Chapter 27
Reproductive System

The Reproductive System

- **Gonads**: organs that produce gametes and hormones
- **Ducts**: receive and transport gametes
- **Accessory glands**: secrete fluids into ducts
- **Perineal structures**: collectively known as external genitalia
- **Reproductive Tract**: all chambers and passageways that connect ducts to the exterior of the body

Quick tour of male reproductive anatomy

- **Pathway of Spermatozoa**: Testis → Epididymis → Ductus deferens (vas deferens) → Ejaculatory duct → Urethra
- **Accessory Organs** Secrete fluids into ejaculatory ducts and urethra:
  - seminal vesicles
  - prostate gland
  - bulbourethral glands
- **External Genitalia**
  - Scrotum
  - Penis

Testes

- Remember the parts of the testes from lab
- **Seminiferous tubules = spermatogenesis and production of testosterone**
  - large **Interstitial cells (cells of Leydig)**
    - Produce androgens (male sex hormones) including testosterone (T) (key androgen)
  - **Sustentacular (Sertoli) cells**
    - Secrete
      - ABP (androgen binding protein) to bond to and raise conc of T in the testes
      - MIF
      - Inhibin (inhibits FSH)

The Male Reproductive System

Overview

- Male anatomy
- Spermatogenesis
- Male reproductive hormones
- Female anatomy
- Oogenesis
- Female reproductive hormones:
  - ovarian cycle
  - uterine cycles
Steps in Spermatogenesis
1. Stem cells (spermatogonia) divide by mitosis to produce 2 daughter cells:
   - One remains as spermatogonium
   - second differentiates into primary spermatocyte
2. Primary spermatocytes:
   - begin meiosis, form secondary spermatocytes
3. Secondary spermatocytes:
   - differentiate into spermatids (immature gametes)
4. Spermatids:
   - differentiate into spermatozoa
5. Spermatozoa:
   - lose contact with wall of seminiferous tubule
   - enter fluid in lumen

Chromosomes in Mitosis and Meiosis

Meiosis
- Is a specialized form of cell division that only occurs in the gonades to produce of gametes:
  - spermatozoa in males
  - ova in females
- Divides the number of chromosomes in half
- Produces four daughter cells

Meiosis
- In seminiferous tubules: begins with primary spermatocytes and produces spermatids (undifferentiated male gametes)
- Basically, in meiosis one, you separate the homologues (meaning each of the resulting daughter cells gets only one of your two copies of chromosome #4 and one of your two copies of chromosome #21, etc. (Both cells contain 23 chromosomes with 2 chromatids each (reductional division)
- Meiosis two is just like mitosis, only it is different than mitosis in somatic cells because there are only 23 chromosomes at this point yields 4 cells, each containing 23 chromosomes (equational division)

Spermatogenesis

Cells in Spermatogenesis
- Spermatogonium produces 2 daughter cells
- One is primary spermatocyte, contains 46 individual chromosomes (before any meiosis)
- Secondary spermatocytes: after meiosis I contains 23 chromosomes (2 duplicate chromatids each)
- These divide in meiosis II to yield haploid spermatids (23 chromosomes each)
- Each primary spermatocyte produces 4 spermatids interconnected by bridges of cytoplasm → mature into spermatozoa
Spermiogenesis

- Is the last step of spermatogenesis
- Each spermatid (small, relatively unspecialized cell) matures into 1 spermatozoon (highly specialized cell) attached to cytoplasm of sustentacular cells; involves major structural changes
- At spermiation, a spermatozoon:
  - loses attachment to sustentacular cell
  - enters lumen of seminiferous tubule
- Spermatogonial division to spermiation:
  - takes about 9 weeks

Functions of Sustentacular Cells

1. Maintain blood–testis barrier
2. Support mitosis and meiosis
3. Support spermiogenesis
4. Secrete inhibin
5. Secrete androgen–binding protein
6. Secrete Müllerian–inhibiting factor

Support of Mitosis and Meiosis

- Sustentacular cells are stimulated by FSH and testosterone to promote division of spermatogonia and meiotic divisions of spermatocytes (spermatogenesis)
- Inhibin gives feedback control of spermatogenesis:
  - Basically, inhibin increases in proportion to spermatogenesis, exerting negative feedback on FSH and thus on spermatogenesis (because FSH activates spermatogenesis)

Sperm Lack Most Organelles

- Mature spermatozoon lacks:
  - endoplasmic reticulum
  - Golgi apparatus
  - lysosomes
  - peroxisomes
  - inclusions
  - other intracellular structures
- Reduces sperm size and mass
- Sperm must absorb nutrients (fructose) from surrounding fluid
- Nucleus?

