Chapter 27
Reproductive System

Slides by Karen Dunbar Kareiva and W. Rose.
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Why This Matters

• Understanding the anatomy and physiology of the reproductive system will help you recognize symptoms of disorders like STIs, give you the ability to treat your patients with reproductive diseases and help you educate your patients on how to have a healthy reproductive system.
Reproductive System

• Primary sex organs (gonads): testes and ovaries
  – Produce **gametes** (sex cells): sperm and ova
  – Secrete steroid **sex hormones**
    • Androgens (males)
    • Estrogens and progesterone (females)

• **Accessory reproductive organs:** ducts, glands, and external genitalia
Male Reproductive System

- **Testes** (within *scrotum*) produce sperm
- Sperm delivered to exterior through system of ducts
  - *Epididymis* → *ductus deferens* → *ejaculatory duct* → urethra
Part 1 – Anatomy of Male Reproductive System

- **Testes**: sperm-producing *male gonads* that lie within the scrotum
- Sperm is delivered to body through system of ducts: *epididymis, ductus deferens, ejaculatory duct,* and *urethra*
- Accessory sex glands: *seminal glands, prostate,* and *bulbo-urethral glands*
Figure 27.1
Reproductive organs of the male, sagittal view.

- Peritoneum
- Seminal gland (vesicle)
- Ampulla of ductus deferens
- Ejaculatory duct
- Rectum
- Prostate
- Bulbo-urethral gland
- Anus
- Bulb of penis
- Ductus (vas) deferens
- Epididymis
- Scrotum
- Testis
- Ureter
- Urinary bladder
- Prostatic urethra
- Pubis
- Intermediate part of the urethra
- Urogenital diaphragm
- Corpus cavernosum
- Corpus spongiosum
- Spongy urethra
- Glans penis
- Prepuce (foreskin)
- External urethral orifice
27.1 Scrotum and Testes

The Scrotum

- Sac of skin and superficial fascia
  - Hangs outside abdominopelvic cavity
  - Contains paired testes
    - 3°C lower than core body temperature
    - Lower temperature is necessary for sperm production
  - Midline septum divides scrotum into two compartments, one for each testis
The Scrotum (cont.)

- Temperature is kept constant by two sets of muscles
  - **Dartos muscle**: smooth muscle; wrinkles scrotal skin; pulls scrotum close to body
  - **Cremaster muscles**: bands of skeletal muscle that elevate testes
The Testes

• Each testis is surrounded by two tunics
  – *Tunica vaginalis*: outer layer derived from peritoneum
  – *Tunica albuginea*: inner layer forms fibrous capsule

• Septa divide testis into ~250 *lobules*, each containing one to four *seminiferous tubules*
  – Site of sperm production
Figure 27.2
Relationships of testis, scrotum, spermatic cord.

- Urinary bladder
- Superficial inguinal ring (end of inguinal canal)
- Spermatic cord
- Penis
- Septum of scrotum
- Cremaster muscle
- External spermatic fascia
- Scrotum containing dartos muscle
- Skin
- Testicular artery
- Ductus (vas) deferens
- Autonomic nerve fibers
- Pampiniform venous plexus
- Epididymis
- Tunica vaginalis (from peritoneum)
- Tunica albuginea of testis
- Internal spermatic fascia
The Testes (cont.)

- Seminiferous tubules have thick, stratified epithelium surrounding central fluid-containing lumen
  - Epithelium contains spheroid spermatogenic cells (sperm-forming cells) embedded in support cells called sustentocytes
- Myoid cells surround each seminiferous tubule
  - Smooth muscle–like cells that may squeeze sperm and testicular fluids out of testes
- Tubules of each lobule converge to form the straight tubule
The Testes (cont.)

- Sperm is conveyed from seminiferous tubules to straight tubule → rete testis → efferent ductules → epididymis
  - Epididymis is made up of the head, the body, and the tail
  - Sperm are stored in the tail until ejaculation

- **Interstitial endocrine cells**: located in soft tissue surrounding seminiferous tubules
  - Produce androgens, such as testosterone
  - Secrete it into interstitial fluid
The Testes (cont.)

