I. THE URINARY SYSTEM

CONSISTS OF:
- Kidneys
- Urinary tract (calyces, renal pelvis, ureter, urinary bladder, urethra)

GENERAL FEATURES OF KIDNEY
- Hilum
  - Slit-like opening on concave medial surface where blood vessels enter & leave, & where renal pelvis leaves to become ureter
- Renal sinus
  - Fat-filled cavity within the kidney; entered by passing through the hilum
  - Contains minor & major calyces, most of the renal pelvis, & branches of renal blood vessels
- Cortex: Outer, darker staining region (in H&E)
- Medulla: Inner, lighter staining region (in H&E)

CORTEX VS. MEDULLA OF KIDNEY
- Cortex
  - Includes:
    - Cortical arches (between the capsule & the bases of the pyramids)
    - Renal columns (the areas between pyramids)
  - NOTE: Ross includes renal columns in medulla (we don’t)
  - Consists of two histological components:
    - Medullary rays
    - Cortical labyrinths (contain renal corpuscles)
- Medulla:
  - A discontinuous tissue mass made up of renal pyramids
  - Base of pyramid faces the cortex
  - Papilla = conical apex of each pyramid; projects into a minor calyx
  - Large collecting ducts (ducts of Bellini) open into the minor calyx on the part of a papilla called the area cribrosa (Latin, cribrosa = sieve)

RENAL LOBES VS. RENAL LOBULES
- Renal lobe:
  - Defined as all the tissue whose nephrons drain into the same minor calyx
  - Includes both cortex & medulla
  - Consists of:
    - A renal pyramid
    - Its cortical arch
    - Half of the renal column on either side of pyramid
    - Interlobar arteries & veins are located in the renal columns at the boundaries between lobes
    - Each lobe contains many lobules
- Renal lobule:
  - Defined as all the tissue whose nephrons drain into the same medullary ray
  - Includes cortex but no medulla
MICROSCOPIC ANATOMY

Consists of:
- A medullary ray (which forms the center of the lobule)
  - a medullary ray is a bundle of cortical tubules, running parallel
to one another & perpendicular to the capsule, so that it
  seems to radiate from the medulla into the cortex
  - does not contain renal corpuscles
- Half the width of the cortical labyrinth that surrounds the ray

Interlobular arteries & veins – located at the boundaries between lobules

MEDULLARY RAY VS. CORTICAL LABYRINTH

Medullary ray
- Looks very different when cut in cross section vs. longitudinal
- Contains 3 kinds of tubules:
  - Collecting tubules
  - Straight proximal tubules (= thick descending limb of Henle’s loop)
  - Straight distal tubules (= thick ascending limb of Henle’s loop)
- These tubules continue on into the medulla

Cortical labyrinth
- Is the area that completely surrounds each medullary ray
- Contains:
  - Renal corpuscles
  - Proximal convoluted tubules
  - Distal convoluted tubules
  - Arched collecting tubules (= connecting tubules)
- Due to the random coiling of the tubules, a cortical labyrinth looks the
  same no matter what the plane of the section

RENAL CORPUSCLE

- Includes glomerulus and Bowman’s capsule
  - Glomerulus includes
    - 10-20 loops of fenestrated capillaries (glomerular capillaries) whose
      endothelial cells have no diaphragms
    - Intraglomerular mesangial cells
      - phagocytic cells that clean the basal lamina of the capillaries
      - located between capillary endothelium & the basal lamina
      - are also contractile
  - Bowman's capsule has a visceral layer & a parietal layer
  - Visceral layer = podocytes
    - cover the outer surface of capillaries
    - have long primary processes, which give rise to secondary
      processes, which give rise to pedicels (foot processes)
    - pedicels interdigitate with pedicels of neighboring podocytes to
      form filtration slits that are covered by a slit diaphragm
  - Parietal layer = simple squamous epithelium making up the wall of
    the capsule
  - Visceral & parietal layer are separated by Bowman’s space (urinary
    space) which receives the glomerular filtrate
Bowman’s capsule has 2 poles:

**Vascular pole:**
- Where afferent & efferent arterioles enter & leave, respectively
- Where visceral & parietal layers of Bowman’s capsule are continuous with one another
- Macula densa is located outside the corpuscle near the vascular pole

**Urinary pole:**
- Where proximal convoluted tubule is continuous with parietal layer of Bowman’s capsule (lumen of proximal tubule is continuous with urinary space)
- Epithelium changes abruptly from simple squamous to simple cuboidal

**JUXTAGLOMERULAR APPARATUS**

Located near vascular pole of each renal corpuscle. It has 3 components:

- **Macula densa** (Latin = dark spot)
  - Is in the terminal portion of the distal straight tubule near the junction with the distal convoluted tubule
  - Formed by cells of the distal tubule that are located on the side of the tubule nearest the renal corpuscle. Macula densa cells are narrower and generally also taller than ordinary distal tubule cells.
  - The closely packed nuclei make the macula stain darker
  - Located adjacent to the juxtaglomerular cells (JG cells)
  - Basement membrane is absent between macula densa and JG cells
  - Macula densa cells respond to a variety of stimuli including changes in blood pressure, blood flow rate, and composition of the fluid in the distal tubule.
  - Example: A decrease in Na$^+$ concentration in the distal tubules stimulates macula densa cells to signal the juxtaglomerular cells, causing them to release renin. Renin activates the angiotensin-aldosterone system. Aldosterone stimulates Na$^+$ reabsorption from collecting tubules, which decreases Na$^+$ loss in the urine, & increases blood pressure & renal blood flow.

- **Juxtaglomerular cells** (JG cells, or granular cells)
  - Are modified smooth muscle cells in the tunica media of the afferent arteriole (sometimes also the efferent)
  - Contain renin in cytoplasmic secretory vacuoles

- **Extraglomerular mesangial cells** (lacis cells)
  - Located in the triangular region bounded by afferent arteriole, efferent arteriole, & macula densa

**THE MINIMUM BLOOD-FILTRATE BARRIER:**

- Is the thinnest possible layer of tissue that separates the glomerular capillary lumen from the urinary space
- It has three components:
  - Fenestrated endothelium of glomerular capillary (no diaphragms)
  - Fused basal lamina between capillary endothelium & podocytes
  - Filtration slits between pedicels of podocytes
  - Covered by a filtration slit diaphragm (a protein complex, not a lipid bilayer)
NEPHRON vs. URINIFEROUS TUBULE:

A nephron consists of:
- A renal corpuscle
- Proximal convoluted tubule
- Loop of Henle
  - Thick descending limb (= proximal straight tubule)
  - Thin limb
  - Thick ascending limb (= distal straight tubule)
- Distal convoluted tubule

