Functional Histology of the Gastrointestinal Tract

Robert A. Anders M.D., Ph.D.
September 16th, 2011
Gastrointestinal System

- Esophagus
- Stomach
- Small intestine
- Large intestine
- Pancreas
- Liver

Contact info:
- Robert A. Anders MD PhD
- CRB II 346
- Phone 955-3511
- rander54@jhmi.edu
- Don’t hesitate to contact me!
Goals

• Know the general *layers* of the GI tract

• Know the *function* of the organs of the GI tract
General Organization of the GI tract

Layers:
- Mucosa
- Submucosa
- Muscularis Externa
- Serosa

Structures:
- Surface Epithelium
- Basal Lamina
- Lamina Propria
- Muscularis Mucosa
- Meissner’s nerve plexus
- Muscularis: Inner Circular
- Auerbach’s myenteric nerve plexus
- Muscularis Outer Longitudinal

Layers:
- Fibroblasts
- Nerves
- Blood vessel
- Immune cells
- Connective tissue

Fat cells / Adipocytes
Esophagus

- **Function:** transit tube
- **Histology:** keratinized stratified squamous epithelium, submucosal mucus glands
- **Disease burden:**
  - Non-neoplastic – gastric reflux
  - Neoplastic – adenocarcinoma & squamous cell carcinoma
Gross Anatomy
Endoscopic view of GE junction
Fig. 13.1 Regional variations of the gastrointestinal tract. a Esophagus in cross-section shows a stellate-type lumen resulting from folding of the mucosa (M) typical of the relaxed state. The muscularis mucosae (MM) of smooth muscle is noted; surrounding the submucosa (SM) the muscularis externa of smooth muscle shows the inner circular (IC) and outer longitudinal (OL) layers. With the introduction of a food bolus, a peristaltic wave of contraction of the muscle is initiated, lasting 6–7 seconds. The upper and lower ends of the esophagus have sphincters (the lower one is not histologically distinct), which relax in association with the transport of a bolus along the esophagus. The stratified squamous epithelium (E) protects against wear and tear.
Histology
Histology
Gastric Reflux

Normal

Reflux
Carcinoma

Adenocarcinoma

Squamous cell carcinoma
Stomach

- **Function:** Endocrine controlled digestive bag of acid and enzymes

- **Histology:**
  - **Body**
    - Surface epithelium of columnar mucous cells
    - Deeper glands of parietal (oxyntic) and endocrine cells
  - **Antrum**
    - Surface cuboidal epithelium of mucous cells
    - Deeper loosely coiled glands of cuboidal epithelium of mucous and endocrine cells
Stomach cont.

• **Disease burden:**
  – Non-neoplastic – gastritis, gastric ulcer
  – Neoplastic – adenocarcinoma carcinoma
Fig. 13.7 Regional variations of the gastric mucosa. a Principal regions of the stomach. The histologically distinct regions are in **bold**. The lower esophageal sphincter (LES) is a physiological sphincter with no structural specialization, whereas the pyloric sphincter (PS) is a thickening of the circular muscle in the muscularis externa. The muscularis externa may show three layers: the inner oblique (distal half of stomach), the middle circular (whole stomach), and the outer longitudinal layer (upper two-thirds of stomach).
Histology
-glandular profile-

ANTRUM

BODY
CARDIA

ANTRUM

BODY
ANTRUM

G cell

Gastrin +

Histamine +

Endocrine cell

Enterochromaffin Like Cell (ECL Cell)

H+

Negative Feed back

BODY

= Parietal Cell

= Endocrine cell

Endocrine System

-negative feedback loop-
Fig. 13.7c Body (or corpus) mucosa. This occupies about 80% of the lining of the stomach and is identified by shallow gastric pits (P), which are lined by surface mucous cells. Long, straight tubular glands extend downward from these cells toward the muscularis mucosae (MM). These gastric glands contain mucous, stem, acid-secreting, enzyme-secreting, and endocrine cells. The volume of fluid secreted by the stomach mucosa is about 1.5–2 L per day, most of which is secreted by the gastric glands of the body of the stomach.
Histology

