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This atlas is a series of photographs ranging from low to high magnifications of the individual tissue specimens. The low magnification images should be used for orientation, while the higher magnification images show details of cells, tissues, and organs. Although every effort has been made to faithfully reproduce the colors of the tissues, a full appreciation of histological structure is best achieved by examining the original specimens with a microscope. This atlas is a preview of what should be observed.

The photomicrographs found in this atlas come from the collection of microscope slide used by medical, dental and undergraduate students of histology at the University of Minnesota. Most of these slides were prepared by Anna-Mary Carpenter M.D., Ph.D. during her tenure as Professor in the Department of Anatomy (University of Minnesota Medical School).

Each tissue specimen, in its entirety, has been digitized with a high resolution 40X or 60X lens to generate virtual microscope slides. The Virtual Microscope Collection includes additional slides which complement and extend the core slide collection. Producing the virtual slide collection and developing the web site for their presentation was done with the very capable assistance of Todd C. Brelje Ph.D.

The drawings that appear in the atlas are the product of Jean E. Magney, who is accomplished both as an histologist and an artist. Her talented interpretation of biological structure and its artistic rendering greatly facilitate the learning and comprehension of histology. These drawings first appeared in "Color Atlas of Histology" Stanley L. Erlandsen and Jean E. Magney, Mosby 1992.

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## Introduction:

What is histology? Histology is the study of cells, tissues and organs as seen through the microscope. Although this atlas is a guide to biological structure that can be observed through the light microscope, histology also includes cellular detail down to the molecular level that can be observed using an electron microscope. The importance of histology is that it is the structural basis for cell, tissue and organ biology and function (physiology) and disease (pathology).

What is the plan for the study of cells, tissues and organs? Histology is organized into four basic types of tissues.

1. Epithelium
2. Connective tissue including

Cartilage and bone
Blood and blood formation
3. Muscle
4. Nervous tissue

Chapters 2-8 are concerned with the features of the four basic tissues. The remaining chapters focus on features of organs. Organs are typically made up of more than one type of tissue and cells with varying degrees of differentiation.

The light microscope, tissue preparation, limits and challenges.

The bright field light microscope is a two lens compound optical instrument. The two lenses are the objective and the oculars. The oculars have a 10 fold magnification and the objectives range from 10X, 20X, 40X to 100X. Thus the total magnification typically ranges from 100 fold to 1000 fold. In practice this means that while using the 10X objective you have a wide field of view, but with low resolution. While using the 100X objective you have high resolution, but with a very small field of view. To use a metaphor what this means is that when using the low power objective you can see the forest but not the trees and while using the high power objective you can see the leaves on the trees but not the forest. Therefore when examining a specimen it is essential to start with the low power objective to gain perspective and then work up to the highest power magnification as needed to observe the necessary detail.

Examination of tissues requires that they be prepared for viewing with a microscope. This is a multi-step process that includes fixation (preserves the tissue), embedment (stabilizes the tissue for sectioning), sectioning (cuts the specimen into thin slices of about 5 um ) then placing the sections on a glass slide so they can be stained for viewing.

A note about resolution and detection. Resolution refers to the ability to discriminate between two adjacent objects. For the light microscope with optimal lenses and sample preparation this approaches 0.2 um, which is the theoretical limit for light microscopes. [The eye can resolve about 250-500 um and the electron microscope can resolve about 1 nm ) Detection refers to the ability to detect something and this can be much smaller than the limit of resolution. For fluorescence molecules this can be as little as a few molecules!


There are several challenges in learning histology. The first being that the view observed through a microscope gives you a perspective that you are unlikely to have experienced previously. It is a complex data set - one with a broad range of shapes and sizes, with varying shades of red and blue. This complex image offers very few clues that are intuitive. Also, the tissue specimen is a two dimensional slice of a complex three dimensional
structure. So, once the two dimensional image has been ascertained you still have the challenge of imagining its three dimensional elaboration. The ideal situation is to have the student and teacher viewing the same specimen simultaneously such as in a dual view microscope. Since this is not always possible, this atlas was written as if a teacher was always at your side to help guide you from low power to the highest power necessary to observe the essential features of the tissue specimens. Thus you will notice that images of all of the slides range from a macroscopic view of the microscope slide itself and then progress through higher magnifications as needed.

