SLIDE REVIEW
GI TRACT

I. ORAL CAVITY

A. TONGUE

Divided into anterior 2/3 & posterior 1/3 by V-shaped sulcus terminalis
Lingual tonsils are embedded in the dorsal surface of the posterior 1/3
Papillae are present on the dorsum & lateral aspect of the anterior 2/3
Characteristic feature at low mag: bundles of intrinsic skeletal muscle that run in 3 mutually perpendicular planes
- adipose tissue, mucous glands, & serous glands are also present

FOUR TYPES OF PAPILLAE

All found anterior to sulcus terminalis
Distinguished from one another by their size, shape, location, abundance, & whether or not they carry taste buds

Filiform papillae
Most numerous and smallest type
Carry no taste buds
Have an elongated conical shape
Cover most of the dorsum of anterior 2/3 of tongue

Foliate papillae
Located on lateral edge of tongue just anterior to sulcus terminalis
Consist of parallel vertical ridges separated by deep clefts
Walls of clefts carry many taste buds in neonates & children
- taste buds of foliate papillae degenerate with age

Fungiform papillae
Mushroom shaped
Scattered individually among filiform papillae
Taste buds tend to be located on their dorsal surface
Thin stratified squamous epithelium & tall connective tissue (CT) papillae bring capillaries close to surface, so the papillae look redder than filiform papillae in the living state

Circumvallate (vallate) papillae
~ 6-12 extremely large papillae arranged in a V-shaped line
located just anterior to sulcus terminalis
Each surrounded by a circular moat (sulcus or valley) and then a solid ring of tissue forming a wall
Taste buds tend to be on the sides of papilla
Von Ebner’s glands (serous) empty into base of moat
TASTE BUDS
Pale oval structures extending through full the thickness of the epithelium
Contains at least 3 major cell types by LM:

- **Neuroepithelial cells** (gustatory cells, Type II and Type III cells)
  - sensory cells whose basal ends form synapses with afferent axons
  - apical microvilli carry receptors for taste

- **Sustentacular cells** (supporting cells, Type I cells)

- **Basal cells** (Type IV cells) are the stem cells

Apical ends of cells converge to form a **taste pore**
Also found on areas other than papillae, e.g., epiglottis, palate

PARAKERATINIZED EPITHELIUM
Is a type of stratified squamous epithelium that is intermediate between minimally and maximally keratinized stratified squamous epithelium
Has nucleated cells in its surface layer (like minimally keratinized), but the surface cells are very flat (as in maximally keratinized)
Parakeratinized is often found on parts of gingiva & hard palate

B. SALIVARY GLANDS

THE THREE MAJOR SALIVARY GLANDS ARE PAROTID, SUBMANDIBULAR, & SUBLINGUAL
They are distinguished from one another by their relative content of serous & mucous secretory cells

WHAT DO THE TERMS “SEROUS” & “MUCOUS” MEAN?
Serous & mucous glands both produce glycoprotein secretions
Mucous cells produce a viscous secretion rich in glycoproteins called mucinogens
Serous cells produce a watery secretion with a lower glycoprotein content

MORPHOLOGY OF MUCOUS VS. SEROUS CELLS

- **Mucous cells**
  - Nucleus usually flattened against basal plasma membrane
  - Cytoplasm usually pale or foamy (products extracted during tissue preparation)
  - Tend to form tubular rather than spherical secretory units

- **Serous cells:**
  - Usually have a round nucleus in the basal half of the cell
  - Apical cytoplasm not as pale as in mucous cells (products are less soluble)
  - Eosinophilic secretory granules may be visible
  - When abundant, serous cells can form pure serous acini
  - When less abundant, serous cells tend to form serous demilunes
MICROSCOPIC ANATOMY

PAROTID
Paired “pure” serous glands located on the face, just anterior to ears
Empty into oral cavity opposite upper molar teeth
Are the largest salivary glands, but produce only ~ 30% of salivary volume
Resemble pancreas except that parotid has striated ducts, & lacks islets of Langerhans and centroacinar cells
Secretions include salivary amylase
Transport IgA into the ducts in the form of secretory IgA
Adipose tissue increases with age
CLINICAL CORRELATION: Become enlarged in mumps

SUBMANDIBULAR
Paired seromucous glands, with serous cells predominating
Has many pure serous acini; relatively few serous demilunes
The striated ducts are long, and thus commonly observed in sections
Produce most of the salivary volume (~ 60%)
Located inferior to floor of oral cavity, near inner surface of mandible
Empty onto the floor of the oral cavity

SUBLINGUAL
Paired seromucous glands, with mucous cells predominating
Many serous demilunes; pure serous acini are rare
Smallest of the 3 major salivary glands; short striated ducts
Contribute the least to total salivary volume
Located in floor of oral cavity
Empty into oral cavity via multiple short ducts

SALIVARY GLAND DUCTS
Intralobular – directly surrounded by secretory units
Intercalated ducts are the smallest intralobular ducts
Simple low cuboidal epithelium
Receive “primary saliva” directly from the secretory units
Striated ducts
Larger intralobular ducts with basal striations that push the nucleus away from the basal end of cell & toward the center
Modify the content of saliva to product “secondary saliva”
Interlobular – between lobules in the CT septa
Epithelium becomes stratified as ducts merge & become larger
Eventually unite to form the main excretory duct
C. TEETH

GROUND SECTIONS VS. DECALCIFIED SECTIONS

In ground sections the inorganic components of all 3 hard tissues (enamel, dentin & cementum) are preserved.