KEY CONCEPT

- Spermatogenesis:
  - begins at puberty and continues past age 70
  - is a continuous process
- All stages of meiosis are observed within seminiferous tubules
Functionally Immature Spermatozoa

- Spermatozoa:
  - detach from sustentacular cells
  - are free in lumen of seminiferous tubule
  - are functionally immature
- Are incapable of locomotion or fertilization
- Are moved by cilia lining efferent ductules into the epididymis

Functions of the Epididymis

1. Monitors and adjusts fluid produced by seminiferous tubules
2. Recycles damaged spermatozoa
3. Stores and protects spermatozoa

Spermatozoa Leaving Epididymis

- Are mature, but remain immobile
- To become motile (actively swimming) and functional spermatozoa undergo capacitation
  1. Spermatozoa become motile:
     - when mixed with secretions of seminal vesicles
  2. Spermatozoa become capable of fertilization:
     - when exposed to female reproductive tract

The Vas Deferens

- Lined by ciliated epithelium; peristaltic contractions propel spermatozoa and fluid
- Can store spermatozoa for several months in a state of suspended animation (low metabolic rates)
- Carries sperm to Ejaculatory Duct
  - short passageway (2 cm) at junction of vas defens ampulla and seminal vesicle duct
  - Penetrates wall of prostate gland and empties into urethra

Accessory Glands

- Semen = sperm and fluids from testes (5%) + seminal fluid, which comes from:
  - seminal vesicles (60% of semen volume)
    - fibrinogen, prostaglandins, fructose (makes sperm motile)
  - prostate gland (20-30%)
    - antibiotic: seminalplasmin, fibrinogen activator
  - bulbourethral glands (<5%)
    - Lubricant and buffer (for acidic urine and vagina)
- Typical ejaculation releases 2–5 ml

Penis
The Penis

- **Glans** = the expanded distal end of penis
- Erectile Tissue Consists of network of vascular channels incompletely separated by partitions of elastic connective tissue and smooth muscle fibers
  - Corpora Cavernosa (2)
  - Corpus Spongiosum
- Flaccid: blood flow restricted, smooth muscle tensed
- **Erection:** parasympathetic nervous system causes release of NO, dilates blood vessels and relaxes smooth muscles = engorgement
- **Viagra** prolongs NO signal

Summary

- **GnRH** (pulses) \(\rightarrow\) LH, FSH
  - LH \(\rightarrow\) interstitial cells \(\rightarrow\) T \(\rightarrow\) many effects
  - FSH \(\rightarrow\) sustentaculars \(\rightarrow\) inhibin
    - ABP
    - spermatogenesis
    - (T also necessary)

Androgens

- **T** \(\rightarrow\) (aromatase) \(\rightarrow\) Estradiol
  - (5 alpha reductase) \(\rightarrow\) DHT
- **Propecia** blocks 5 alpha reductase because DHT is implicated in baldness
- Some people lack 5 alpha reductase and DHT is necessary for external male genital development. Look like girls… until puberty

The Female Reproductive System

- **Ovaries** or female gonads
  - release 1 immature gamete (oocyte) per month
  - produce hormones
- **Uterine tubes:**
  - carry oocytes to uterus
- If sperm reaches oocyte:
  - fertilization is initiated and oocyte matures into ovum
- **Uterus:** encloses and supports developing embryo
- **Vagina:** connects uterus with exterior
- External genitalia
- Accessory glands
Ovary Functions

1. Production of immature female gametes (oocytes)
2. Secretion of female sex hormones (estrogens, progestins)
3. Secretion of inhibin for feedback control of pituitary FSH