A uriniferous tubule consists of:
- Nephron + collecting tubule/duct

NOTE: Each collecting duct receives the filtrate from many nephrons

MORPHOLOGY OF NEPHRONS VARIES BETWEEN TWO EXTREMES

Juxtamedullary nephrons:
- Renal corpuscle is located deep in the cortex, near medulla
- Long loop of Henle that extends deep into medulla

Cortical nephrons:
- Renal corpuscle is located closer to the surface of kidney
- Loop of Henle that extends only a short distance into medulla

HOW TO IDENTIFY TUBULE TYPES BY LIGHT MICROSCOPY:

Proximal Tubules
- Simple cuboidal epithelium
- Abundant microvilli form a brush border visible by LM
  - Poorly fixed microvilli may slough off into lumen as debris
  - Poor fixation may cause stellate shaped lumen
- Large cells, therefore nuclei are farther apart, i.e., relatively few present in a cross section
- Often more eosinophilic than distal tubules due to many mitochondria
- Lateral cell boundaries are indistinct by LM; due to many folds of the plasma membrane that interdigitate with folds of neighboring cells
- Basal striations may be visible by LM (typical ion pumping cell)

Proximal convoluted tubules:
- Are found in a cortical labyrinth
- Are longer than distal convoluted tubules, therefore make up a larger percentage of the tubule profiles seen in a section through a cortical labyrinth

Proximal straight tubules:
- Found in medullary rays of the cortex and in the outermost medulla

Distal Tubules

Distal convoluted tubules:
- Found in a cortical labyrinth
- Fewer profiles of distal convoluted tubules than proximal convoluted tubules
Distal straight tubules:
- Found in medullary rays of the cortex and in the medulla
- Extend deeper into the medulla than proximal straight tubules
All distal tubules are similar to proximal tubules in that they have:
- Simple cuboidal epithelium
- Lateral cell boundaries indistinct by LM due to interdigitating folds
Distal tubules differ from proximal tubules in that distals have:
- Fewer microvilli; no prominent brush border visible by LM
  - Gives a cleaner, sharper edge to the lumen
- Smaller cells (more nuclei in each cross section of a tubule)
- Nuclei that are often very close to the apical plasma membrane so that they seem to bulge into the lumen
- Often smaller in diameter than proximal convoluted
- Basal striations less prominent than in proximal tubules by LM

Collecting Tubules and Ducts
- Lateral cell membranes are visible by LM because the cells interdigitate less with neighboring cells
- No brush border by LM; a few microvilli by EM
- Nuclei don't bulge into lumen; are near the center of cuboidal cells
- Contain two cell types:
  - Principal cells (light cells) – are most common
    - Have a single nonmotile cilium (primary cilium) visible by EM
    - Membrane contains water channels (aquaporins) regulated by ADH that determine permeability of collecting duct
  - Intercalated cells (dark cells)
    - Have many small folds of their apical membrane (microplicae)
    - Number gradually decreases until there are none at the papilla
    - Involved in the secretion of H+ (α-intercalated cells) or bicarbonate (β-intercalated cells)

Collecting tubule vs. collecting duct terminology
- If it’s small, with a low cuboidal to cuboidal epithelium, call it a tubule
- If epithelium is columnar call it a duct, unless it’s clearly in the cortex
- If it’s in the medulla, call it a duct
- If it opens into a minor calyx at the renal papilla it’s a duct of Bellini

Thin limb of the Loop of Henle
- Found in medulla
- Simple squamous epithelium that is slightly thicker (taller) than the endothelial cells of the vasa recta

HOW TO IDENTIFY TUBULE TYPES BY ELECTRON MICROSCOPY (EM):
- Proximal tubules (straight and convoluted)
  - Well-developed brush border
  - Folds of basal plasmalemma & mitochondria between the folds
  - Extensive interdigitation of lateral plasma membranes
Distal tubules (straight and convoluted)
   Many fewer microvilli than proximal
   Basal folds and mitochondria between folds
   Considerable interdigitation of lateral plasma membranes

Collecting tubules/ducts by EM
   Only sparse apical microvilli
   Relatively straight lateral plasma membranes
   Fewer mitochondria than proximals or distals

IDENTIFICATION OF KIDNEY REGIONS BASED ON COMBINATIONS OF TUBULE TYPES PRESENT

Cortex has:
   Convoluted tubules (more profiles of proximal than distal)
      Located in cortical labyrinths
   Straight proximal, straight distal and collecting tubules
      Located in medullary rays
   Renal corpuscles in the cortical labyrinths

Subdivisions of the medulla:
   Outer stripe of outer medulla:
      Contains straight proximal tubules, straight distal tubules & collecting ducts (“no” thin limbs)
      Extends as far into medulla as the point where straight proximal tubules become thin descending limbs of the loop of Henle
   Inner stripe of outer medulla:
      Contains thin limbs, straight distal tubules, & collecting ducts (no proximal tubules)
      Extends as far into medulla as the deepest point where ascending thin limbs become straight distal tubules
   Inner medulla:
      Contains collecting ducts & thin limbs (no proximal or distal tubules)
      Has more interstitial CT between tubules than in the outer medulla

RENAL BLOOD SUPPLY

Renal artery divides into anterior and posterior divisions near the hilum
   Each division gives off segmental branches in the renal sinus
You should be able to identify the following based on their location:
   Interlobar arteries (bisect the renal columns; run toward capsule; give rise to arcuate arteries)
   Arcuate arteries (run parallel to base of pyramids, near the border between cortex & medulla; give off numerous interlobular arteries)
   Interlobular arteries (bisect cortical labyrinths; run toward capsule)
   Afferent glomerular arterioles (many arise from each interlobular artery; they lead to glomeruli)
   Glomerular capillaries
   Efferent glomerular arterioles (one from each glomerulus
They break up into either peritubular capillaries or vasa recta

**Peritubular capillaries**
- An irregular network of anastomosing vessels found mainly in cortex
- Arise from efferent arterioles of most nephrons
- Empty into an interlobular or arcuate vein

**Vasa recta**
- Long straight vessels found in the medulla
- Arise from efferent arterioles of juxtamedullary nephrons
- Empty into an interlobular or arcuate vein

Note the existence of an arterial portal system in the kidney:
- Glomerular capillary bed → efferent arteriole → peritubular capillary bed
  or vasa recta

**URINARY TRACT (MINOR CALYCES THROUGH URETHRA):**

**CALYCES & PELVIS:**
- **Minor calyces**
  - Funnel-shaped structures
  - One renal papilla protrudes into lumen of each minor calyx
  - Epithelium covering the papilla becomes continuous with the epithelium lining the calyx
  - Several ducts of Bellini deliver urine into each minor calyx
    - Openings of ducts of Bellini (papillary ducts) form the area cribrosa

- **Major calyces are formed by the union of 2 or more minor calyces**

- **Renal pelvis**
  - Formed by the union of all the major calyces
  - Narrows down and becomes the ureter at the hilum