**Fig. 13.7d** Pyloric antral mucosa. The pyloric region extends proximally up to 5 cm from the pylorus or commencement of the duodenum. The gastric mucosa within this area is characterized by deep gastric pits (P), again lined by mucous cells that occupy more than half of the depth of the mucosa. Arising from the gastric pits, the pyloric glands (G) are coiled and branched and contain mostly mucous cells but some acid-secreting and endocrine cells, notably gastrin cells. Aggregations of lymphoid cells (L) are indicated in the lamina propria.
Histology

*Fig. 13.8 Surface mucous cells.*

a The entire surface of the gastric mucosa is lined by simple columnar epithelial cells that extend into the gastric pits (GP) but are infrequent in the gastric glands in the body of the stomach. Surface mucous cells resemble goblet cells of the intestine in that the apical cytoplasm is eosinophilic with H&E stains resulting from the high content of mucous granules. These give a lightly stained cytoplasm. The secreted mucus contains mucins, that is, glycoproteins that form a viscid gel layer which is resistant to pepsin (enzymatic) degradation. Mucus is produced via mechanical irritation and in response to stimulation of the vagus nerve. Mucin also coats luminal contents, assisting slippage through the stomach.
Fig. 13.9b Body of gastric mucosa shows gastric pits (GP) and gastric glands consisting of the isthmus (I), neck (N) and base (B). Parietal cells (P) are pink stained, and chief cells (C) are blue-purple stained with a foam-type cytoplasm. The supporting issue of the lamina propria contains a loose network of collagen and reticular fibers, wandering cells of the immune system, capillaries and strands of smooth muscle extending vertically from the deeper muscularis mucosae.
Histology
-glandular profile-

ANTRUM

BODY
Histology

Parietal Cell

Endocrine Cell
Stomach

• **Disease burden:**
  – Non-neoplastic - gastritis, gastric ulcer
  – Neoplastic - gastric adenocarcinoma
    • Diffuse infiltrating single cells, non mass forming
    • Discrete mass forming
Gastric ulcer
Gastric Ulcer Etiology

*Helicobacter pylori*
Gastric Adenocarcinoma
-mass forming-
Gastric Adenocarcinoma

-non mass forming-
Small Intestine

- **Function:** Absorption!

- **Histology:**
  - Villous forms covered with columnar cells with a brush boarder.
  - Submucosal Brunner’s gland in duodenum
  - Lymphoid follicles throughout, most prominent in ileum
  - Surface area amplification
    - Plica circularis – grossly evident folds
    - Villous – microscopic finger like projections
    - Microvilli – form the brush border

- **Disease burden:**
  - Malabsorption
  - Adenocarcinoma, rare
Gross Anatomy
Histology
-villi-
Histology

Fig. 13.16b Downward extensions of the surface epithelium of the villi, often branched, are termed intestinal glands or crypts of Lieberkühn. These open upward into the lumen between the bases of the villi. Each crypt is surrounded by the loose connective tissue of the lamina propria (LP), which is richly supplied with lymphoid cells, notably lymphocytes. Crypts terminate at the muscularis mucosae (MM). Some major functions of the crypts are (1) to provide new epithelial cells that migrate to the villi to replace cells lost there, (2) to secrete mucus via scattered goblet cells (G), and (3) to produce ions and isotonic alkaline fluid (approximately 2 L per day) that assist in keeping the epithelium wet and diluting chyme. This fluid is reabsorbed by the villi thus assisting their absorption of nutritive...
Histology
Fig. 13.17b Thin epon resin section of surface epithelium of two villi shows goblet cells (G) with mucous granules, some released onto the surface of the brush border (BB). The precise role of mucus in the small bowel is unknown, but, it may provide barrier protection for the epithelium against harmful agents (microorganisms or toxins), envelop exfoliated cells and clear them by distal transport, or stabilize immunoglobulins directed against bacteria or viruses. Tall columnar absorptive cells (A) display a clear zone or terminal web (TW) subjacent to the brush border, representing an anchoring site for the core of microvilli. Lymphocytes (L) are usually T-suppressor/cytotoxic cells serving as an immunological defense. Basal epithelial cells with granules represent enteroendocrine cells (EC). There are at least 16 types of ECs that secrete a variety of peptides or amines that perform local stimulatory or inhibitory functions regulating secretory or absorptive activities of the mucosa. Numerous ECs are classified as amine precursor uptake and decarboxylation (APUD) cells, which provide protein or biogenic amine hormones acting locally.