In decalcified sections of:

- Developing teeth: Organic components of all 3 hard tissues are preserved, e.g., collagen of dentin & cementum, enamelins of enamel.
- Mature teeth: The enamel is often missing because most of the original organic matrix of enamel is lost during the maturation process.

FEATURES OF A MATURE TOOTH

**Crown:**

- Clinical definition – the part that projects above the gum
- Anatomical definition – the part covered by enamel
- Enamel forms the outer layer, dentin forms the inner layer of the crown

**Enamel**

- is the hardest substance in the body
- mature enamel is at least 95% inorganic and < 1.0% organic
- organic matrix of mature enamel is mainly enamelins & tuftelins (not collagen)
- produced by ameloblasts – ectodermal origin
- ameloblasts are lost when tooth erupts

**Dentin**

- second hardest substance in the body
- mature dentin is ~70% inorganic, 20-25% organic; the rest is water
- organic matrix of mature dentin is mainly collagen type I
- produced by odontoblasts – mesenchymal origin from dental papilla (from mesenchymal cells derived from neural crest)
- odontoblasts line the inner surface of the dentin
- they are present throughout life
- odontoblasts first lay down predentin, which then mineralizes to form mature dentin
- dentin contains narrow channels called dentinal tubules that extend from pulp cavity to dentin-enamel junction
- dentinal tubules contain odontoblast processes

**Neck (cervix):**

Where enamel & cementum meet (cemento-enamel junction)

**Root:**

Cementum forms the outer layer, dentin forms inner layer of the root
Cementum
- is similar in composition to bone (~50% inorganic, 50% organic)
- usually avascular
- produced by cementoblasts – mesenchymal origin from the part of the dental sac (dental follicle) that surrounds the root
- is acellular near the neck
- is cellular near the root, where cementoblasts become cementocytes that get trapped within lacunae in the cementum

Root has an apical foramen through which nerves & blood vessels enter to reach the dental pulp

Root fits into the tooth socket (alveolus)

Pulp cavity:
- Lies interior to the dentin in the crown & root
- Contains loose CT
- Highly innervated and vascularized
- Develops from the dental papilla
- Odontoblasts line the pulp cavity (in contact with the dentin)

Periodontal ligament:
- Collective name for CT bundles that suspend the tooth in the alveolar socket
  - composed mostly of collagen type I
  - bundles are embedded in cementum at one end & in alveolar bone on the other
  - the embedded portions of these bundles are called Sharpey’s fibers
- Prevents direct contact between root & alveolar bone, which would cause resorption of bone

TOOTH DEVELOPMENT (ODONTOGENESIS)

1. Primary Dental Lamina
- A thickening of the oral epithelium caused by locally increased mitotic activity
- Forms a horseshoe-shaped ridge, one in upper jaw, one in lower
- Defines the line along which teeth develop
- Additional mitotic activity forms a placode in the dental laminae at each site where tooth development will begin

2. Bud Stage
- Bud grows downward into the ectomesenchyme, which begins to condense beneath the bud
- Bud is connected to the oral epithelium by a strand of tissue called the secondary dental lamina
- For deciduous (milk) teeth there are 10 buds in each of the 2 laminae
3. **Cap Stage**

The rounded free end of each bud indents to form a cap-shaped structure called the **enamel organ**

Enamel organ:
- Is derived from ectoderm
- Still connected to surface epithelium by the secondary dental lamina
- Forms a cap over the **dental papilla** (the region of condensed ectomesenchyme)

Enamel organ at first consists of:
- **Outer enamel epithelium (OEE)**
- **Inner enamel epithelium (IEE)**
  - continuous with OEE at the **cervical loop**
- **Stellate reticulum**
  - fills the space between OEE & IEE

Dental papilla will become the pulp cavity of the mature tooth

Enamel organ plus dental papilla are called the **tooth germ**

Ectomesenchyme surrounding the tooth germ is called the **dental sac or dental follicle**
- Will give rise to cementum and periodontal ligament