- **Wall of minor calyces, major calyces & pelvis consists of:**
  - Transitional epithelium
  - Lamina propria
  - A thin smooth muscle layer
  - Adventitia that blends with fat of renal sinus

**URETERS:**
- Renal pelvis narrows to become ureter
- Ureter has a narrow lumen, often stellate in cross section due to muscle contraction
- **Mucosa** = Transitional epithelium and lamina propria
  - No muscularis mucosae, so the one CT layer is usually called a lamina propria by histologists, but clinicians sometimes call it a submucosa

- **Muscularis**
  - Inner longitudinal, outer circular in the proximal 2/3 (i.e. the reverse of the GI tract)
  - Distal 1/3 adds an outer longitudinal layer, so the arrangement there is:
    - Inner longitudinal, middle circular, outer longitudinal

- Adventitia is present (not serosa)
Transitional epithelium
Plasma membrane includes thickened plaques visible by EM
In empty bladder the plaques fold up (like closing a book) to form
discoid (fusiform) vesicles in the cytoplasm

URINARY BLADDER:
Lumen is lined by transitional epithelium
Lamina propria
In many species there is no muscularis mucosae
Humans often have a thin discontinuous or continuous muscularis mucosae,
and in that case would have a lamina propria and a submucosa
The muscularis (= muscularis propria or the detrusor muscle of the bladder):
Is thicker than in ureter
3 smooth muscle layers (less regularly arranged than in ureter)
Forms the internal (involuntary) sphincter (sphincter vesicae)
Adventitia is present over most of bladder
Serosa is present where the roof of the bladder contacts the peritoneum

MALE URETHRA
Has three parts:
Prostatic
Membranous, where it passes through the urogenital (UG) diaphragm
Penile
Prostatic urethra
Is lined mainly by transitional epithelium
Receives secretions of prostatic glands
Receives sperm & secretions of seminal vesicles via ejaculatory ducts
Membranous urethra
Lined by stratified & pseudostratified columnar epithelium
Surrounded by the skeletal muscle of the UG diaphragm
Penile urethra
Lined by pseudostratified columnar epithelium proximally (with patches
of stratified columnar), & by stratified squamous near its termination
Surrounded by erectile tissue of corpus spongiosum
Receives mucous secretions from bulbourethral glands and glands of
Littré (urethral glands)

FEMALE URETHRA:
Extends from bladder to vestibule (space between the two labia minora)
Epithelium changes from:
Transitional epithelium in a short segment near bladder
Then patches of pseudostratified &/or stratified columnar
Then most of its length is lined by minimally keratinized stratified
squamous epithelium
Receives mucous secretions from urethral glands in lamina propria
Where urethra penetrates the urogenital (UG) diaphragm, skeletal muscle
of the diaphragm forms the external (voluntary) urethral sphincter
Extensive venous plexus in the lamina propria resembles erectile tissue
II. MALE REPRODUCTIVE SYSTEM

TESTES:

- Are exocrine and endocrine glands
  - Exocrine portion = the seminiferous tubules, which “secrete” spermatozoa into the duct system in a “holocrine” fashion
  - Endocrine portion = interstitial cells (Leydig cells), which secrete testosterone, & Sertoli cells, which secrete inhibin into the blood

STRUCTURAL ORGANIZATION OF TESTES

- Tunica albuginea
  - Is a dense irregular CT capsule; surrounds the entire testis
  - Thickens along posterior border of testis to form the mediastinum
  - Is covered on part of its surface by a mesothelium called the visceral layer of the tunica vaginalis

  At the mediastinum
  - Blood vessels enter and leave testis
  - CT septa radiate out to divide testis into ~ 250 lobules
  - The rete testis tubules are present

- Lobules
  - Each lobule contains 1-4 seminiferous tubules
  - Each tubule is U-shaped, and connects at both ends to a tubulus rectus (straight tubule) near the mediastinum

- Tunica vaginalis
  - Is a closed sac lined by a mesothelium
  - Is a remnant of the embryonic processus vaginalis
  - Parietal layer lines the wall of the sac
  - Visceral layer covers part of testis & part of epididymis
  - Visceral layer is in direct contact with the tunica albuginea

SEMINIFEROUS TUBULES

- The seminiferous epithelium that lines the tubule lumen includes:
  - Spermatogenic cells (in various stages of development)
  - Sertoli cells

- The epithelium rests on a basement membrane

- Several layers of flat myoid cells (contractile) surround each tubule exterior to the basement membrane

- The CT between tubules contains:
  - Clusters of Leydig cells (= interstitial cells)
  - Fenestrated capillaries
The entire process of sperm production from stem cell (A dark spermatogonium) to mature spermatozoan is called spermatogenesis. It includes:

- Early stages where the cells (spermatogonia) divide by mitosis
- Intermediate stages where the cells (spermatocytes) divide by meiosis
- Late stages where the cells (early spermatids) no longer divide, but do undergo morphological maturation into late spermatids & spermatozoa

The morphological maturation is called spermiogenesis.

Spermiation, the final step in spermiogenesis, is the release of late spermatids from the epithelium into the tubule lumen as free spermatozoa.

NOTE: Among the spermatogenic cells, you are responsible for identifying spermatogonia (but not distinguishing between Ad, Ap, & B), primary spermatocytes, early spermatids, late spermatids, & spermatozoa.

**SPERMATOGENIC CELLS**

- The most immature spermatogenic cells in the epithelium (spermatogonia) rest on the basement membrane.
- The most mature (late spermatids) are nearest the lumen.

**TYPES OF SPERMATOGENIC CELLS**

**SPERMATOGONIA**

- Small cells with round or oval nuclei
- Located on the basement membrane
- Type A dark (Ad or A₁) spermatogonia
  - Are the stem cells of the spermatogenic cell line
  - Have dark oval nuclei
  - Divide by mitosis to yield either two Type A dark spermatogonia or two Type A pale (Ap or A₂) spermatogonia
- Type Ap spermatogonia
  - Have pale oval nuclei
  - Are committed to spermatogenesis (i.e., are no longer stem cells)
Divide several times by mitosis, eventually forming Type B spermatogonia

Type B spermatogonia
Have round nuclei
Divide by mitosis to produce primary spermatocytes

NOTE: The Ap spermatogonia derived from a single Ad spermatogonium (and all the progeny of those Ap cells – type B spermatogonia, primary and secondary spermatocytes, early and late spermatids) remain connected to one another by cytoplasmic bridges until spermiation

PRIMARY SPERMATOCYTES
Largest of the spermatogenic cells
Located just luminal to spermatogonia (i.e., not in contact with basement membrane)
Cells replicate their DNA and enter meiosis I (where homologous pairs of chromosomes separate)
Have a large round nucleus with evidence of chromosome condensation
Prophase of meiosis I is much longer than the other stages (~ 22 days); therefore this is the most commonly observed stage