Oogenesis

- Begins before birth, pauses
- Continues at puberty
- Does not actually complete until fertilization!
- Ceases at menopause
- Ovarian Cycle Includes monthly oogenesis between puberty and menopause

- Oogenesis = females reproductive stem cells
  - complete mitotic divisions before birth (not thought to happen at all after birth, but...)
- Between third and seventh months:
  - primary oocytes begin meiosis but stop at prophase of meiosis I
- At birth, a baby girl’s ovaries have about 2 million primordial follicles each containing a primary oocyte arrested in prophase I of meiosis
- At puberty rising FSH triggers start of ovarian cycle
- Each month thereafter some primary oocytes are stimulated to develop further by FSH
- One per month will complete meiosis I and become a secondary oocyte just prior to ovulation
- Ovary releases secondary oocyte (not mature ovum) that is suspended in metaphase of meiosis II
- Meiosis II is only completed upon fertilization
The Ovarian Cycle

Ovarian Cycle: Follicular Phase
- Primary Oocytes, located in outer part of ovarian cortex and the follicle around them form a primordial follicle in clusters called egg nests
- Follicular phase (preovulatory phase)
  - Follicle cells become granulosa cells and work with surrounding thecal cells to produce estrogens
  - Secondary follicles form when granulosa cells secrete Follicular fluid that accumulates (NOTE: still a primary oocyte)
  - Tertiary follicle forms when follicle becomes enlarged and oocyte breaks free into the antrum
  - Just prior to ovulation, LH causes primary oocyte to complete Meiosis I and start meiosis II

The Ovarian Cycle: Luteal Phase
- Corpus luteum develops from granulosa cells left behind
- Forms a large structure that secretes progestins (progesterone) to prepare the uterine lining for pregnancy
- If fertilization does not occur, corpus luteum automatically degenerates about 12 days after ovulation, fills with scar tissue to become corpus albicans
- Loss of progesterone secretion causes menses and also restarts the ovarian cycle

The Uterine Tubes
- Fallopian tubes or oviducts are hollow, muscular tubes about 13 cm long
- Epithelium lining uterine tube contains scattered mucin secreting cells
- Mucosa is surrounded by concentric layers of smooth muscle
- Transport oocyte from ovary to uterus involves:
  - Ciliary movement
  - Peristaltic contractions in walls of uterine tube
- From infundibulum to uterine cavity normally takes 3–4 days
- For fertilization to occur:
  - Secondary oocyte must meet spermatozoa during first 12–24 hours
  - Usually occurs about halfway down the tube

The Uterus
Regions of the Uterus

- **Body**
  - Fundus: rounded portion of uterine body superior to attachment of uterine tubes
- **Cervix**
  - Inferior portion of uterus, extends from isthmus to vagina
  - Distal end projects about 1.25 cm into vagina

The Uterine Wall

- **Myometrium**
  - 90% of the mass of the uterus
  - Arranged into longitudinal, circular, and oblique layers
  - Provides force to move fetus out of uterus into vagina
- **Endometrium**
  - 10% of uterine mass
  - Thin, inner, glandular mucosa
  - Glandular and vascular tissues support physiological demands of growing fetus

The Functional Zone

- Contains most of uterine glands
- Contributes most of endometrial thickness
- Undergoes dramatic changes in thickness and structure during menstrual cycle
- Radial arteries:
  - Supply straight arteries (to basilar zone)
  - Supply spiral arteries (to functional zone)
- Functional zone undergoes cyclical changes:
  - In response to sex hormone levels
  - Produce characteristic features of uterine cycle

The Uterine Cycle

- Also called **menstrual cycle**
- Is a repeating series of changes in endometrium that usually lasts from 21 to 35 days (average = 28 days)
- Responds to hormones of ovarian cycle:
  - Menses and proliferative phase occur during ovarian follicular phase (estrogen)
  - Secretory phase occurs during ovarian luteal phase (progesterone)
Uterine Cycle Phases

• **Menses**
  – degeneration of functional zone caused by constriction of spiral arteries (affects entire functional zone only)
  – Lasts from 1-7 days