Bud of permanent (secondary) tooth begins to develop from the dental lamina

4. **Bell Stage**

Defined by the appearance of a layer called the **stratum intermedium**
- Located in the stellate reticulum, in contact with the IEE
- Formed as the stellate reticulum loses fluid & “collapses”
- Produces growth factors that regulate differentiation
  - induces inner enamel epithelium to differentiate into **ameloblasts**
- Ameloblasts then induce differentiation of **odontoblasts** from mesenchyme of dental papilla
  - ameloblasts will be lost when tooth erupts; odontoblasts will remain

Enamel organ takes on a bell shape (i.e., concavity of IEE deepens)

5. **Appositional Stage**

Odontoblasts produce **predentin**
- This induces production of **enamel** (amelogenensis) by ameloblasts
  - Enamel is composed of enamel rods (enamel prisms) & interrod enamel
- The oldest predentin (nearest the enamel) begins to mineralize to become **dentin**
Odontoblasts continue lay down new predentin
Dentin and enamel thus lie in direct contact (apposition) with one another to form the dentin-enamel junction (DEJ)
Production of dentin & enamel begins at the top of the crown & proceeds toward the cervix

6. Root Formation
   Begins after development of the crown
   Involves formation of a structure called Hertwig’s root sheath
   Formed when IEE & OEE come into direct contact in the narrowing cervical loop (i.e., no stellate reticulum or stratum intermedium remains between them)
   Odontoblasts in papilla begin to produce the dentin of the root
   Root sheath becomes a perforated layer
   Ectomesenchymal cells from dental sac migrate through perforations & begin to produce cementum in direct contact with the dentin

7. Formation of the secondary (permanent, succedaneous) tooth bud

D. TONSILS:
   Consist of aggregated lymphoid nodules embedded in diffuse lymphocytic tissue
   Organized around either tubular invaginations (crypts) or folds of the mucosa
   Respond to ingested or inhaled antigens
   Distinguished from one another by:
      Anatomical location
      Type of epithelium that overlies them
      Crypts (present or absent, multiple or single, deep & branching or short and “unbranched”)

THREE TYPES OF TONSILS
   Palatine (faucial) tonsils:
      Paired structures, one on each lateral wall of the throat between two folds called the palatoglossal and palatopharyngeal folds
      These folds are sometimes referred to as the fauces, or the anterior pillar and posterior pillars of the fauces, respectively
      Hence the tonsils that lie between them are the faucial tonsils
      Covered by minimally keratinized stratified squamous epithelium
      Has multiple deep, branching crypts
      Many nodules are located along each crypt
Pharyngeal tonsil:
Unpaired; located in roof of nasopharynx
Covered at least in part by respiratory epithelium
Also by areas of minimally keratinized stratified squamous epithelium
No crypts, but has a pleated (ridged) mucosa that can look like crypts when sectioned at a right angle to a ridge
CLINICAL CORRELATION: Enlarged pharyngeal tonsils are adenoids

Lingual tonsils:
Embedded on the dorsum of the posterior 1/3 of the tongue
Smaller & more numerous than other tonsils
Covered by minimally keratinized stratified squamous epithelium
Each usually has a single short crypt with few, if any, branches
Judge the depth of a crypt by how many nodules you could line up along its length (2-4 = short crypt; 8-10 or more = deep crypt)
NOTE: To identify lingual tonsil at low mag, look for evidence that it is located in the tongue (e.g., characteristically oriented bundles of skeletal muscle, papillae)

II. GUT TUBE
A. THE FOUR LAYERS OF THE DIGESTIVE TUBE WALL
   Mucosa
   Submucosa
   Muscularis externa (called “muscularis propria” by many clinicians)
   Serosa or adventitia

Mucosa includes:
   Epithelium: simple columnar except in esophagus & lower anal canal
   Lamina propria
     Loose CT (highly cellular from stomach onward)
     Contains glands in stomach, intestines, & parts of esophagus
   Muscularis mucosae
     Always smooth muscle
     Two (indistinct) layers in most places (inner circular, outer longitudinal)

Submucosa
   CT layer
   Contains submucosal (Meissner’s) plexus of the enteric nervous system
   Contains larger blood vessels that give rise to the capillary beds of the lamina propria
   Contains mucous glands in esophagus (esophageal glands proper) and in duodenum (Brunner’s glands)
**Muscularis externa**

Generally an inner circular & outer longitudinal layer (stomach is more complex)
Smooth muscle except in pharynx (skeletal) & esophagus (changes from skeletal to smooth as you move toward stomach)

**Myenteric (Auerbach’s) plexus** is located between the muscle layers

Outermost layer is either a **serosa** or an **adventitia**
Both are CT layers

A serosa is CT plus a simple squamous epithelium (**mesothelium**) that covers its outer surface
Intraperitoneal parts of GI tract have a serosa
A serosa is continuous with a **mesentery** that connects the intraperitoneal organ to the abdominal wall or to another intraperitoneal organ
The mesentery carries blood vessels, nerves, lymphatics to & from the organ
An adventitia is only CT; it lacks a mesothelium
Its CT blends into the CT of surrounding structures
Retroperitoneal parts of GI tract have an adventitia