SECONDARY SPERMATOCYTES
Produced in the first meiotic division
Haploid for chromosome number, each chromosome consists of 2 sister chromatids
Located closer to lumen than primary spermatocytes
Smaller than primary spermatocytes
During the very brief interphase between meiosis I & II they resemble early spermatids but are larger
Since meiosis II is rapid, secondary spermatocytes are rare in sections (assume that all spermatocytes you see that have condensed chromosomes are primary spermatocytes)

EARLY SPERMATIDS
Round cells with round nuclei
Produced in the second meiotic division (where sister chromatids separate)
Haploid for chromosome number and DNA content

LATE SPERMATIDS
Differentiate from early spermatids via spermiogenesis, which involves morphological changes, but no cell division
Morphological changes visible by LM include:
Nucleus elongates and chromatin condenses greatly
Tail develops
Spermatids reorient themselves with their head toward the basement membrane of the seminiferous epithelium & tail toward the lumen
Still connected by cytoplasmic bridges to all the other spermatids that developed from the same Type Ap spermatogonium

SPERMATOZOA (SPERM)
By definition spermatozoa are individual cells that are free in the lumen. The cytoplasmic bridges that connect spermatids are lost when residual bodies pinch off during spermiation.

STAGES OF SEMINIFEROUS EPITHELIUM

A stage is a characteristic combination of different spermatogenic cell types that are consistently seen together in sections of a seminiferous tubule. Stages are identified by comparing the cell types present between the basement membrane and the lumen in any given region of a tubule. Human tubules have 6 stages (i.e., 6 different combinations) numbered I-VI.

In some species each cross section of a tubule includes only one stage, and the stages are arranged in linear order along the length of the tubule, forming what is called a wave of the seminiferous epithelium. A wave is a measure of the distance along a tubule from the first to the last stage.

In humans each cross section of a tubule usually includes multiple stages, and the stages are less regularly arranged, forming what is called a mosaic pattern (i.e., there are no waves in humans).

A CYCLE OF THE SEMINIFEROUS EPITHELIUM

If you could watch a part of a tubule that was in stage I, it would proceed in order to stage II, III, IV, V, VI & back to stage I again. A cycle is the time it takes for a region of seminiferous epithelium to go through all the different stages (6 in humans) and return to the stage at which you initially observed it.

Maturation of a cell from an Ad spermatogonium to a spermatozoan takes a little more than 4 cycles or ~ 74 days.

MORPHOLOGY OF A SPERMATOZOAN

Head contains:
- Elongated & highly heterochromatic nucleus
- Acrosome (a large flattened lysosome that covers anterior 2/3 of nucleus)

Tail is subdivided into 4 regions:
- **Neck** or connecting piece (contains modified centrioles)
- **Middle piece** contains (from superficial to deep):
  - Mitochondrial sheath
  - 9 outer dense fibers
  - Axoneme of the flagellum (9+2 arrangement of microtubules)
- **Principal piece** contains:
  - A fibrous sheath that replaces the mitochondria of the middle piece
  - 7 outer dense fibers
  - Axoneme
- **End piece** contains only the axoneme, which loses its characteristic 9+2 arrangement toward the end of the end piece.
SPERMIOGENESIS (THE MATURATION OF SPERMATID TO SPERMATOZOAN)
Has 4 phases:

Golgi phase
**Acrosomal vesicle** (containing acrosomal granule) forms from the Golgi
Attaches to nuclear membrane at what will become its anterior pole
Centrioles migrate toward the posterior pole of the nucleus

Cap or early acrosomal phase
Acrosomal vesicle flattens to become the **acrosomal cap**, covering the
anterior half of the nucleus
Contains hydrolytic enzymes needed for penetration of zona
pellucida of ovum (e.g., acrosin)

Late acrosomal phase
Cell is now called a late spermatid
Spermatid has reoriented itself with head toward basement membrane
and tail toward lumen
Chromatin has condensed and the nucleus has elongated
Centrioles become modified to form the connecting piece (neck)
9 outer dense fibers (ODF) develop from the modified centrioles
Mitochondrial sheath develops in middle piece
Fibrous sheath develops in principal piece

Maturation phase
Excess cytoplasm (including cytoplasmic bridges between spermatids)
is shed as the residual body
Results in the release of the cell into the lumen as a spermatozoan
(process of release = spermiation)
Sertoli cells phagocytize residual bodies

SERTOLI CELLS
Functions include:
Provide physical & nutritional support for spermatogenic cells
Phagocytize residual body that is shed from each spermatid
Form the blood-testis barrier via Sertoli-Sertoli membrane junctions
Secrete fluid that pushes the sperm out of the testis
Secrete androgen-binding protein (ABP) into lumen (binds testosterone
or dihydrotestosterone & keeps hormone levels high in tubules)
Secrete inhibin, which inhibits FSH release from pituitary
Secrete (during embryogenesis) Müllерian-inhibiting factor (MIF) also
called anti-Müllерian hormone (AMH), which suppresses
development of the female reproductive tract

Are part of the seminiferous epithelium
Have a large, irregular, euchromatic nucleus
Prominent nucleolus
In some nonhuman species the nucleolus is flanked by 2 prominent
DNA-containing bodies, forming a “Mickey Mouse-ear nucleolus”
Extend from basal lamina to luminal surface of tubule
Joined together by membrane junctions that form the blood-testis barrier
Location of junctional complexes is unusual in that they are near the basal end of the lateral plasma membranes (not apical ends)
Extensive infoldings of lateral plasma membrane, therefore lateral cell boundaries are not visible by light microscopy
Developing spermatogenic cells are located between the lateral folds

**BLOOD-TESTIS BARRIER**
- Creates basal & luminal compartments in the seminiferous tubule
- Basal (aboluminal) compartment
  - Is bounded by:
    - The basement membrane of the seminiferous tubule
    - The membrane junctions between Sertoli cells
  - Contains spermatogonia and early primary spermatocytes (preleptotene spermatocytes)
  - Mitosis occurs in basal compartment
- Adluminal (luminal or apical) compartment
  - Is bounded by:
    - The membrane junctions between Sertoli cells
    - The apical surface of the seminiferous epithelium
  - Contains late primary spermatocytes (pachytene spermatocytes and later), secondary spermatocytes, & spermatids
  - Meiosis and spermiogenesis occur in the adluminal compartment

**LEYDIG (INTERSTITIAL) CELLS:**
- Usually found in clusters between seminiferous tubules
- Large polygonal, eosinophilic cells usually with cytoplasmic lipid droplets
  - Pale, foamy cytoplasm by LM (if lipid droplets were extracted)
- EM appearance is that of a typical steroid-secreting cell
- After puberty they secrete testosterone upon stimulation by LH
- Secrete into fenestrated capillaries
- Cytoplasm may contain elongated proteinaceous crystals (of Reinke) with unknown function
- In prepubertal boys the inactive cells resemble fibroblasts