## How to study microscope slides:

1. Know what structures are important to learn. This atlas shows and identifies the structures and how to find them.
2. The next task in learning is to see if you can identify the structures when examining a slide. Always start at the lowest power (this is important for context and orientation). Increase the magnification as needed so that additional features of the specimen can be observed.
3. Take notes on the features that are observed in the slide. This is best done by drawing pictures and writing a description of the specimen. As in any science laboratory, it is essential that observations be recorded. Not only is this good practice but in research and medicine it is also a legal requirement.
4. Each chapter has a section "Observe and note". This lists the features that are essential to learning histology and are noteworthy.

## How to take Histology Laboratory Notes:

A. Draw a picture of the object of interest. (A blue and red pencil is sufficient for nearly all drawings)
B. Write notes about its appearance, characteristics and features.

Nearly every cell can be described by taking note of:

1. Size
2. Shape
3. Nuclear size and shape and nuclear/cytoplasmic ratio
4. General Staining properties (H\&E)
a. Basophilia \& eosinophilia
b. Hetero- and euchromatin
5. Special staining properties
a. Verhoeff, Azan, silver etc.
6. Cellular specializations
a. Microvilli, cilia, secretion granules, myofilaments etc.
b. Unusual amounts of mitochondria, RNA etc
7. Cellular constituents such as secretion granule contents (hormones, enzymes)
8. Polarity
9. Extracellular material
a. Extent
b. Appearance
10. Location
a. Example
i. Adjacent to similar cells
ii. Borders a lumen
iii. Surrounded by extensive extracellular matrix
iv. Etc.
11. Organization (cells, tissues and organs)
a. Arrangement of cells of similar and different types
b. Arrangement of cells with respect to extracellular material
12. Compare and contrast with similar/different cells.
13. Heterogeneity among homologous cells:
a. Cell development and differentiation
b. Cell Cycle
c. Active and resting cycles
d. Exposure to a concentration gradient of nutrients
i. Example
14. Skin cells
15. Liver hepatocytes
C. Include questions in the notes.

Carefully formulated questions can often reveal the answer.
D. Drawing (and taking notes) is a way of thinking, seeing and understanding.


## Chapter 14 Gastrointestinal Tract

The gastrointestinal tract is a hollow muscular tube that starts at the esophagus and ends with the anus. It is divided into four regions, the esophagus, stomach, small intestine and large intestine. The esophagus is a passage for transporting food to the stomach. The stomach adds gastric juices to begin digestion. It is divided into three histologic regions: cardiac, fundus/body and pyloric. The small intestine is the principle site for digestion and absorption. It transfers chyme from the stomach to the large intestine and is divided into three regions: duodenum, jejunum and ileum. The large intestine has the main function of re-absorbing water from the chyme and adding mucus to facilitate transport of the feces. The parts of the large intestine are the cecum, appendix, colon, rectum and anal canal.

## General Plan for Hollow Tubular Organs

The walls of hollow organs have four layers or tunics: mucosa, submucosa, muscularis externa and adventitia or serosa.

Mucosa (mucous membrane): Mucous membranes line internal passages and provide a barrier between the tissues of the body and the external environment. The membranes are constantly wet and lubricated by mucus. The mucosa has three parts: an epithelium, lamina propria and muscularis mucosa. The epithelium varies in different regions depending on its function (i.e. protective, secretory or absorptive). The lamina propria is a connective tissue layer that supports the epithelium and contains small arteries, veins, lymphatics and nerves. Lymphocytes and plasma cells are also frequently seen in this layer. When glands are found in this layer they are referred to as mucosal glands. The muscularis mucosa, when present, consists of two or three layers of smooth muscle. It facilitates localized movement of the mucous membrane, aiding expression of secretions and movement of fluid across the surface of the epithelium.

Submucosa: The submucosa is a layer of fibroelastic connective tissue that supports the mucosa. Found in this layer are blood and lymphatic vessels and nerves. Parasympathetic ganglia found in this layer are called Meissner's submucosal plexus. When glands are found in this region (esophagus and duodenum) they are referred to as sub-mucosal glands.

Muscularis externa: This is a separate layer not to be confused with muscularis mucosa. The muscularis externa consist of two thick layers of smooth muscle - and inner circular layer and an outer longitudinal layer. Between the layers is a
vascular plexus and an autonomic nerve plexus associated with small parasympathetic ganglia of (Auerbach's) myenteric plexus. The muscularis externa maintains tonus in the tube and propels luminal contents by peristalsis.