• **Proliferative phase**
  – uterine gland growth and vascularization with new spiral arteries completely restores functional zone stimulated by estrogen
  – Occurs at same time as enlargement of primary and secondary follicles in ovary
  – stimulated and sustained by estrogens secreted by developing ovarian follicles

• **Secretory phase**
  – Endometrial glands enlarge, manufacture mucus rich in glycogen
  – essential for survival of fertilized egg
  – Begins at ovulation and persists as long as corpus luteum remains intact (lack of progesterone signals shedding)
  – Generally lasts 14 days (stimulated by progesterone mostly)

Histology of the Vagina

The Vagina

• An elastic, muscular tube
• Extends between cervix and vestibule
• Passageway for elimination of menstrual fluids
• Receives spermatozoa during sexual intercourse
• Forms inferior portion of birth canal

The Vaginal Wall

• Contains a network of blood vessels and layers of smooth muscle
• Mucosa is moistened by:
  – secretions of cervical glands
  – water movement across permeable nonkeratinized, stratified squamous epithelium
  – Forms folds (rugae)
  – Changes with ovarian cycle
  – Lamina Propria is thick and elastic
    • Contains small blood vessels, nerves, and lymph nodes
• Is surrounded by elastic muscularis layer:
  – arranged in circular and longitudinal bundles continuous with uterine myometrium

Vaginal Muscles

• 2 bulbospongiousus muscles along either side of vaginal entrance cover vestibular bulbs
  – masses of erectile tissue on either side of vaginal entrance
  – Have same embryological origins as corpus spongiosum of penis

Vaginal Bacteria

• A population of harmless resident bacteria:
  – supported by nutrients in cervical mucus
  – creates acidic environment
  – restricts growth of many pathogens
  – Acidity must be neutralized by semen or sperm will die
The Female External Genitalia

• **Vulva**: area containing female external genitalia
• **Vestibule**: central space bounded by small folds (labia minora):
  - Urethra opens into vestibule anterior to vaginal opening
• **Clitoris**: a small protruberance in vestibule
  - Similar embryonic structures as penis (contains same tissue that forms the erectile corpora cavernosa)
• Extensions of labia minora form prepuce or hood
• **Labia Majora**: larger folds that form outer limits of vulva (from same tissue as scrotum)
• **Mons Pubis**: adipose overlying pubic symphysis

Accessory Glands

• **Paraurethral Glands** (Skene's glands; analogous to the male prostate)
  - Discharge into urethra near external opening
• **Vestibular Glands**:
  - **Lesser vestibular glands**: secrete lubricant onto exposed surface of vestibule near urethra
  - **Greater vestibular glands** (Bartholin’s glands: similar to bulbourethral glands in males): secrete mucous into vestibule near vaginal entrance (at about 5 and 7 o’clock) during sexual arousal

The Mammary Glands

• Secrete milk to nourish an infant (lactation)
• Are specialized organs of integumentary system (like elaborated sweat glands)
• Are controlled by:
  - hormones of reproductive system
  - Placenta

An Active Mammary Gland

• Is a tubuloalveolar gland:
  - consisting of multiple glandular tubes (lactiferous ducts)
  - ending in secretory alveoli
• Some development occurs during each menstrual cycle
• Glands only become “active” at about 6 months gestation and can secrete **colostrum**:
  - Initial protein containing serous secretions, contain passive immunity in the form of IgA antibodies.
  - Do not secrete milk until a few days after delivery
Hormonal Control of Female Reproductive Cycle

- A complex pattern of circulating hormones that coordinates ovarian and uterine cycles thus coordinating ovulation and uterus preparation

GnRH

- GnRH from hypothalamus regulates reproductive function
- GnRH pulse frequency is key to its effects and changes over the course of ovarian cycle (in males it is relatively constant)
- Changes are controlled by estrogens and progestins:
  - Estrogens increase pulse frequency
  - Progestins decrease pulse frequency

Pituitary Response to GnRH

- Gonadotrope cells of anterior pituitary that release FSH and LH respond differently to different GnRH pulse frequencies:
  - Very low pulse frequency \(\rightarrow\) LH released (more)
  - Low pulse frequency \(\rightarrow\) FSH released
  - High pulse frequency \(\rightarrow\) LH released

One more wrinkle..