**THE EXCURRENT DUCT SYSTEM:**
- Tubules located inside the testis (listed in order):
  - Seminiferous tubules
  - Tubuli recti (straight tubules)
  - Rete testis
- Tubules located outside the testis (listed in order):
  - Efferent ductules (ductuli efferentes)
  - Epididymis (ductus epididymis)
  - Ductus deferens (vas deferens)
  - Ejaculatory duct
  - Urethra (with prostatic, membranous and penile parts)
TUBULI RECTI (straight tubules)
- Present near the mediastinum at both ends of each U-shaped seminiferous tubule
- Connect seminiferous tubules to the rete testis
- Begin within a lobule as tubules lined only by Sertoli cells
- Lining changes to simple cuboidal near the rete testis
- Very short, and hence not easy to find

RETE TESTIS:
- Anastomosing network of very irregular tubules (variable diameter)
- Located in mediastinum
- Usually lined by simple cuboidal epithelium
- Receive sperm from tubuli recti; empty into efferent ductules

EFFERENT DUCTULES (DUCTULI EFFERENTES)
- About 10-20 efferent ductules in man
- They coil to form conical masses called coni vasculosi that connect to the head of the epididymis
- Lined by pseudostratified columnar epithelium containing:
  - Tall columnar ciliated cells
  - Cuboidal nonciliated cells
    - Absorb most of the fluid produced in seminiferous tubules
    - By doing so they aid the ciliated cells in drawing the nonmotile sperm toward the epididymis
  - Basal cells (stem cells) – few in number
- Clusters of columnar ciliated cells alternate with clusters of nonciliated cuboidal cells, giving the luminal surface a scalloped appearance
- Are the first tubules to contain true smooth muscle (thin circular layer), which also helps to move sperm through the ductules

EPIDIDYMIS (DUCTUS EPIDIDYMIS):
- Becomes a single highly coiled tubule with a head, body & tail
- Pseudostratified columnar epithelium with principal cells & basal cells
- Principal cells:
  - Have stereocilia (long, branching microvilli) that “pull” sperm along by absorbing additional fluid from tubule lumen
  - Phagocytize any remaining residual bodies
  - Secretions include decapacitation factors that are added to the glycocalyx of sperm, & later removed during capacitation in the female reproductive tract
- Epithelium is of uniform height (no alternating groups of columnar & cuboidal cells as in efferent ductules)
- May see intraepithelial lymphocytes (halo cells)
  - Lymphocytes are not normally present in ducts proximal to epididymis
  - Head & most of body have circular smooth muscle; undergoes peristalsis
Inner & outer longitudinal smooth muscle layers are added in the tail, resulting in the following arrangement: IL, MC, OL
Sperm are stored in tail, where there is little peristalsis until sympathetic stimulation triggers emission
Sperm become motile in epididymis
Tail of epididymis leads to the ductus deferens

**DUCTUS DEFERENS (VAS DEFERENS):**
- Lined by pseudostratified columnar epithelium with shorter stereocilia than epididymis
- 3 very thick muscle layers: inner & outer longitudinal, middle circular
- Often see longitudinal folds in wall, due to muscle contraction
- Vas travels in the spermatic cord to reach and then pass through the inguinal canal and into the abdominal cavity
- Spermatic cord also includes:
  - Branches of testicular artery
  - Pampiniform plexus of veins around artery branches (countercurrent heat exchanger to lower temperature of blood reaching the testis)
  - Cremaster muscle (skeletal muscle derived from the internal abdominal oblique muscle)
- Near the prostate the duct widens to form the ampulla of the vas
  - Ampulla has extensive mucosal folds that resemble seminal vesicle
  - Ampulla unites with duct of seminal vesicle to form ejaculatory duct

**SEMINAL VESICLES:**
- Paired glands lateral to vas deferens on posterior surface of urinary bladder
- Each is a single highly coiled tubule with a thick mucosa and muscularis
- Mucosa has distinctive, interconnected folds that form arches (“arcades”)
  - Gives a “honeycomb” appearance to the mucosa
  - Lamina propria makes up the core of the folds
  - Lamina propria contains very little smooth muscle
- Lumen has an open central portion with no folds (vs. ampulla of oviduct)
- Lined by pseudostratified columnar epithelium, but basal cells are rare
- Muscle of the muscularis does not usually extend into the mucosal folds
- Seminal vesicles produce a viscous secretory product:
  - Rich in fructose, prostaglandins, ascorbic acid, flavins, & semenogelin
    - semenogelin is involved in formation of a gel matrix (coagulum) that encases ejaculated sperm; it is a substrate for prostate specific antigen (PSA), which is an enzymes that liquefies the gel
  - Flavins are yellow pigments that give semen its pale color, and fluoresce under UV light
- Secretory function of the seminal vesicle is testosterone-dependent

**PROSTATE:**
Walnut-sized gland located inferior to urinary bladder
Has a capsule with CT and smooth muscle
Ejaculatory ducts run through prostate & empty into the prostatic urethra
The bulk of the gland is composed of 30-50 tubuloalveolar serous glands
Empty into prostatic urethra
Surrounded by stroma containing intermingled CT & smooth muscle

Prostate can be divided into regions according to several different schemes including the following:
- Periurethral zone – immediately around urethra
- Transitional zone – surrounds proximal part of the periurethral zone & extends anteriorly
- Central zone – posterior to transitional zone; includes ejaculatory ducts
- Peripheral zone – surrounds distal part of periurethral zone & extends out to the capsule posteriorly and laterally
  Contains the majority of prostatic glandular tissue

Prostatic glands can be classified into the following types according to their size, location, and where their ducts enter the prostatic urethra
NOTE: it is not necessary for you to distinguish between them by LM or EM

**Mucosal glands**
- Are the smallest
- Lie in the periurethral zone
- Each empties directly into urethra at any point around its circumference

**“True” prostatic glands**
- Larger and more highly branched than mucosal glands
- Empty into the prostatic urethra in only 2 regions (the prostatic sinuses)
- Can be subdivided into:
  - **Submucosal glands** in transitional & somewhat in central zones
  - **Main prostatic glands**
    - Are the largest
    - Found in peripheral zone, & are therefore the ones that are most easily palpated through the anterior wall of the rectum in digital rectal exams

Prostatic secretions include acid phosphatase, PSA, fibrinolysin, and citrate
Secretory function is dependent on dihydrotestosterone (DHT), which is synthesized from testosterone
Glandular epithelium is pseudostratified columnar with few basal cells
Prostatic adenocarcinomas typically have a simple epithelium
Smooth muscle is common in the stroma between glands
Especially in older men, prostatic concretions (corpora amylacea) accumulate within gland lumens
  - Have a layered appearance in sections
  - Formed by precipitation of secretory material around cell fragments

**CLINICAL CORRELATIONS:**
Mucosal & submucosal glands can become enlarged in benign prostatic hypertrophy and impinge on the prostatic urethra. Prostatic carcinoma most often develops in the main prostatic glands in the peripheral zone.