**B. ESOPHAGUS**

Lumen may have a scalloped or collapsed appearance in cross section due to contraction of the muscularis externa

**Mucosa:**

**Minimally keratinized stratified squamous epithelium**
Lamina propria contains scattered mucous glands called **esophageal cardiac glands**
- found mainly at lower end of esophagus (which leads into cardiac stomach), less often near upper end, least often in middle

Muscularis mucosae is mainly a single longitudinally oriented layer of smooth muscle
- thin or missing in upper esophagus; thickens near stomach

**NOTE:** This is the reverse of the description given in the Ross text

**Submucosa:**
Contains mucous glands called **esophageal glands proper** that are scattered throughout the length of the esophagus

Muscularis externa contains:

**Skeletal muscle** in upper portion

**Mixed skeletal & smooth** muscle in mid-portion

**Smooth muscle** in lower portion
Adventitia or serosa:
Cervical and thoracic portions of esophagus have an adventitia
Short abdominal portion has a serosa

Gastroesophageal junction
Abrupt transition to the simple columnar epithelium of the stomach
A physiological sphincter exists at the gastroesophageal junction, but
there is no consistent anatomical sphincter
- an anatomical sphincter = a thickening of circularly arranged muscle

C. STOMACH
ANATOMIC VS HISTOLOGICAL REGIONS OF STOMACH
Four anatomical regions of stomach:
Cardia
Fundus
Body
Pylorus
Three histological regions of stomach:
Cardiac
Fundic (body is histologically identical to fundus)
Pyloric

STRUCTURAL FEATURES SHARED BY ALL REGIONS
Rugae (temporary folds involving submucosa and mucosa) are
present, but there are no villi (which are permanent folds of the
epithelium and lamina propria)
There is a serosa, since the stomach is intraperitoneal
Simple columnar epithelium lines lumen
- Has one major cell type – the surface mucous cell (surface lining cell)
Surface mucous cells also line the gastric pits
Gastric pits (foveolae):
- Tubular in shape
- Epithelial lining also includes some DNES cells
  - DNES cells of the GI tract are called enteroendocrine cells
Gastric glands:
- One or more gastric glands empty into the base of each pit
- Glands have a simple columnar epithelium, but cell types vary in
different parts of stomach (see below)
Muscularis externa:
- Traditionally described as having 3 layers (outer longitudinal, middle
circular, inner oblique)
- Longitudinal & oblique layers are incomplete; in many places only 2
  of the 3 layers are present
- An anatomical sphincter (pyloric sphincter) is present at
gastroduodenal junction
HISTOLOGICAL REGIONS ARE DEFINED BY THE STRUCTURE OF GASTRIC PITS & GLANDS

Criteria that help to distinguish the three regions include:
- Length of the pits vs. length of the glands
- Overall height (thickness) of the mucosa
- Whether the glands are mostly straight or coiled
- Major cell type(s) in the glands
  NOTE: The surface mucous cell is the major cell type that lines the surface and the pits in all three regions

Cardiac stomach:
- Thinnest (shortest) mucosa of all three regions
- Short pits & short coiled glands
  Glands contain mainly mucous cells & some DNES cells

Pyloric stomach:
- Deepest pits & short coiled glands
  Glands contain mainly mucous cells & some DNES cells

Fundic stomach:
- Short pits and long glands
- Usually has thickest mucosa because of the very long glands
  Glands are mostly straight; lower ends coil
  Glands contain mostly parietal cells & chief cells; also smaller numbers of mucous neck cells & DNES cells
Mucosa has a 3-zoned appearance in good H&E-stained specimens due to the distribution of different cell types:
- pits (usually pale due to surface mucous cells)
- upper part of glands (eosinophilic due to many parietal cells)
- lower part of glands (basophilic due to many chief cells)

EPITHELIAL CELL TYPES OF THE STOMACH:

Surface Mucous Cell
- Rectangular cells (i.e., not goblet-shaped)
- Mucus-containing vacuoles at apical end form a light-staining “apical cup”
- Produces “visible mucus” (i.e., viscous & cloudy) that is alkaline and strongly PAS-positive

Stem Cell
- Few in number; found in the neck of the gland
- Gives rise to surface epithelium & gland epithelium

Turnover times:
- Surface epithelium every few days
- Gland epithelial cells live longer (parietal live up to 200 days)
**Mucous Neck Cell**

Small cells scattered between parietal cells in upper part of the glands
Contains less apical mucus than surface mucous cells, hence usually no apical cup by LM; best identified by EM
Secretes a more water-soluble mucus than surface mucous cells