- At low and moderate levels, E inhibits LH (negative feedback)
- At high levels of E, this switches to positive feedback and suddenly E causes more LH to be released

Overall view

- Low GnRH pulse freq \(\rightarrow\) FSH released \(\rightarrow\) causes ovarian folicles to develop \(\rightarrow\) secrete more E (granulosa + thecal cells)
  - increases GnRH pulse freq, to high \(\rightarrow\) now LH is released \(\rightarrow\) signals ovulation \(\rightarrow\) luteum produces high levels of P \(\rightarrow\) very low pulse frequency \(\rightarrow\) keeps LH high
- Death of corpus luteum causes P to drop \(\rightarrow\) GnRH pulse frequency rises a little to low \(\rightarrow\) repeat
Ovarian Cycle: Follicular Phase

- Begins with FSH stimulation
- Monthly, some primordial follicles develop into primary follicles
- In follicular phase estrogen levels are low
- As follicles enlarge ovaries produce estrogen
- As tertiary follicles form, concentration of circulating estrogens rises steeply

Ovarian Cycle: Follicular Phase

- When estrogen levels exceed a threshold value for about 36 hours, switchover from negative to positive feedback occurs resulting in massive release of LH from anterior pituitary gland
- Sudden surge in LH concentration triggers:
  1. completion of meiosis I by primary oocyte
  2. rupture of follicular wall
  3. ovulation

Ovarian Cycle: Luteal Phase

- High LH levels trigger ovulation
  - promote progesterone secretion
  - trigger formation of corpus luteum
- Low frequency of GnRH pulses stimulates LH more than FSH
  - LH maintains structure and secretory function of corpus luteum
- When luteum dies, progesterone and estrogen levels drop
- GnRH pulse frequency increases:
  - stimulating FSH secretion
  - ovarian cycle begins again

Menstrual/Uterine Cycle

- Corpus luteum degenerates
- Progesterone and estrogen levels decline resulting in menses (day 0 = start of menses)
- Endometrial tissue sheds over several days:
  - until rising estrogen levels (from developing follicle) stimulates regeneration of functional zone
- Proliferative phase continues under the control of E until ovulation (day 14) when:
  - rising progesterone starts secretory phase
- Increase in progesterone (and estrogen):
  - causes enlargement of endometrial glands
  - and increase in secretory activities
- After 12 days or so, corpus luteum degenerates…

Uterine Cycle
**KEY CONCEPT**

- Cyclic changes in FSH and LH levels maintain ovarian cycle
- Hormones produced by ovaries regulate uterine cycle

**Male Sexual Arousal**

- Leads to increase in parasympathetic outflow over pelvic nerves which leads to erection and bulbourethral gland activity
- Leads to coordinated processes of emission and ejaculation
- Ejaculation occurs as powerful, rhythmic contractions in skeletal ischiocavernosus and bulbospongiosus muscles that stiffen penis and help push semen toward external urethral opening
  - Causes pleasurable sensations (orgasm)
  - Followed by subsidence of erectile tissue (detumescence)

**Female Sexual Arousal**

- Parasympathetic activation leads to:
  - engorgement of erectile tissues
  - increased secretion of cervical mucous and greater vestibular glands
- Blood vessels in vaginal walls fill with blood
- Fluid moves from underlying connective tissues to vaginal surfaces
- Female orgasm is accompanied by:
  - peristaltic contractions of uterine and vaginal walls
  - rhythmic contractions of bulbospongiosus and ischiocavernosus muscles

**Successful Function of Male Reproductive System**

- Sperm count must be adequate
- Semen must have correct pH and nutrients
- Erection and ejaculation must function properly

**Successful Function of Female Reproductive System**

- Ovarian and uterine cycles must coordinate properly
- Ovulation and oocyte transport must occur normally
- Environment of reproductive tract must support:
  - survival and movement of sperm
  - fertilization of oocyte