URETHRA:
Functions in both micturition and ejaculation
Divided into 3 parts:
Prostatic urethra
  From neck of bladder through prostate
  Receives ejaculatory ducts
  Receives ducts of the prostatic glands
  Usually U-shaped in cross section due to urethral crest on its posterior wall; the ends of the U are the prostatic sinuses
Membranous urethra
  Passes through urogenital diaphragm & is thus surrounded by the skeletal muscle that makes up the diaphragm
Penile urethra
  Passes through corpus spongiosum (surrounded by erectile tissue)
  Receives ducts of bulbourethral glands
  Has mucus-secreting glands of Littré (urethral glands) in its wall
  Opens onto the surface of the glans penis
Epithelium of urethra varies along its length:
  Transitional epithelium is found in most of the prostatic urethra
  Most of its remaining length is stratified columnar or pseudostratified columnar
  Finally a short region of stratified squamous epithelium near the urethral orifice

BULBOURETHRAL GLANDS (Cowper’s glands):
  Pair of small mucous glands embedded in the skeletal muscle of the urogenital diaphragm
  Height of epithelial cells varies directly with testosterone level
  Secretes the majority of the pre-ejaculation fluid
  Secretion contains small nutrient molecules
  Produces most of the pre-ejaculate fluid that lubricates the urethra

PENIS:
Contains 3 cylindrical bodies of erectile tissue:
  2 corpora cavernosa
  1 corpus spongiosum
Each erectile body is surrounded by a tunica albuginea (dense CT)
Penis has thin skin & a superficial fascia of loose CT that contains little or no fat
Corpora cavernosa
  Are located dorsally in an erect penis
Tunica albuginea of corpora cavernosa are fused to form a midline septum which may be incomplete in places. The thick tunica albuginea limits expansion of the corpora cavernosa; increased blood pressure within the 2 cavernosa creates the rigidity of the erect penis.

Corpus spongiosum
- Single, smaller, erectile body
- Ventrally located in an erect penis
- Contains the penile urethra
- Surrounded by a thinner tunica albuginea than corpora cavernosa
- Thinner tunica albuginea results in less compression of the spongiosum during erection, & thus prevents collapse of the urethra
- Corpus spongiosum expands at its distal end to form the glans penis
  - Glans covers the ends of the 2 corpora cavernosa like a cap

Erectile tissue has two components:
- Cavernous spaces (lacunae)
  - Thin-walled irregular blood vessels lined by endothelium
  - Become engorged with blood during erection
  - Receive blood from helicine arteries
- Fibromuscular trabeculae
  - The CT between cavernous spaces
  - Contains some bundles of smooth muscle, plus helicine arteries

II. FEMALE REPRODUCTIVE SYSTEM

OVARIES:

GENERAL STRUCTURE
- Cortex: outer region; contains the ovarian follicles, corpora lutea & corpora albicantia
- Medulla: central region; contains large blood vessels, but no follicles or remnants of follicles
- Hilum: Location where blood vessels & nerves enter & leave ovary
- Germinal epithelium covers the outer surface of the ovary
  - Is a simple low cuboidal epithelium
  - Continuous with mesothelium of the mesovarium (the mesentery that connects ovary to posterior surface of broad ligament)
- Tunica albuginea: dense connective tissue (CT) layer beneath the germinal epithelium; lies just superficial to the follicles

STAGES OF FOLLICULAR MATURATION:

PRIMORDIAL FOLLICLES
- Are small unstimulated follicles
- Most are located just deep to the tunica albuginea
- Primordial follicles have:
  - A small (~ 30µm) primary oocyte
    - Arrested in prophase of meiosis I
  - 4 N for DNA, 2N for chromosome number
  - Homologous chromosomes are paired
A layer of flat follicular cells
A basement membrane between follicular cells & the surrounding stroma
May have a Balbiani body (a cluster of organelles including Golgi, RER, mitochondria & lysosomes) visible by LM in cytoplasm

PRIMARY FOLLICLES
Defining characteristic is that follicular cells become cuboidal
Oocyte enlarges (~ 80µm)
Usually found deeper in the cortex than primordial follicles

Unilaminar primary follicles:
Have one layer of follicular cells
Zona pellucida (ZP) begins to develop between oocyte & follicular cells
  Composed of 3 main classes of glycoproteins (ZP1, ZP2, ZP3)
  ZP3 is a receptor for sperm binding

Multilaminar primary follicles:
Have multiple layers of follicular cells (which are now called granulosa cells; collectively they form the membrana granulosa)
Membrana granulosa layer is avascular
Cytoplasmic processes of the innermost granulosa cells extend into the ZP and form gap junctions with processes of the oocyte
Theca folliculi develops from the stroma
  Still separated from the granulosa by a basement membrane
  Contains blood vessels
  Theca initially composed of flat cells oriented around the follicle
  Later in this stage it differentiates into:
    Theca interna (rounder cells; steroid-producers)
    Theca externa (cells remain flat; are contractile)
Steroid products of ovarian follicles:
Theca interna produces androstenedione from cholesterol supplied mainly by LDLs
Membrana granulosa cells convert androstenedione to estradiol
  Membrana granulosa is avascular, so cells have no access to LDL cholesterol, and can’t carry out a complete steroid synthesis from cholesterol by themselves
  Conversion of androstenedione to estradiol requires an aromatase enzyme activity that is present in membrana granulosa cells
Other secretory products of granulosa cells
  Inhibins (inhibit FSH secretion)
  Components of zona pellucida (others are produced by the oocyte)
  OMI (oocyte maturation inhibitor)

SECONDARY FOLLICLE
Microanatomists disagree as to when a follicle becomes a secondary follicle
Some say it is when small pools of liquor folliculi are visible by LM in the membrana granulosa
Like the Ross text, we say it is when the pools coalesce to form the antrum. Oocyte reaches ~125 mm diameter; it undergoes no further enlargement in later stages although the follicle continues to grow. Follicle increases in size due to proliferation of granulosa cells and enlargement of antrum. Oocyte is surrounded by the cumulus oophorus (a mound of granulosa cells that projects into the antrum). Note: Some books define the cumulus oophorus as being only the pedestal of granulosa cells on which the oocyte sits rather than the entire mound of cells that completely surrounds the oocyte. Corona radiata = the cells of the cumulus oophorus that remain with the oocyte after ovulation.