• Blood supply
  – Testicular arteries arise from abdominal aorta
  – Testicular veins arise from pampiniform venous plexus surrounding each testicular artery
    • Cooler; absorb heat from testicular arteries
    • Keep testes cool

• Spermatic cord encloses nerve fibers, blood vessels, and lymphatics that supply testes
Figure 27.3a
Structure of the testis.

- Spermatic cord
- Blood vessels and nerves
- Ductus (vas) deferens
- Head of epididymis
- Efferent ductule
- Rete testis
- Straight tubule
- Body of epididymis
- Duct of epididymis
- Tail of epididymis
- Testis
- Seminiferous tubule
- Lobule
- Septum
- Tunica albuginea
- Tunica vaginalis
- Cavity of tunica vaginalis
Figure 27.3b
Structure of the testis.

- Spermatic cord
- Ductus deferens
- Epididymis
- Testis
• Testicular cancer
  – Rare, but most common cancer in men age 15–35
    • Having mumps that lead to orchitis (inflammation of testis) could be a risk factor
    • Cryptorchidism is most common risk factor
      – Nondescent of testes
  – Sign: painless, solid mass in testis
  – 90% cured by surgical removal of testis and often radiation or chemotherapy
27.2 Penis

- **Penis**: male copulatory organ
- **External genitalia**: scrotum and penis
- Penis consists of:
  - Root and shaft that ends in **glans penis**
  - **Prepuce**, or foreskin: cuff of loose skin covering glans
    - Circumcision: surgical removal of foreskin
      - 60% of males in U.S. circumcised, but only 15% in other parts of world
      - Studies show 60% reduction in HIV risk and reduced risk for other reproductive infections
27.2 Penis

- Internally, penis made up of spongy urethra and three cylindrical bodies of *erectile tissue*, spongy network of connective tissue and smooth muscle with vascular spaces
- **Corpus spongiosum**: surrounds urethra and expands to form glans and bulb
- **Corpora cavernosa**: paired dorsal erectile bodies
• *Erection*: erectile tissue fills with blood, causing penis to enlarge and become rigid

• *Crura*: proximal ends of corpora cavernosa surrounded by ischiocavernosus muscle; anchors penis to pubic arch
Figure 27.4
Male reproductive structures.
The Male Perineum

• Diamond-shaped region between pubic symphysis, coccyx, and ischial tuberosities
• Suspends scrotum
• Contains root of penis and anus
Figure 27.5 The male perineum, inferior view.
• Ducts carry sperm from testes to body exterior
  – Epididymis
  – Ductus deferens
  – Ejaculatory duct
  – Urethra
Epididymis

- **Head**: contains efferent ductules and is located on superior aspect of testis
- **Body and tail**: located on posterolateral area of testis
- **Duct of the epididymis** is ~ 6 m in length
  - Microvilli (stereocilia) absorb testicular fluid and pass nutrients to stored sperm
- Nonmotile sperm enter, pass slowly through (~ 20 days), become motile
  - Can be stored several months
- During ejaculation, epididymis contracts, expelling sperm into ductus deferens

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Epididymis (cont.)

• Nonmotile sperm enter, pass slowly through (~ 20 days), become motile
  – Can be stored several months
• During ejaculation, epididymis contracts, expelling sperm into ductus deferens
Ductus Deferens and Ejaculatory Duct

- **Ductus deferens** (vas deferens) ~ 45 cm long
  - Passes through inguinal canal to pelvic cavity
  - Expands to form **ampulla**
  - Joins duct of seminal vesicle to form **ejaculatory duct**
- Smooth muscle in walls propels sperm from epididymis to urethra
- **Vasectomy**: cutting and ligating ductus deferens
  - Nearly 100% effective form of birth control
Figure 27.3a
Structures of the testis.