(Biopsy specimen courtesy of Dr P. Gibson, Department of Medicine, University of Melbourne, Australia)
Microvilli

Fig. 13.18 Surface of the villous epithelium. Brush border of microvilli (MV) lines the surface of the intestinal absorptive cells. Note the flocculent appearance of the terminal web (TW) containing filaments of actin. The lateral plasma membranes of adjacent cells interdigitate extensively (arrows) and contain ion pumps, which facilitate transport of fluids and absorbed nutrients into the intracellular space that opens up during periods of intestinal absorption. The contents flow into capillaries in the lamina propria and then into the portal system en route to the liver.
Surface Area Amplification

- plicae circulares
- villi
- microvilli
Malabsorption

Normal

Celiac disease
Fig. 13.19a Villous core. a The villous core is filled with loose connective tissue of the lamina propria containing many free cells of the immune system, particularly plasma cells and lymphocytes with a rich vascular and muscular framework. A central blind ending lacteal (L) is seen, and strips of smooth muscle (M) run the length of the villous core and provide motility for each villus. Numerous lymphocytes appear in the mucosal epithelium (arrows), having migrated across the basement membrane from the lamina propria.

Fig. 13.19b When viewed in transverse section the villous core displays a central lymphatic capillary (L) surrounded by cells of connective tissue and a variety of leukocytes. The blood vessels (arrows) are located just deep to the epithelium and represent either capillaries or postcapillary vessels that form from the branching of one or more arterioles supplying the villus. Goblet cells (G) and intraepithelial lymphocytes (circles) are indicated in the mucosal epithelium.
Colon

- **Function**: Extract water
- **Histology**:  
  - Goblet and absorptive columnar cells
- **Disease burden**:  
  - Diarrhea  
  - Colonic adenocarcinoma
FIG. 1. Diagram of the major regions of the colon.
Gross Anatomy
Histology

\[ \text{Fig. 13.22 Colon. a The principal components of the large intestine are the mucosa (M), submucosa (SM), and muscularis externa (ME). Folds in the mucosa are not permanent, being formed by local contractions of either of the above muscle layers. The mucosal epithelium should not be mistaken for villi, since the latter are comparatively large and arise independently with separation between neighbouring villi.} \]
Histology

Fig. 13.22b Colonic crypts or glands with numerous goblet cells have a pale supranuclear region filled with mucous granules. On the surface, columnar absorptive cells are seen, and these cells outnumber the goblet cells in the colon. The characteristic features of colonic crypts are their alignment similar to test tubes in a rack and the abundance of goblet cells together with the columnar enterocytes. In the base of the crypts, new cells arise by mitosis and mature and migrate upward through the crypts until ultimately exfoliated from the surface. Many immunocompetent cells, notably plasma cells, occupy the lamina propria (LP). T lymphocytes also occur there and within the mucosal epithelium.
Fig. 13.23b Transverse section through several colonic crypts shows the radial arrangement of goblet cells (G) and the tall intervening columnar absorptive cells. The central lumen of the gland or crypt is quite narrow and is partly filled with mucoid materials. Each gland or crypt is surrounded by the supporting lamina propria, and the fluids/electrolytes taken up by the surface epithelium of the glands are transported from the mucosa via numerous blood vessels (arrows) leading to the portal system. Colonic crypts also secrete an isotonic fluid rich in potassium and bicarbonate ions, acting as a buffering agent in the lumen.
Mechanisms of cholera toxin
Diarrhea Histology

Fig. 13.22b Colonic crypts or glands with numerous goblet cells have a pale supranuclear region filled with mucous granules. On the surface, columnar absorptive cells are seen, and these cells outnumber the goblet cells in the colon. The characteristic features of colonic crypts are their alignment similar to test tubes in a rack and the abundance of goblet cells together with the columnar enterocytes. In the base of the crypts, new cells arise by mitosis and mature and migrate upward through the crypts until ultimately exfoliated from the surface. Many immunocompetent cells, notably plasma cells, occupy the lamina propria (LP). T lymphocytes also occur there and within the mucosal epithelium.
Colonic Adenocarcinoma
General Organization of the GI tract