**GRAAFIAN (TERTIARY OR MATURE) FOLLICLE**
- Follicle continues to enlarge while oocyte remains constant in size
- Follicle extends through full thickness of cortex and even forms a bulge on surface of ovary
- You can use oocyte as a ruler to judge diameter of the antrum when trying to decide if a follicle is secondary or Graafian
- Eventually, the cells that surround the oocyte loosen from the rest of the granulosa; the oocyte & its attached granulosa cells float free in antrum, just prior to ovulation, LH surge triggers oocyte to complete 1st meiotic division, producing secondary oocyte and first polar body. In 1st meiotic division homologous chromosome pairs separate. Secondary oocyte is 2N for DNA, 1N for chromosome number. Becomes arrested at metaphase II until fertilization occurs.

**CORPUS LUTEUM (CL, literally “yellow body”)**
- Develops from the follicle after ovulation
- Functions as a temporary endocrine gland
- Former antral cavity initially contains a blood clot, & entire structure is then called a corpus hemorrhagicum
- Follicular wall becomes deeply folded around the former antrum
- Wall has two layers:
  - Granulosa lutein is the inner layer
    - Derived from membrana granulosa cells of the follicle
    - Composed of large, pale-staining, steroid-producing cells
    - Becomes vascularized after basement membrane breaks down
      - gives cells access to LDLs
      - they convert LDL cholesterol to progesterone
    - Cells secrete mostly progesterone, some estradiol (from androstenedione supplied by theca lutein), inhibin, & relaxin
  - Theca lutein
    - Derived from theca interna of follicle
    - Small, dark-staining cells
Cells form thin strands on outer surface of CL, between folds of granulosa lutein. Cells secrete mainly androstenedione and some progesterone. By EM, granulosa lutein & theca lutein cells are typical steroid secretors. Blood clot resorbs, & antrum gradually decreases in size as the CL matures.

CORPUS ALBICANS (literally “white body”) is a degenerating corpus luteum. Granulosa lutein and theca lutein cells degenerate and are replaced by fibroblasts & collagen. Thus has fewer nuclei and more extracellular matrix than a corpus luteum (which is formed by closely packed epithelial cells).

ATRETIC FOLLICLES are follicles that degenerate without ever ovulating. 99% of follicles become atretic. Atresia can occur at any stage of follicular development. Morphology depends on what stage the follicle reaches before degenerating. Atresia of primordial & small primary follicles leaves little or no trace. Atresia of multilaminar primary follicles:
- Oocyte degenerates
- Zona pellucida collapses, folds, & gradually disappears
- Basement membrane thickens to form the glassy membrane

Atresia of secondary follicles (in addition to the above):
- Granulosa cells degenerate & slough off into the antrum
- Follicle becomes irregular in shape
- Some theca cells can persist & form interstitial glands resembling Leydig cells

FEMALE REPRODUCTIVE TRACT:

UTERINE TUBES (OVIDUCTS; FALLOPIAN TUBES) HAVE 4 REGIONS
- Infundibulum: Funnel-shaped free end of tube near the ovary
- Ampulla: The longest segment of the tube
- Isthmus: Narrower part between ampulla & uterine wall
- Intramural segment (interstitial segment): Passes through the wall of the uterus and empties into uterine lumen

WALL OF UTERINE TUBE HAS 3 LAYERS: MUCOSA, MUSCULARIS, SEROSA
- Mucosa (epithelium & lamina propria): Lumen is lined by simple columnar epithelium with 2 cell types:
  - Ciliated cells (cilia beat toward uterus)
  - Peg cells: tall nonciliated cells that protrude into the lumen
  - Secrete fluid rich in nutrients for the ovum & sperm
Hormones affect epithelial cells:
- Height of epithelial cells is maximal at ovulation (hypertrophy)
- Estrogen increases the number of ciliated cells (hyperplasia)
- Progesterone increases number of peg cells (hyperplasia)

Mucosa has longitudinal folds that are best developed in ampulla

Muscularis
- Gradually becomes thicker as you move toward uterus
- Inner circular & outer longitudinal layers for most of its length (i.e., same arrangement as in GI tract)
- Near the uterus, may add an inner longitudinal layer, yielding the same arrangement as in the vas deferens & lower ureter (i.e., IL, MC, OL)

Serosa (formed by the broad ligament with its mesothelium)

THE FOUR REGIONS OF THE UTERINE TUBE

Infundibulum:
- Has fimbriae at its free end
- Are finger-like extensions of the free end of the oviduct that project toward the ovary
- Covered by the same that lines lumen of oviduct
- Fimbriae & mucosal folds lining the oviduct lumen contain many large, thin-walled veins that become engorged at the time of ovulation

Ampulla
- Mucosal folds are very extensive & more branched than in infundibulum, almost filling the wide lumen
- Folds have fewer thin-walled venous vessels than infundibulum
- Most common site of fertilization

Isthmus
- Narrow lumen, with fewer, less elaborate mucosal folds
- Thicker muscle layer

Intramural segment
- Fewest mucosal folds
- Muscularis blends with myometrium of the uterus

UTERUS HAS THREE LAYERS:

PERIMETRIUM
- Is a serosa over the fundus and body of the uterus
- Is an adventitia around the cervix

MYOMETRIUM
- Smooth muscle that forms the thickest layer of uterus
- Muscle cells are arranged in interlacing bundles
- Sometimes described as having 3 layers (inner, middle or “stratum vasculare” which contains large blood vessels, & outer)
These are not well-defined layers. They are identified only on the basis of the presence or absence of the large vessels.

Muscle cells undergo hyperplasia & hypertrophy during pregnancy
Prostaglandins & oxytocin stimulate myometrial contractions at parturition

**ENDOMETRIUM**

Luminal surface is lined by simple columnar epithelium with many secretory cells and a few ciliated cells
Has simple tubular glands (some branch near base)
   - Lined mainly by secretory cells
CT stroma surrounds glands
   - Is the equivalent of a lamina propria
   - Stromal cells differentiate into predecidual cells at midcycle, & become decidual cells in placenta

Endometrium is composed of 2 layers:
- **Stratum basalis** (stratum basale)
  - Thin layer that lies in contact with the myometrium
  - Not shed during menstruation
  - Contains the coiled basal portions of endometrial glands
  - Glands show little change in morphology during menstrual cycle
  - Often darker staining than functionalis due to more cells in stroma
  - Gland cells re-epithelialize luminal surface after menstruation
- **Stratum functionalis** (stratum functionale)
  - Contains the upper portions of the uterine glands
  - Is shed during menstruation
  - Layer thickens during proliferative stage & most of the secretory stage
  - Shows cyclic changes in gland morphology that are controlled by ovarian hormones (see below)
  - Changes are used to define uterine stages