- Ductus (vas) deferens
- Head of epididymis
- Efferent ductule
- Rete testis
- Straight tubule
- Body of epididymis
- Duct of epididymis
- Tail of epididymis
- Spermatic cord
- Blood vessels and nerves
- Testis
- Seminiferous tubule
- Lobule
- Septum
- Tunica albuginea
- Tunica vaginalis
- Cavity of tunica vaginalis
Urethra

• Conveys both urine and semen (at different times)
• Has three regions
  – **Prostatic urethra**: surrounded by prostate
  – **Intermediate part of the urethra (membranous urethra)**: in urogenital diaphragm
  – **Spongy urethra**: runs through penis; opens at *external urethral orifice*
Figure 27.4 Male reproductive structures.
27.4 Male Accessory Glands

- **Seminal glands**
  - On posterior bladder surface
  - Contains smooth muscle that contracts during ejaculation
  - Produces viscous alkaline seminal fluid
    - Fructose, citric acid, coagulating enzyme (vesiculase), and prostaglandins
    - Yellow pigment fluoresces with UV light
    - Comprises 70% volume of semen
  - Duct of seminal gland joins ductus deferens to form ejaculatory duct
27.4 Male Accessory Glands

• Prostate
  – Encircles urethra inferior to bladder
  – Contains smooth muscle that contracts during ejaculation
  – Secretes 1/3 of semen fluid volume
    • Contains citrate, enzymes, and prostate-specific antigen (PSA)
    • Plays a role in sperm activation
    • Enters prostatic urethra during ejaculation
• Prostate disorders
  – Prostatitis: inflammatory disorders
    • Bacterial infection; acute and chronic; treated with antibiotics
    • Chronic prostatitis: also called pelvic pain syndrome is most common form; two types:
      – Inflammatory type: urinary tract infection symptoms; pain in external genitalia and lower back; leukocytes in urine
      – Noninflammatory type: same as inflammatory but no leukocytes or bacteria in urine
Benign prostatic hyperplasia

- May be age-related
- Distorts urethra
- Treated with surgery, but newer options include:
  - Using microwaves or drugs to shrink prostate
  - Balloon compression
  - Radio-frequency radiation
– Prostate cancer

• Second most common cause of cancer death in males
• Digital exam screening, PSA levels
  – Biopsy if abnormal
• Treatment may include: surgery, radiation (incl. brachytherapy), “castration” (surgical or chemical, to reduce T levels, since prostate cancer cell growth is stimulated by T), chemotherapy
• In clinical trials: cryosurgery, ultrasound, proton beam therapy
27.4 Male Accessory Glands

- **Bulbo-urethral glands**
  - Pea-sized glands inferior to prostate
  - Produce thick, clear mucus during sexual arousal
    - Lubricate glans penis
    - Neutralize traces of acidic urine in urethra
Figure 27.4 Male reproductive structures.
Semen

- Mixture of sperm and accessory gland secretions
  - 2–5 ml semen per ejaculate; 20–150 million sperm/ml
- Contains fructose for ATP production
- Alkaline fluid neutralizes acidity of male urethra and female vagina, enhances motility
- Prostaglandins decrease viscosity of cervical mucus, stimulate reverse peristalsis in uterus

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Erection

- Arterioles are normally constricted
  - Sexual excitement causes CNS activation of parasymathetic neurons, which releases nitric oxide (NO)
    - NO release causes relaxation of local vascular smooth muscle
- When smooth muscles relax, arterioles dilate
Erection (cont.)

- Corpora cavernosa expands and retards venous drainage, leading to engorgement of erectile tissues with blood
- Initiated by sexual stimuli (touch; mechanical stimulation; erotic sights, sounds, smells)
- Can be induced or inhibited by emotions or higher mental activity
- Corpus spongiosum keeps urethra open
Ejaculation

- Propulsion of semen from male duct system
- *Sympathetic* spinal reflex
  - Bladder sphincter muscle constricts, preventing expulsion of urine
  - Ducts and accessory glands contract and empty their contents
  - Bulbospongiosus muscles undergo rapid series of contractions that cause expulsion of semen
  - Ejaculatory event is called **climax** (*orgasm*)
Erectile dysfunction

- Parasympathetic nerves of penis release too little NO
- Possible causes: alcohol, drugs, hormones, blood vessel or nervous system problems, incompetent venous valves that fail to retain blood in penis
- “ED” drugs (Viagra, Cialis, etc.) potentiate existing NO effects
Sildenafil (Viagra) mechanism of action.
Sildenafil (Viagra) mechanism of action

eNOS, nNOS: endothelial & neural nitric oxide synthase
NO: nitric oxide (synthesized by eNOS & nNOS)
sGC: soluble guanylate cyclase (enzyme activated by NO)
cGMP = cyclic guanosine monophosphate (made by sGC, causes smooth muscle relaxation which causes vasodilation)
PDE5 = phosphodiesterase 5 (enzyme that breaks down cGMP)
Sildenafil & related drugs inhibit PDE5, so slow breakdown of cGMP.
Spermatogenesis: production of sperm (spermatozoa) in seminiferous tubules