**Layers**

- **Mucosa**
  - Fibroblasts
  - Nerves
  - Blood vessel
  - Immune cells
  - Connective tissue

- **Submucosa**
  - Meissner’s nerve plexus

- **Muscularis Externa**
  - Auerbach’s myenteric nerve plexus
  - Muscularis: Inner Circular

- **Serosa**
  - Fat cells / Adipocytes

**Structures**

- Surface Epithelium
- Basal Lamina
- Lamina Propria
- Muscularis Mucosa
- Meissner’s nerve plexus
- Muscle: Inner Circular
- Auerbach's myenteric nerve plexus
- Muscularis Outer Longitudinal
Pancreas

• **Function:** production of digestive enzymes and hormones

• **Histology:**
  – Acinar cells secrete digestive proteins
  – Ductal cells transport secretions
  – Islets secrete insulin and other hormones

• **Disease burden**
  – Non-neoplastic – diabetes
  – Neoplastic – ductal adenocarcinoma
Gross Anatomy
Fig. 14.9b Acini, the enzyme-secreting units in the exocrine pancreas, are ovoid-elliptical clusters of acinar cells bordering a common luminal space. In hematoxylin and eosin sections, the basal cytoplasm (B) associated with the nuclei is deeply stained and shows a blue or purple color. This basophilia represents cisterns of rough endoplasmic reticulum. In the apical regions, pale-staining zymogen (Z) granules (containing packages of inactive enzymes) face the narrow lumen. The supporting tissue is thin, composed of delicate strands of extracellular matrix and collagen. Unique to the acinar complex are the centroacinar cells (C) which form the start of the pancreatic ducts, intercalated within the acini. Acini are not associated with myoepithelial cells commonly observed in other exocrine glands.
Fig. 14.11b The pathway taken in the synthesis of secretory proteins involves preprotein synthesis in the rough endoplasm reticulum (R), transport of the Golgi complex (G), processing, sorting, and routing into condensing vacuoles (CV), and concentration into mature zymogen granules (Z), which contain about 20 different zymogens and enzymes. Lysosomes (L) containing a mixture of about 75 acid hydrolases are also formed by the Golgi, but these are mostly sorted into endosomal compartments.
Islet
Diabetes
Pancreatic Cancer

NORMAL, PanIN-1A, PanIN-1B, PanIN-2, PanIN-3, INVASIVE CARCINOMA

Telomere shortening
Mutations of K-RAS

Inactivation of p16

Inactivation of p53
SMAD4
BRCA2

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Liver

• **Function**: Metabolic converter
  – Bile, glucose, lipids, proteins

• **Histology**: Hepatocytes, portal vascular system and bile drainage

• **Disease burden**
  – Non neoplastic – Cirrhosis
  – Neoplastic – Hepatocellular carcinoma
Portal System

All intestinal venous drainage
Liver Anatomy

- Hepatic vein
- Hepatic artery
- Gallbladder
- Common bile duct
- Portal vein
Gross Anatomy

Diagram of liver anatomy:
- Hepatic artery branch
- Portal vein branch
- Bile ductules
- Sinusoids
- Liver cell plates
- Normal lobular pattern of liver
- Central veins (tributary to hepatic vein via sublobular veins)
- Portal triad
- Proper hepatic artery
- Portal vein
- Common hepatic duct
- Sublobular vein
- Central vein
- Fibrous (Glisson's) capsule extending into porta hepatitis along vessels and bile duct

Image: Normal lobular pattern of liver
Hepatic lobule
Histology
Cirrhosis
Hepatocellular Carcinoma
Cost of GI Diseases

• What are the five most costly (direct and indirect) GI diseases?
Cost of GI Diseases

- GE reflux 10 billion
- Gallbladder 6
- Colon cancer 5
- Peptic ulcer 3
- Diverticular disease 2.6
Inflammatory vs Neoplastic