**Blood supply of endometrium:**
- Uterine artery → arcuate arteries in myometrium → radial arteries
- Radial arteries enter the endometrium
  - Give off side branches (straight arteries) to supply stratum basalis
  - Radial arteries end as spiral (helicine) arteries to supply stratum functionalis
- Spiral arteries drain into capillaries & dilated venules called lacunae or venous lakes
- Spiral arteries undergo pulsatile constriction
  - Prolonged constriction prior to menstruation causes ischemic necrosis of the constricted portion of the artery and the surrounding tissue
  - Relaxation of damaged vessels results in bleeding that washes away the stratum functionalis (= menstrual flow)
  - The stumps of the spiral arteries remaining in stratum basalis regrow into functionalis during the next cycle
3 STAGES OF MENSTRUAL CYCLE:

PROLIFERATIVE PHASE
From end of menstruation (~ day 4) to one day after ovulation (~ day 15)
Occurs at same time as follicular phase of ovarian cycle
Influenced by estrogen from ovarian follicles
At onset, stratum functionalis is gone but stratum basalis is present
Characteristic features:
  Glands:
    Epithelial cells in glands of stratum basalis divide to rebuild glands of
    the functionalis & re-epithelialize the luminal surface
    Functionalis glands are straight narrow tubules that become slightly
    wavy by the end of the phase
  Stromal cells:
    Are spindle-shaped or stellate mesenchymal cells
    Mitotically active
    Synthetically active (produce extracellular matrix)
  Spiral (helicine) arteries:
    Vessels grow ~ 2/3 of the way into the endometrium (are not yet
    highly coiled & therefore hard to find)

SECRETORY PHASE (~ day 15-28; i.e., until menstruation)
Corresponds to luteal phase of ovarian cycle
Influenced mainly by progesterone from corpus luteum
Endometrium continues to increase in thickness until late secretory
Glands of the functionalis become more coiled
Early secretory phase:
  Glands have a corkscrew appearance (like a "sine wave"), with walls
  that curve but remain parallel to one another
  Glycogen accumulates at basal end of cell (basal vacuolization) and
  nucleus is pushed toward the center of the cell
  - basal vacuolization is maximal at ~ day 17 (early secretory)
  - then glycogen moves to the apical end of the cell (the “glycogen
    shift”), and the nucleus moves toward the basal end
  - secretory material rich in glycogen & glycoproteins is then
    released into the lumen of the gland
Late secretory phase:
  Glands have a sacculated (sawtooth) appearance with small
  epithelial projections like the teeth of a saw projecting into the
  glandular lumen
Stroma:
  Becomes edematous in early secretory
  Edema declines precipitously just before menstruation
  Fluid moves into the lacunae, which become prominent
Some stromal cells become "pre-decidual" cells in late secretory phase (rounder cells, more cytoplasm, euchromatic nucleus) Will become the decidual cells of the placenta if pregnancy occurs Leukocyte infiltration (mostly neutrophils) begins a few days before menstruation starts

Spiral arteries:
Continue to lengthen, reaching almost to the endometrial surface
Become more highly coiled
Constrict rhythmically for gradually longer times until ischemia causes necrosis of the stratum functionalis and of the constricted portion of the spiral artery itself late in the secretory phase

MENSTRUAL PHASE (~ day 1-4)
Morphologically defined by:
Absence of epithelium from large areas of the luminal surface
Irregular luminal surface as chunks of functionalis wash away
Extravascular blood (from ruptured spiral arteries) in stroma & uterine lumen
Thinning of stratum functionalis as the layer is shed

CERVIX
Internal os – a constriction that separates it from the body of the uterus
External os – the opening of the cervix into the vagina
Cervical canal (endocervix) – the lumen between internal os & external os
Ectocervix – the part of the cervix that projects into the vaginal lumen
In a pelvic exam, the external os and ectocervix are visible
Gross anatomists consider the cervix to be a part of the uterus
But the cervix differs from the rest of the uterus in that the cervix:
Has folds of mucosa called plicae palmatae
Has a less muscular, more fibrous wall
Has large compound glands (not simple tubular as in uterus proper)
Secretes mainly mucus (not glycogen) from its glands & surface epithelium
Epithelium (surface & glands) is simple columnar, with mostly mucous cells and some ciliated
Does not shed its mucosa during menstruation
Lacks spiral arteries (therefore there is no ischemic necrosis of the cervix)
Has an adventitia rather than a serosa
Amount & properties of mucus vary during the cycle, under the control of ovarian hormones
Mucus production can be used to estimate when ovulation is about to occur (i.e., the time of greatest fertility)
Near ovulation the mucus:
Is produced in greater amounts
Is more stretchable (increased spinnbarkeit), i.e. less viscous
Shows a “ferning pattern” (due to higher salt concentration) when allowed to dry on a slide

Squamo-columnar junction:
The epithelium changes abruptly to vaginal epithelium (minimally keratinized stratified squamous) at the squamo-columnar junction.

Location of the squamo-columnar junction varies at different stages of life:
In prepubertal females it is usually in the cervical canal.
During reproductive years, the cervix enlarges & everts slightly into the vagina, possibly under the influence of estrogen, so that the original junction comes to be located on the ectocervix.
The acidic environment of the vagina induces squamous metaplasia of the delicate simple columnar epithelium that is newly exposed on the ectocervix; this produces a more resistant type of epithelium.
This gradual metaplasia causes the squamocolumnar junction to "migrate" back into the endocervix.
In postmenopausal women it is back in the endocervix.

The transition zone (transformation zone) is the region between the current location of the squamocolumnar junction and the furthest point that the junction had reached on the ectocervix, i.e., the region where columnar to squamous metaplasia has occurred.

Nearly all cervical dysplasia & cervical cancer occurs in the transition zone.

Exfoliated cells from the transition zone are examined in a Pap (Papanicolaou) smear to detect precancerous & cancerous cells.
Normal cells are squamous with small pycnotic nuclei & abundant cytoplasm; abnormal cells have larger nuclei and less cytoplasm.
Blockage of ducts of cervical glands as squamous metaplasia occurs results in retention of secretion & formation of dilated cysts (Nabothian cysts).

VAGINA

Ends inferiorly in the vestibule (the space between labia minora that also contains the urethral orifice).
Vagina has a mucosa, muscularis & adventitia.
Mucosa:
Lined by minimally keratinized stratified squamous epithelium.
Cells in the superficial layers accumulate glycogen that is released when the cells desquamate (holocrine secretion).
Bacteria metabolize the released glycogen to lactic acid, producing a low pH in vaginal lumen that helps kill infectious microorganisms.
Mucosa lacks glands (vagina is lubricated by mucus from cervical glands and by transudate from vaginal blood vessels).
Many large thin walled veins in the mucosal CT become engorged with blood and act as an erectile tissue during sexual arousal.
Muscularis:
Contains smooth muscle.
Skeletal muscle fibers from the pelvic diaphragm form a vaginal sphincter as vagina goes through the diaphragm to pass from the pelvis into the perineum.

THE END!