Most body cells have 46 chromosomes:
- Two sets (23 pairs) of chromosomes (2n, diploid)
  - One maternal, one paternal: homologous chromosomes

Gametes have 23 chromosomes (n, haploid)
Meiosis Compared to Mitosis

• Gamete formation involves meiosis, which differs from mitosis
  – Involves two consecutive cell divisions (*meiosis I and II*), but only one round of DNA replication
    • Produces four daughter cells

• Functions of meiosis
  – Number of chromosomes are cut in half (*2n* to *n*)
  – Introduces genetic diversity, as all daughter cells are genetically different from original cell
Figure 27.6-1 Mitosis and meiosis in a mother cell with $2n = 4$.
Figure 27.7-1: Meiosis I.

**Interphase events**
As in mitosis, meiosis is preceded by DNA replication and other preparations for cell division.

**Prophase I**
Prophase events occur, as in mitosis. Additionally, synapsis occurs: Homologous chromosomes come together along their length to form tetrads. During synapsis, the “arms” of homologous chromatids wrap around each other, forming several crossovers. The nonsister chromatids trade segments at points of crossover. Crossover is followed through the diagrams below.

**Metaphase I**
The tetrads align randomly on the spindle equator in preparation for anaphase.

**Anaphase I**
Unlike anaphase of mitosis, the centromeres do not separate during anaphase I of meiosis, so the sister chromatids (dyads) remain firmly attached. However, the homologous chromosomes do separate from each other and the dyads move toward opposite poles of the cell.

**Telophase I**
The nuclear membranes re-form around the chromosomal masses, the spindle breaks down, and the chromatin reappears as telophase and cytokinesis end. The 2 daughter cells (now haploid) enter a second interphase-like period, called interkinesis, before meiosis II occurs. There is no second replication of DNA before meiosis II.
Meiosis Compared to Mitosis (cont.)

• Meiosis I
  – Reduction division of meiosis: reduces chromosome number from $2n \rightarrow n$
  – Prophase I has events not seen in mitosis or meiosis II
    • Synapsis: homologous chromosomes pair up forming tetrads consisting of 4 chromatids
    • Crossover (chiasmata): exchange of genetic material between maternal & paternal chromatids
      – Results in unique chromosomes that are mixtures of maternal and paternal chromosomes
Meiosis Compared to Mitosis (cont.)

• Meiosis I (cont.)
  – During *metaphase I*, tetrads line up randomly at spindle equator
  – During *anaphase I*, sister chromatids of one homologous chromosome are separated from sister chromatids of other
Meiosis Compared to Mitosis (cont.)

• Meiosis I (cont.)
  – At end of *meiosis I*, each daughter cell has:
    • Two copies (sister chromatids) of one member of each homologous pair (either maternal or paternal) and none of the other
    • Haploid chromosomal number because still-united sister chromatids are considered one chromosome (twice amount DNA in each chromosome)
Figure 27.8  Independent assortment of homologous chromosomes in meiosis.

Possibility 1

Two equally probable arrangements of chromosomes at metaphase I

Possibility 2

Metaphase II

Combination 1
Combination 2

Daughter cells

Combination 3
Combination 4
Meiosis Compared to Mitosis (cont.)

• **Meiosis II**
  – **Equational division of meiosis**
    • Events are similar to mitosis, except there is no chromosome replication before process begins
    • Sister chromatids from meiosis I are separated and pulled toward opposite poles
    • Results in one of each chromosome per daughter cell
Meiosis II begins with the products of meiosis I (2 haploid daughter cells) and undergoes a mitosis-like nuclear division process referred to as the equational division of meiosis.