Adventitia or serosa: This outermost layer is dense irregular connective tissue. When it blends with connective tissue of the surrounding area it is an adventitia. If it has a free surface projecting into the peritoneal cavity it is covered with a single layer of mesothelial cells (epithelial cells derived from mesoderm) and is called a serosa.

## Esophagus

The epithelium is stratified squamous and non-keratinized. This is a thick layer of $40-60$ cells measuring 300-500 um. This is supported by a lamina propria. A well developed muscularis mucosa is present (200-300 um) and surrounded by the submucosal region. Submucosal mucous glands are scattered in this region. The muscularis externa consists of an inner circular layer and an outer longitudinal layer. In the upper third of the esophagus the muscularis is skeletal muscle. In the middle third both smooth and skeletal muscle is present and in the lower third only smooth muscle is present. The myenteric plexus of nerves and ganglia (Auerbach's plexus) are found between the inner and outer layers of the muscularis externa. A tunica adventia is present.

## Stомасн

An abrupt transition occurs at the cardio-esophageal junction, where stratified squamous epithelium gives way to simple columnar epithelium. The simple columnar epithelium (surface mucous cells) dips into the lamina propria to form gastric pits (150-300 um deep). Gastric glands (simple tubular branched) empty into the bottom of the gastric pits. The base of gastric glands rests on a muscularis mucosa. The submucosa is quite prominent and contains numerous arteries, veins, lymphatics and nerves. In the stomach the muscularis externa consists of three layers: a discontinuous inner oblique layer, then an inner circular layer and an outer longitudinal layer. When the stomach is empty the surface is thrown into folds (rugae).

The stomach is divided into three histological regions (cardiac, body/fundus, pyloric) based on their anatomical location and appearance of the glands. The cardiac region of the stomach is a narrow rim of tissue around the esophageal opening. The cardiac glands are short tubular glands that are
coiled at the base. The glands consist mostly of mucus secreting cells. Parietal cells may be found in these glands. The fundus and body make up more than $90 \%$ of the stomach and have the same histological appearance. The glands of the body and fundus are straight tubular and have three regions: The upper third is the isthmus and empties into the gastric pits, the middle third is the neck and the bottom third is the base. There are five types of cells associated with the glands. Regenerative cells are found at the boundary between the isthmus and the gastric pit. These cells are few in number and not readily distinguished in routine preparations. These cells divide and migrate upwards to replenish the surface mucous cells and downward to replenish the rest of the cells in the gastric glands. Mucous neck cells are found in the isthmus and neck region. These cells are scattered among parietal cells and secrete an acidic form of mucus. Parietal cells are distinctive eosinophillic cells with a centrally located nucleus and secrete hydrochloric acid. The eosinophilia is due to the large quantity of mitochondria in these cells. Some parietal cells are also be found in the base of the gland. The primary cell type in the base is the chief cell which has a basophilic cytoplasm in its basal region. Chief cells secrete pepsinogen and gastric lipase. Gastric enteroendocrine cells are part of the diffuse neuroendocrine system (DNES) are few in number and secrete enteric hormones (these can not be identified with H\&E). The pyloric region has short coiled tubular glands that only secrete mucus - chief cells and parietal cells are absent.

## Small Intestine

One of the main functions of the small intestine is nutrient absorption. Specializations for increasing surface area for absorption involve three magnitudes of folds or projections.

1. Circular transverse folds (plicae circulares or valves of Kerckring) of the entire mucosa (with a core of submucosa) project permanently into the lumen. The plicae are prominent in the duodenum and jejunum and diminish in the later part of the ileum.
2. Villi are projections (evaginations) of the mucous membrane (with a core of lamina propria) into the lumen. The shape of villi varies in the different regions of the small intestine: They start as tall, narrow, fin-ger-like projections in the duodenum and evolve to a short broad leaf-like projection in the distal ileum.
3. Microvilli are cytoplasmic projections (1-2
um in length) on the surface of the simple columnar epithelial cells. These surface projections make up the striate border of intestinal epithelium.

