stimulates testosterone synthesis
  (↑ cholesterol desmolase activity)

Follicle stimulating hormone (FSH):
(Target = Sertoli cells)
- Stimulates spermatogenesis
- Stimulates Sertoli cell function

Hypothalamus

Anterior Pituitary

Testes

Target tissues

Arcuate nucleus

Gonadotrophs

FSH (+)

FSH (-)

LH (+)

LH (-)

GnRH (+)

GnRH (-)

Testosterone

Inhibin

**Testes - Testosterone Action:**

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
  - Acne
- ↑ hair growth (axillary / pubic)
  - Deepens voice

Stimulates growth of musculature

Anabolic steroids:
Promote general body growth without masculinizing other regions
Testes:
- Spermatogenesis
- Testosterone production

Vas deferens:
Passageway from testis to urethra
- Propels sperm via peristaltic contractions

Epididymis:
Sperm maturation / storage site
- Monitors / adjusts fluid composition
- Recycles damages / non-utilized sperm
- Secretes chemicals that prevent capacitation (e.g., mobility)

Accessory Glands:

Prostate:
(30 % of semen volume)
- ↑ [citrate]; sperm activation
- Seminalplasmin; antibiotic
- Buffers; neutralize acids

Benign prostate hyperplasia

Seminal vesicles:
(60% semen volume)
- ↑ [fructose]; sperm activation
- Prostaglandins; smooth muscle contractions
- Fibrinogen; temporarily clots vagina
- Buffers; neutralize acids

Bulbourethral glands:
(5 % of semen volume)
- Thick, alkaline solution (buffer / lubricant)

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 27.3

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 27.4
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

Ovaries:

Oogenesis (ovum production – long process):

- Primary Oocytes (~ 2,000,000)
- Oogonia (~ 7,000,000)
- Mitosis

Atresia: Degeneration of primary oocytes
- Puberty = ~ 400,000 primary oocytes remaining
- Menopause = ~ 0 primary oocytes remaining

Remember: ~ 500 eggs released / life

Before Birth

At Puberty

After Fertilization
Ovary:

Oogenesis occurs within ovarian follicles

Primordial Follicle:
Primary Oocyte + Granulosa cells

Ovarian Cycle: (~ 28 days)

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 develops

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

- Cholesterol
  - Cholesterol desmolase
  - 17α-hydroxylase
  - 17,20-lyase
  - 3β-hydroxysteroid dehydrogenase
  - Androstenedione

Dehydroepiandrosterone

Testosterone

Aromatase

Androstenedione

Progesterone synthesized by thecal cells

- Cholesterol
  - Cholesterol desmolase
  - 3β-hydroxysteroid dehydrogenase
  - Progesterone

Basal lamina

Blood
Estrogen / Progestone levels vary during female reproductive cycle

Predominately estradiol
Predominately progesterone

Ovary:

Estrogen / Progestone levels regulated via positive & negative feedback

Follicular Phase:

Hypothalamus
GnRH (+) Gonadotroph-releasing hormone
Anterior Pituitary
FSH (+) LH (-)

Luteinizing hormone (LH):
- Stimulates Estrogen synthesis
  \((\uparrow\) cholesterol desmolase activity\)

Follicle stimulating hormone (FSH):
- Stimulates growth of granulosa cells
  - Stimulates Estrogen synthesis
    \((\uparrow\) aromatase activity\)

M (Menstrual) P (Proliferative) S (Secretory) M (Menstrual)
Reproductive System

Ovary:

Estrogen / Progestone levels regulated via positive & negative feedback

Midcycle:

(Hypothalamus)

GnRH

Anterior Pituitary

FSH

LH

Estrogen [high]

• 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:

(Hypothalamus)

GnRH

Anterior Pituitary

FSH

LH

Corpus luteum

Progesterone

• Corpus luteum forms; begins synthesizing progesterone
  (granulosa cells reduce / abolish aromatase activity)

Birth Control Pill
**Endocrine System**

Ovary:

**Estrogen**

- 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

- Stimulates breast development
  - Growth of lobular ducts
  - Enlargement of areola
  - ↑ adipose tissue

**Progesterone**

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

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

Duct / Development System:

Fimbriae: Finger-like projections (collect egg)

Isthmus: Connection of tube to uterus wall

Infundibulum: Expanded funnel

Ampulla: Middle segment of tube

Uterine Cycle: (28 days)

Follicular Phase:
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

Luteal Phase:
3) Secretory Phase: Endometrial glands enlarge / increase secretions (~ 14 days)
   • If no implantation, lymphocytes invade endometrium; sloughing begins due to loss of progesterone

Uterine Cycle:

Uterus layers = Endometrium / myometrium