**Parietal (Oxytic) Cell**

A large cell that is occasionally binucleate
Located mostly in the upper half of the fundic glands
Has eosinophilic cytoplasm due to many mitochondria supplying ATP for active transport
Secretes $H^+$, $Cl^-$, and *intrinsic factor*

Has multiple methods for increasing the surface area of its plasma membrane in order to accommodate many transporters. These include:

- **Intracellular canaliculi** (deep tubular invaginations of the apical plasma membrane)
- **Microvilli** that extend into canaliculi
- A **tubulovesicular system** of membranes in the cytoplasm
  - Represents a membrane reservoir that can be rapidly incorporated into the plasma membrane to increase its surface area during active transport of ions
  - Number of microvilli therefore increases greatly in an active cell, and amount of tubulovesicular system in the cytoplasm decreases

**Chief (Zymogen) Cell**

Secretes **pepsinogens, rennin (= chymosin) and gastric lipase**
Smaller, more basophilic than parietal cells
Most abundant in the basal half of fundic glands
Morphology is typical of cells that synthesize protein & secrete it in a regulated fashion

**DNES (Diffuse Neuroendocrine System) Cell**

Usually scattered individually throughout gastric epithelium
Have small secretory granules clustered near the basal end of the cell
Secrete into the lamina propria (not into gut lumen)
Pale-staining cytoplasm by LM & often by EM as well
All lie on basement membrane of the epithelium

- Some reach the lumen (= *open* enteroendocrine cells)
- Others do not reach the lumen (= *closed* enteroendocrine cells)

Several different types exist in stomach, each producing a different hormone
Different types are often distinguishable on the basis of the morphology of their secretory granules. IT IS NOT NECESSARY FOR YOU TO BE ABLE TO MAKE THESE DISTINCTIONS.

GASTRODUODENAL JUNCTION
At the gastroduodenal junction:
- Inner circular layer of the muscularis externa is greatly thickened to form the pyloric sphincter
- Epithelium remains simple columnar in small intestine, but cell types change (see below)

D. GENERAL CHARACTERISTICS OF SMALL INTESTINE
Villi (permanent surface projections) are unique to small intestine
- Covered by a simple columnar epithelium that contains:
  - Absorptive cells (enterocytes) – the main cell type
  - Goblet cells
  - DNES cells
- Core of villus is formed by lamina propria (no submucosa)
  - Contains fenestrated capillaries
  - Contains lymphatic capillaries called lacteals

Intestinal glands (= crypts of Lieberkühn)
- Simple tubular glands located in the lamina propria
- The mouths of the glands open between villi in the small intestine
- The bases of the glands usually lie near the muscularis mucosae
- Found in small intestine & large intestine

Muscularis externa has:
- Inner circular layer
- A complete outer longitudinal layer of uniform thickness (no teniae coli)

Serosa vs. adventitia
- A serosa is present on intraperitoneal portions (jejunum, ileum, & first & last parts of duodenum)
- An adventitia is present on retroperitoneal portions (2nd & 3rd of the four parts of the duodenum)

Plicae circulares (= valves of Kerckring)
- Permanent folds involving submucosa & mucosa
- Oriented mainly transversely
- Found mostly in duodenum, jejunum & proximal part of ileum
EPITHELIAL CELL TYPES OF SMALL INTESTINE:

**Absorptive Cells (Enterocytes)**
- Tall columnar cells, oval nuclei
- Striated border (brush border) formed by **microvilli**
- Thick glycocalyx on microvilli (visible by hi mag EM or by LM with a PAS stain)
- Apical junctional complexes between cells
- Supranuclear Golgi involved in processes such as assembling **chylomicrons**
- Many mitochondria in apical cytoplasm provide energy for ion pumps (active transport systems) in cell membranes
- Considerable SER in apical cytoplasm for re-synthesis of triacylglycerols from absorbed fatty acids & glycerol

**Goblet Cells**
- Secrete **acidic mucinogens** that stain with Alcian blue
  - Secreted mucinogens absorb water to become mucins, which are abundant in mucus
- Goblet cells increase in abundance from duodenum through large intestine
- Base of cell is narrower than apex (like the stem of a goblet)
- Nucleus is compressed in the basal cytoplasm
- Supranuclear Golgi is well developed
  - Involved in processing & packaging of mucinogens
- Secretory vacuoles fill the apical cytoplasm

**Stem cells**
- Found near the base of the crypts (not at the necks of the glands as in stomach)

**Paneth Cells**
- Found mainly in jejunum
- Located at the base of the crypts
- Very large intensely eosinophilic secretory granules in apical cytoplasm
- Products include **lysozyme** (an antibacterial enzyme) & **α-defensins**

**DNES (Enteroendocrine) Cells**
- More common in crypts than on villi
- Produce peptide hormones and amines that control gut motility & secretion
- Morphology similar to DNES cells in stomach, & they produce some of the same hormones
REGIONAL DIFFERENCES OF SMALL INTESTINE:

Duodenum

Duodenal (Brunner's) glands
Mucous glands that are located in the submucosa
Empty into the bases of crypts of Lieberkühn
Produce an alkaline mucus that neutralizes the acidity of the chime from the stomach
Epithelium contains fewer goblet cells than jejunum or ileum

Jejunum

Many plicae circulares
Many Paneth cells
Intermediate number of goblet cells between duodenum & ileum
“No” Brunner's glands or Peyer's patches

Ileum

Has Peyer's patches
Characteristic of ileum, less often seen in jejunum
Are part of the gut-associated lymphoid tissue (GALT)
Each patch includes many lymphoid nodules
A patch is large enough to be grossly visible as a whitish spot
Often found on the side of the gut tube opposite the attachment of the mesentery (abmesenteric border)
Nodules are located in lamina propria; often extend into submucosa
Lymphocytes usually enter Peyer's patches by crossing the wall of HEVs located in or near the nodules
Lymphocytes usually leave Peyer's patches in efferent lymphatics
The epithelium covering a nodule is called the dome epithelium
Lacks villi (but villi are found between the domes of adjacent nodules)
Has “no” goblet cells
Contains M cells and absorptive cells

M Cells (Microfold Cells)
Apical plasma membrane has microfolds rather than microvilli
Basal plasma membrane has a very deep invagination
- forms a pocket occupied by lymphocytes & macrophages
M cells transport antigen from the lumen across their cytoplasm via transcytosis, and deliver it to lymphocytes & macrophages in the pocket
Difficult to see M cells by LM; look for the cluster of lymphocytes within the pocket of each M cell
E. LARGE INTESTINE

Includes cecum, appendix, colon, rectum, & anal canal

Has crypts of Lieberkühn, but no villi
  Major cell types are: Goblet cells, absorptive cells, stem cells & DNES cells

Has three characteristic external features that are grossly visible:
  Haustra (sacculations defined by folds that involve all 4 layers of the wall)
  Teniae coli (thickenings of the outer longitudinal layer of muscularis externa)
  Epiploic appendages (omentum appendices) – small fat-filled tags protruding from the serosa

There are no permanent plicae circulares, but there can be temporary folds that involve only submucosa & mucosa, & are therefore distinct from haustra

Mucosa:
  Simple columnar epithelium
  Goblet cells are more abundant than in small intestine; increase in number as you go distally toward the rectum
  Intestinal glands (crypts of Lieberkühn)
    - stems cells at base of crypts
    - crypts contain “no” Paneth cells
  Lamina propria lacks lymphatics – may contribute to slow rate of metastasis of colon cancers

Muscularis externa:
  Inner circular layer is uniform in thickness
  Outer longitudinal layer includes 3 thickened bands (teniae coli)
    Between the teniae the longitudinal muscle is thin or discontinuous

Has a serosa on its intraperitoneal portions and an adventitia on its retroperitoneal portions

REGIONAL VARIATION IN THE LARGE INTESTINE

Appendix:
  Fewer & shorter crypts than colon
  Many lymphoid nodules in lamina propria & submucosa
  Nodules are located all around lumen, i.e., not limited to abdomesenteric side of wall as is common in Peyer’s patches
  Often has debris in lumen
  Has a continuous outer longitudinal layer of muscularis externa (i.e., the 3 teniae coli meet & form a continuous layer)

Rectum:
  Typical morphology of the large intestine except that, like the appendix, rectum has a continuous uniformly thick outer longitudinal layer of the muscularis externa (no teniae coli)
  Has 2-4 (usually 3) transverse rectal folds (Houston’s valves)
    These are semilunar transverse folds that protrude into the lumen
RECTO-ANAL JUNCTION:

Epithelium changes to:
- Minimally keratinized stratified squamous at the **pectinate line** in the anal canal
- Then to maximally keratinized stratified squamous in the inferior part of the anal canal

**Internal anal sphincter** is **smooth muscle** (involuntary control)
  - Derived from inner circular layer of muscularis externa

**External anal sphincter** is **skeletal muscle** (voluntary control)
  - Derived from pelvic diaphragm

III. LIVER:

Largest gland in body

**Dual blood supply** from portal vein & hepatic artery
  - Portal vein carries blood that:
    - comes from intestines (rich in absorbed nutrients), pancreas (rich in pancreatic hormones), and spleen (rich in breakdown products of red cell destruction such as iron and bilirubin)
  - Hepatic artery carries oxygenated blood & chylomicrons

Liver is composed of functional units called lobules

CLASSIC LIVER LOBULE

**Classic lobule** is roughly hexagonal in cross section
  - **Portal triads** are located in **portal canals** near each vertex
  - A **central vein (terminal hepatic venule)** lies at the center
  - Blood flows from periphery toward center
  - Bile flows in opposite direction