The second main function of the small intestine is digestion and is dependent on secretions from three types of glands:

1. Exocrine glands (liver and pancreas) deliver their secretions (bile and digestive enzymes) into the duodenum by way of the cystic duct and main pancreatic ducts.
2. Submucosal glands. Submucosal glands are only found in the duodenum (Brunner's glands). They secrete mucus and resemble the pyloric glands of the stomach.
3. Intestinal crypts (glands) are invaginations of the surface epithelium down into the underlying lamina propria.

Cell types found in the intestinal epithelium include:

1. Simple columnar epithelium absorptive cells have a microvillus (striate) border and are involved in nutrient digestion and absorption.
2. Goblet cells secrete mucin.
3. Columnar crypt cells transport secretory $\lg A$
4. Paneth cells at the base of intestinal crypts produce antibacterial substances. These cells have very eosinophillic secretion granules due to their content of lysozyme.
5. M cells occur in regions where lymphoid nodules abut intestinal epithelium. Here the columnar cells are replaced by the cuboidal to squamous M cells. M cells belong to the mononuclear phagocytic system of macrophages and antigen presenting cells.
6. Stem cells are located in the base of the intestinal crypts
7. Enteroendocrine cells (DNES) produce hormones and are not readily distinguished in routine preparations.

The lamina propria forms the core of the villi and supports the intestinal glands, is highly vascular and rich in lymphocytes and plasma cells. The muscularis mucosa lies at the base of the glands and sends fibers into the core of the villi. The sub-
mucosa is irregular fibroelastic tissue with a rich lymphatic and vascular supply. Meissner's submucosal nerve plexus is found in this layer and controls the muscularis mucosa. In the duodenum submucosal glands are found. The muscularis externa, is responsible for peristalsis, and has an inner circular and outer longitudinal layer. Auerbach's plexus of nerves is found between the two muscle layers.

The small intestine is divided into three regions: duodenum, jejunum and ileum. The pyloric stomach transitions to the duodenum at the pyloric sphincter (thick inner circular layer of the muscularis externa). The duodenum is the shortest segment ( 25 cm ) and receives secretions from the liver (bile) and pancreas (digestive enzymes). A distinguishing feature of the duodenum is the presence of submucosal glands (Brunner's glands, their appearance differs from pyloric glands only with respect to where they are located i.e. submucosal vs. mucosal). The jejunum and ileum have a similar appearance. Lymphoid tissue in the lamina propria progressively increases from the jejunum to the ileum. In the ileum, permanent clusters of lymphoid nodules (Peyer's patches) become a prominent feature. Villi become shorter, broader and have increasingly larger lacteals (blind ending lymphoid vessels in the core of villi) in the ileum. Frequency of goblet cells and Paneth cells increases as one progresses from the duodenum to the ileum.

## Large Intestine

The main function of the large intestine is to reabsorb water and to consolidate and transport the fecal mass. The parts of the large intestine are the cecum, appendix, colon, rectum and anal canal. The cecum and colon are histologically indistinguishable. Having no villi, the inner surface is smooth and even. The intestinal glands (crypts of Lieberkuhn) are frequent and closely packed together. The glands are simple straight tubular glands and quite long (>600 um). The two major cell types are simple columnar absorptive cells with striated border and numerous goblet cells. Paneth cells may or may not be present. Enteroendocrine cells may be seen at the base of the crypts. Lymphocytes are common in the lamina propria. The muscularis mucosa is found at the base of the glands. The submucosa is well developed with prominent blood and lymph vessels. Meissner's submucosal nerve plexus is easily seen in the colon. The muscularis externa consists of an inner circular layer and an unusual outer longitudinal layer. The outer layer is gathered into three distinct bundles (taenia coli) that are equally spaced around the gut. Between the muscle layers the numerous ganglia of Auerbach's plexus are
seen. The colon is mostly covered by a serosa. The appendix is a $4-6 \mathrm{~cm}$ blind ending diverticulum descending from the cecum. Its epithelium is similar to the colon, but with fewer goblet cells. The crypts are short (150-250 um) in comparison to the colon. Enteroendocrine cells are found in the base of the crypts. Numerous lymphocytes and nodules are present in the lamina propria. When nodules are present M cells are frequently observed in the epithelium overlying the nodules. The muscularis mucosa is very thin. The muscularis externa is inner circular and outer longitudinal layers of smooth muscle. The appendix is covered by a serosa.