After progressing through the phases of meiosis and cytokinesis, the product is 4 haploid cells, each genetically different from the original mother cell. (During human spermatogenesis, the daughter cells remain interconnected by cytoplasmic extensions during the meiotic phases.)
Spermatogenesis: Summary of Events in the Seminiferous Tubules

- Occurs in seminiferous tubules of testis
- **Spermatogenic cells** give rise to sperm
- Overview of three steps of spermatogenesis:
  1. **Mitosis of spermatogonia** (stem cell) forms two spermatocytes
  2. **Meiosis**
     - Spermatocytes form secondary spermatocytes, which form spermatids
  3. **Spermiogenesis**
     - Spermatids become sperm
Figure 27.9b Spermatogenesis.

- **Spermatogenesis** (early spermatogenesis)
  - Spermatogonium (stem cell)
  - Enters meiosis I and moves to adluminal compartment
  - Meiosis I completed
  - Primary spermatocyte
  - Meiosis II
  - Secondary spermatocytes
  - Early spermatids
  - Late spermatids
  - Type A daughter cell
    - Remains at basal lamina as a precursor cell
  - Type B daughter cell

- **Spermatogenesis** (late spermatogenesis)
  - Spermatozoa

*Events of spermatogenesis, showing the relative position of various spermatogenic cells*
Spermatogenesis: Summary of Events in the Seminiferous Tubules (cont.)

1. Mitosis of spermatogonia: forming spermatocytes
   – Spermatogenesis begins at puberty
   – Begins with spermatogonia
     • Stem cells that are in contact with epithelial basal lamina
     • Each mitotic division yields one type A daughter cell and one type B daughter cell
       – Type A cells maintain germ cell line at basal lamina
       – Type B cells move toward lumen and develop into primary spermatocytes
Figure 27.9c Spermatogenesis.

- Spermatogonium (stem cell)
- Basal lamina
- Type A daughter cell (remains at basal lamina as a precursor cell)
- Type B daughter cell
- Primary spermatocyte
- Secondary spermatocytes
- Early spermatids
- Late spermatids
- Spermatozoa

(c) A portion of the seminiferous tubule wall, showing the spermatogenic cells surrounded by sustentocytes (colored gold)
2. **Meiosis: spermatocytes to spermatids**

   – **Meiosis I**
     
     • Primary spermatocyte \((2n)\) undergoes meiosis I, forming **two secondary spermatocytes** \((n)\)

   – **Meiosis II**
     
     • Each secondary spermatocyte \((n)\) rapidly undergoes meiosis II to become **two spermatids** \((n)\)
       
       – Spermatids: small, nonmotile cells found close to lumen of tubule
Figure 27.9c Spermatogenesis.

- Type A daughter cell (remains at basal lamina as a precursor cell)
- Type B daughter cell
- Primary spermatocyte
- Secondary spermatocytes
- Early spermatids
- Late spermatids
- Spermatogonium (stem cell)
- Sustentocyte nucleus
- Sustentocytes
- Lumen of seminiferous tubule
- Lumen of adluminal compartment
- Adluminal compartment
- Cytoplasmic bridge
- Tight junction between sustentocytes
- Basal compartment
- Basal lamina

(c) A portion of the seminiferous tubule wall, showing the spermatogenic cells surrounded by sustentocytes (colored gold)
3. Spermiogenesis: spermatids to sperm
   
   – Spermatids
     • Contain correct haploid chromosome number needed for fertilization ($n$)
     • Nonmotile
   
   – Spermiogenesis
     • Streamlining process where spermatid elongates, loses excess cytoplasm, and forms a tail to become a spermatozoon (sperm)
3. **Spermiogenesis: spermatids to sperm (cont.)**

   - Major regions of sperm:
     - **Head**: genetic region that includes nucleus and helmetlike acrosome containing hydrolytic enzymes that enable sperm to penetrate egg
     - **Midpiece**: metabolic region containing mitochondria that produce ATP to move tail
     - **Tail**: locomotor region that includes flagellum
Figure 27.10 Spermiogenesis: transformation of a spermatid into a functional sperm.

Approximately 24 days
Spermatogenesis: Summary of Events in the Seminiferous Tubules (cont.)