Classic lobule is based on venous drainage, i.e., is a region whose sinusoids all drain into the same central vein

Very little connective tissue between classic lobules in humans

PORTAL TRIAD

Located within a portal canal (the space enclosed by the **limiting plate** of hepatocytes)

Components of a portal triad are branches of:
- **Hepatic artery** (usually an arteriole)
- **Portal vein** (usually a venule; larger diameter than hepatic artery branch)
- **Bile duct** (simple cuboidal epithelium)

Lymphatic capillaries are also often present
CENTRAL VEINS (TERMINAL HEPATIC VENULE)
Wall is thin (more like a venule than a vein); consists of endothelial cells (no smooth muscle)
Plates of hepatocytes are organized radially around the central vein
Hepatic sinusoids run between plates of hepatocytes
Central veins receive blood from sinusoids and drain into sublobular veins
Can be distinguished from the components of a portal triad because:
- central veins are not accompanied by other vessels or ducts
- less connective tissue around central veins than around triad

HEPATIC SINUSOIDS
Are highly permeable sinusoidal capillaries
Wall is formed by a mixture of endothelial cells & Kupffer cells
Blood from the inlet branches of the hepatic artery and portal vein first mixes at the level of the sinusoid

KUPFFER CELLS
Are a type of macrophage
Contribute to sinusoidal walls & may extend across the lumen
Phagocytize old or damaged RBCs & other particulate matter

SPACE OF DISSE
Narrow space encircling each sinusoid; separates it from hepatocytes
Microvilli of hepatocytes extend into space of Disse
Is the location of most metabolic exchange between blood & hepatocytes
Reticular fiber stroma is located mainly in the space of Disse

ITO CELLS (HEPATIC STELLATE CELLS)
Located in the space of Disse
Store vitamin A in cytoplasmic lipid droplets
Produce the reticular fiber stroma of the liver in a healthy organ
In cirrhosis they produce collagen type I that results in fibrosis

PATHWAY OF BLOOD FLOW
Interlobular branches of hepatic artery & portal vein in portal canals
Distributing branches leave portal canal & run between classic lobules
Inlet vessels enter lobules
Sinusoids
Central vein
Sublobular vein
Larger collecting veins
3 or more hepatic veins
Inferior vena cava
2 ADDITIONAL WAYS OF DEFINING A LIVER LOBULE

**Portal Lobule**
- Based on bile flow, i.e., is a region whose bile canaliculi all drain toward the bile duct in the same portal canal.
- Roughly triangular in cross section
  - Central vein at each vertex
  - A portal triad at the center
  - Bile flows from periphery toward center

**Hepatic Acinus (of Rappaport) = Liver Acinus**
- Roughly diamond-shaped or oval in cross section
- Central veins and portal triads are located at the periphery
- Short axis connects 2 portal triads (distributing vessels lie on the short axis)
- Long axis connects 2 central veins
- Based on gradients of \( \text{O}_2 \), nutrients, & toxins supplied by distributing vessels
- Consists of 3 zones centered around the distributing vessels
- Used to explain patterns of hepatocyte metabolism & pathology
  - Cells in zone 1 (closest to distributing vessel): First to receive oxygen, nutrients, and toxins from outside the liver (exogenous toxins)
  - Cells in zone 3 (nearest central vein): Are most susceptible to damage from hypoxia & endogenous toxins (those produced within the liver)

**HEPATOCYTES**
- Are epithelial cells
- Are the major parenchymal cells of the liver

**LM characteristics:**
- Polygonal cells with round, euchromatic nuclei
- One or more prominent nucleoli
- **Often binucleate**; if uninucleate, they may be *polyploid*

Plasma membrane has 2 structurally & functionally different domains:
- **Sinusoidal domain** contacts the space of Disse and is the endocrine face of the hepatocyte
- **Lateral domain** faces another hepatocyte
  - is the site where bile canaliculi form
  - canaliculi represent the exocrine face of the hepatocyte

**Bile canaliculi:**
- Plasma membranes of adjacent hepatocytes form a bile canaliculus
  - i.e., they have no epithelial lining of their own other than hepatocytes
- Tight junctions prevent leakage of bile from canaliculi into blood
- Golgi, lysosomes & residual bodies of hepatocytes are often located near canaliculi
  - *lipofuscin* may accumulate within the residual bodies
IV. GALL BLADDER

Stores and concentrates bile

Releases stored bile via the cystic duct into the common bile duct

Cholecystokinin (CCK, pancreozymin) is one stimulus for bile release

CCK is secreted by I cells (a type of DNES cell) in the intestinal mucosa when dietary fat is present in the lumen of the intestine

LAYERS OF THE GALL BLADDER WALL

Has a mucosa, a muscularis & a serosa/adventitia

Has **no muscularis mucosae or submucosa**

**Mucosa:**

**Simple columnar** epithelium and lamina propria

- epithelium consists mainly of **absorptive cells**
- when gall bladder is actively concentrating bile, the lateral spaces between absorptive cells widen (seen best by EM)