## Observe and note:

## Tongue

1. Striated muscle
2. Lingual (minor) salivary glands
3. Foliate and filiform papillae.
4. Taste buds
5. Taste pore

## Esophagus

1. The mucosa consisting of:
a. Epithelium: stratified squamous nonkeratinizing
b. Lamina propria (the connective tissue support for epithelium in mucous
membranes).
c. Muscularis mucosa
2. Submucosa consisting of:
a. Submucosal glands with ducts passing through the mucosa
3. Muscularis externa: inner and outer layers
4. Ganglia of Auerbach's (myenteric) nerve plexus, located between the inner and outer muscle layers of the muscularis externa.

## CARDIOESOPHAGEAL JUNCTION

1. Abrupt transition from stratified squamous non-keratinizing epithelium to a simple columnar epithelium.
2. Mucosa
a. Lamina propria
ii. Pyloric mucosal glands
b. Muscularis mucosa
b. Submucosa
3. Gastric pits
4. Cardiac glands
a. Mucous cells
b. Parietal cells
5. Submucosa
6. Muscularis externa
7. Adventitia

## Fundic stomach

1. Rugae
2. Muscularis mucosa
3. Muscularis externa
4. Gastric pits and glands
5. Four (five) types of cells characteristic of the stomach:
a. Simple columnar epithelium of the surface
b. Mucous neck cells
c. Parietal cells
d. Chief cells
e. Enteroendocrine cells cannot be easily recognized with H\&E

Pyloric stomach

1. Pits and glands
2. Short coiled mucosal glands
a. Glands consists primarily of cells that secrete mucus
i. Absence of parietal cells

Pyloroduodenal junction

1. Sphincter
2. Pyloric stomach
a. Mucosa
i. Gastric pits
3. Duodenum
a. Mucosa
i. Villi
ii. Crypts (glands)
b. Submucosa
i. Submucosal glands (Brunner's glands)

## Duodenum

1. Mucosa
a. Villi
b. Crypts (glands)
c. Surface absorptive cells
i. Brush border - microvilli
d. Goblet cells
e. Lamina propria
f. Muscularis mucosa
2. Submucosa
a. Submucosal glands (Brunner's glands)
3. Muscularis externa
a. Inner circular and outer longitudinal

## Jejunum/leeum

1. Mucosa
a. Villi
i. Compare villi in duodenum, jejunum and ileum
ii. lacteals
b. Crypts (glands)
c. Surface absorptive cells
i. Brush border - microvilli
ii. Terminal web and terminal bar
d. Goblet cells
e. Paneth cells
f. Lamina propria
i. Lymphocytes and plasma cells
ii. Lymph nodules (Peyer's patches)
g. Muscularis mucosa
h. Plicae circulares
2. Submucosa
a. Absence of glands in submucosa
b. Connective tissue, blood and lymph vessels and nerves
3. Muscularis externa
a. Inner circular and outer longitudinal
b. Auerbach's myenteric nerve plexus

## Appendix

1. Mucosa
a. Absence of villi
b. Short crypts
c. Surface absorptive cells
d. Few goblet cells
e. Lamina propria
i. Lymphocytes, plasma cells, eosinophils
ii. Lymph nodules (in some areas M -cells over lie nodule)
f. Submucosa
g. Muscularis externa

## Colon

1. Mucosa
a. Absence of villi
b. Deep crypts (straight intestinal glands)
c. Surface absorptive cells (microvillus border, terminal web)
d. Numerous goblet cells
e. Lamina propria
i. Lymphocytes, plasma cells, eosinophils
f. Muscularis mucosa
2. Submucosa
a. Numerous blood and lymph vessels
b. Meissner's submucosal nerve plexus
3. Muscularis externa
a. Inner circular layer, outer longitudinal layer (taenia coli)
b. Auerbach's myenteric plexus

Slide \# 108 Tongue (H\&E)


Chapter 14 Gastrointestinal tract




Organization of Stomach



Slide \# 111 Stomach,
(Cardiac stomach glands)

Slide \# 112 Fundic Stomach (H\&E)



Slide \# 113 Stomach Fundic


Slide \# 115 Pyloric Stomach (H\&E)



## Intestine Structure and Function



Slide \# 118 Duodenum, Jejunum and Illeum (H\&E)


Illeum


Jejunum


Duodenum





Slide \# 123 Colon (H\&E)

mucosa

Inner circular

Outer longitudinal (taenia coli)



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