- Role of sustentocytes (also called **Sertoli cells**)
  - Extend through wall of tubule and surround developing cells
  - Provide nutrients and signals to dividing cells
  - Move cells along to lumen
  - Secrete testicular fluid into lumen for sperm transport
  - Phagocytize faulty germ cells and excess cytoplasm
  - Produce chemical mediators to regulate spermatogenesis (inhibin)
Spermatogenesis: Summary of Events in the Seminiferous Tubules (cont.)

- Role of sustentocytes (cont.)
  - Sustenocytes contain tight junctions that divide tubule into two compartments
    - **Basal compartment**: area where spermatogonia and primary spermatocytes are located
    - **Adluminal compartment**: area where meiotically active cells and tubule lumen are located
Spermatogenesis: Summary of Events in the Seminiferous Tubules (cont.)

• Tight junctions form **blood testis barrier**
  – Prevents sperm antigens from escaping into blood and causing activation of immune system
  – Sperm is not formed until puberty, so it is absent during immune system development
    • Results in sperm not being recognized as “self”
    • Therefore, sperm needs to be kept separated from rest of body to avoid being attacked by immune system
Figure 27.9c Spermatogenesis.

- **Spermatogonium** (stem cell)
- **Primary spermatocyte**
- **Secondary spermatocytes**
- **Early spermatids**
- **Late spermatids**
- **Spermatozoa**
- **Adluminal compartment**
- **Basal compartment**
- **Basal lamina**
- **Cytoplasmic bridge**
- **Lumen of seminiferous tubule**
- **Tight junction between sustentocytes**
- **Cytoplasm of adjacent sustentocytes**
- **Sustentocyte nucleus**
- **Sustentocyte**
- **Cytoplasm of adjacent sustentocytes**

A portion of the seminiferous tubule wall, showing the spermatogenic cells surrounded by sustentocytes (colored gold).
Spermatogenesis: Summary of Events in the Seminiferous Tubules (cont.)

– Spermatogenesis takes 64–72 days if conditions are hospitable

– Sperm are unable to swim, but pressure of testicular fluid pushes immotile sperm into epididymis, where they gain motility and fertilizing power
The Hypothalamic-Pituitary-Gonadal Axis

- Production of gametes and sex hormones is regulated by sequence of hormonal events involving hypothalamus, anterior pituitary gland, and testes
  - Referred to as hypothalamic-pituitary-gonadal axis
  - Interacting hormones: GnRH, FSH, LH, testosterone, inhibin
Figure 27.11 Hormonal regulation of testicular function, the hypothalamic-pituitary-gonadal (HPG) axis.

1. Anterior pituitary
2. Inhibin
3. FSH
4. LH
5. Testosterone
6. Somatic and psychological effects at other body sites; maintenance of secondary sex characteristics
7. Sustentocyte

Interstitial endocrine cells
FSH
LH
Inhibin
ABP
Spermatogenic cells
Semeniferous tubule
Spermatogenesis

GnRH
Via portal blood

Stimulates
Inhibits
Figure 27.12 Plasma testosterone and sperm production levels versus age in male humans.
Mechanism and Effects of Testosterone Activity

• Testosterone, synthesized from cholesterol, is transformed at some target cells
  – Converted to dihydrotestosterone (DHT) in prostate and estradiol in some brain neurons
  – Prompts spermatogenesis and targets all accessory organs
  – Has multiple anabolic effects throughout body

• Deficiency leads to atrophy of accessory organs, semen volume declines, and erection/ejaculation are impaired; treatment: testosterone replacement
Mechanism and Effects of Testosterone Activity (cont.)

• **Male secondary sex characteristics**: features induced in *nonreproductive* organs by male sex hormones (mainly testosterone)
  – Appearance of pubic, axillary, and facial hair
  – Enhanced growth of chest hair; deepening of voice
  – Skin thickens and becomes oily
  – Bones grow, increase in density
  – Skeletal muscles increase in size and mass
  – Boosts basal metabolic rate
  – Basis of sex drive (libido) in males
Mechanism and Effects of Testosterone Activity (cont.)

• Testosterone
  – Masculinizes embryonic brain
  – Continues to exert effect well into adulthood
  – Although adrenal glands also produce androgens in small amounts, production is insufficient to maintain normal testosterone-mediated functions