Unless gall bladder is full, mucosa usually has many deep irregular folds that look like **arcades (arches)** in sectioned tissue

**Muscularis**

Equivalent to the muscularis externa found in most hollow organs

Is circular near neck of bladder; more random in body

**Rokitansky-Aschoff crypts or sinuses** are deep invaginations of the epithelium that extend into or through the muscularis

- found in chronic inflammation; may perforate

**Serosa/adventitia**

**Adventitia** is present where gall bladder directly contacts liver

**Serosa** covers remainder of organ

V. PANCREAS

Has exocrine & endocrine components

**Exocrine** = Pancreatic acinar cells that secrete digestive enzymes into duodenum via the main (& sometimes an accessory) pancreatic duct

**Endocrine** = Islets of Langerhans that secrete hormones into fenestrated capillaries

**EXOCRINE PANCREAS**

Functional unit of the exocrine pancreas is the **acinus**, which consists of:

- Numerous pancreatic acinar cells
- Centroacinar cells (form the first or intra-acinar part of the duct system)
- Has a very small lumen
MICROSCOPIC ANATOMY

Pancreatic acinar cells
Pyramid-shaped serous cells
Secrete a wide variety of digestive enzymes
- many in proenzyme form (e.g., trypsinogen, chymotrypsinogen)
Basal basophilia due to extensive RER
Acidophilic zymogen granules in apical cytoplasm store the enzymes
Exocytosis occurs in response to signals such as cholecystokinin (pancreozymin) or acetylcholine (from vagal fibers)

Centroacinar cells
Pale, low cuboidal cells that are unique to pancreas
Lie within the lumen of a secretory acinus
Represent the first cells (intra-acinar portion) in an intercalated duct

Intercalated ducts
Are the smallest type of intralobular duct
Simple, low cuboidal epithelium
Secrete a watery, bicarbonate-rich fluid in response to secretin, a hormone produced by S cells in the duodenum
Drain into larger intralobular ducts

Larger intralobular ducts
Lined by simple cuboidal epithelium
No basal striations (there are no striated ducts in pancreas)
Empty into interlobular ducts

Interlobular ducts
Run in the CT septa
Empty into the main pancreatic duct (and in some individuals into an accessory pancreatic duct)

Main duct unites with common bile duct to form the ampulla of Vater, which empties into the duodenum at the major duodenal papilla

ENDOCRINE PANCREAS
Consists of islets of Langerhans
Spherical structures scattered among acini throughout pancreas
Most islets are larger than a secretory acinus
Usually (but not always) paler staining than an acinus
Highly vascular (fenestrated capillaries)
Islet cells have no obvious apical or basal ends (i.e., are not as structurally polarized as acinar cells) because they secrete into capillaries adjacent to any surfaces of the cell
Therefore the cells in an islet appear to be more irregularly arranged than those in an acinus
3 main cell types in most islets
  Usually indistinguishable with H&E
  Listed in order from most abundant to least, they are:

**B (beta) cells:**
- produce **insulin**, which reduces blood glucose levels, and some other hormones such as **amylin** (an appetite suppressant)
- located throughout the islet in humans but concentrated toward center in some other species
- secretory granules may have a dark, angular “crystalline” core

**A (alpha) cells:**
- produce **glucagon**, which increases blood glucose levels
- are mainly located at the periphery of an islet
- granules have a dark spherical core surrounded by a clear halo

**D (delta) cells:**
- produce **somatostatin**, which inhibits motility of gut & gall bladder, secretion by acinar cells, & secretion of insulin & glucagon
- granules are light-staining and almost completely filled with secretory material

Other minor cells types:

**PP cells (F) cells**
- produce **pancreatic polypeptide**
- inhibits secretion by acinar cells & duct cells
- stimulates gastric chief cells

**Epsilon cells**
- produce **ghrelin** (an appetite stimulant)

**Gastrin** is produced transiently in islets during fetal life & in some pancreatic tumors (**Zollinger-Ellison syndrome**) 

**THE INSULOPORTAL (ISLET-ACINAR PORTAL) SYSTEM**

Is a **venous portal system** within the pancreas
Carries islet hormones that affect the activity of other islet cells or acinar cells

First capillary bed is in islets (**fenestrated**)
- Blood flows from periphery to center of an islet
  - thus cells near the center receive blood that may be carrying other islet hormones that affect their activity (e.g., somatostatin from peripheral delta cells can inhibit secretion of centrally located beta cells)

Venules drain first capillary bed & give rise to the second

Second capillary bed (**continuous capillaries**) supplies acini
- thus acinar cell activity can be modulated by islet hormones (e.g., insulin stimulates and somatostatin inhibits acinar cell secretion)