- Panc disease not IDDM (2.4) vs Panc Ca (1.5)
- Hepatitis (0.7+1.7) vs Liver Ca (1.5)
- Diarrhea (2.2+0.4+1.6+0.6+1.1) vs Colon Ca (6.4)
NIH Institutes

**National Cancer Institute (NCI)** - Established in 1937
NCI leads a national effort to eliminate the suffering and death due to cancer. Through basic and clinical research, we can prevent cancer before it starts, identify cancers that do develop at the earliest stage, and that we cannot eliminate so they become manageable, chronic diseases. [more >]

**National Eye Institute (NEI)** - Est. 1968
NEI conducts and supports research that helps prevent and treat eye diseases and other disorders of the visual system, improving the quality of life for people of all ages. NEI-supported research has advanced our knowledge of vision and how to protect it. [more >]

**National Heart, Lung, and Blood Institute (NHLBI)** - Est. 1948
NHLBI provides leadership for a national program in diseases of the heart, blood vessels, lung, and blood, and has responsibility for the NIH Woman's Health Initiative. The Institute plans, conducts, fosters, and supports observational studies, demonstration, and education projects. [more >]

**National Human Genome Research Institute (NHGRI)** - Est. 1989
NHGRI supports the NIH component of the Human Genome Project, a worldwide research effort designed to identify all 40,000 human genes. The NHGRI Intramural Research Program develops and implements technology for basic research in the NHGRI mission areas. [more >]

**National Institute on Aging (NIA)** - Est. 1974
NIA leads a national program of research on the biomedical, social, and behavioral aspects of the aging process, the quality of life for all older Americans. [more >]

**National Institute on Alcohol Abuse and Alcoholism (NIAAA)** - Est. 1970
NIAAA conducts research focused on improving the treatment and prevention of alcoholism and alcohol disease. [more >]

**National Institute of Allergy and Infectious Diseases (NIAID)** - Est. 1948
NIAID research strives to understand, treat, and ultimately prevent the myriad infectious, immunologic, and allergic diseases. [more >]

**National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)** - Est. 1996
NIAMS supports research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases; and dissemination of information on research progress in these diseases. [more >]

**National Institute of Biomedical Imaging and Bioengineering (NIBIB)** - Est. 2000
NIBIB improves health by promoting fundamental discoveries, design and development, and translation in relevant areas of information science, physics, chemistry, mathematics, materials science, and computing. [more >]

**National Institute of Child Health and Human Development (NICHD)** - Est. 1962
NICHD research on fertility, pregnancy, growth, development, and medical rehabilitation strives to ensure healthy outcomes for all children. [more >]

**National Institute on Deafness and Other Communication Disorders (NIDCD)** - Est. 1988
NIDCD conducts and supports biomedical research and research training on normal mechanisms as well as disorders of hearing, balance, speech, language, and related functions in 45 million Americans. [more >]

**National Institute of Dental and Craniofacial Research (NIDCR)** - Est. 1948
...
National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) - Est. 1
NIDDK conducts and supports basic and applied research and provides leadership for a nation-wide effort to advance the health of the public and combat kidney, urologic, and hematologic diseases. Several of these diseases are among the leading causes of death and disability.

National Institute on Drug Abuse (NIDA) - Est. 1973
NIDA leads the nation in bringing the power of science to bear on drug abuse and addiction issues and disseminates results of that research to improve drug abuse and addiction prevention, treatment, and prevention. NIDA also supports research training programs that produce a diversity of scientists to pursue biomedical research careers.

National Institute of Environmental Health Sciences (NIEHS) - Est. 1969
NIEHS reduces the burden of human illness and dysfunction from environmental causes by advancing the environmental sciences and promoting interdisciplinary approaches to scientific research, community service, and public health education.

National Institute of General Medical Sciences (NIGMS) - Est. 1962
NIGMS supports basic biomedical research that is not targeted to specific diseases. NIGMS investigates the workings of cells, how our bodies use energy, and how we respond to medicines. The results are used to develop new treatments, and prevention. NIGMS also supports research training programs that produce a diversity of scientists to pursue biomedical research careers.

National Institute of Mental Health (NIMH) - Est. 1949
NIMH provides national leadership dedicated to understanding, treating, and preventing mental illnesses.

National Institute of Neurological Disorders and Stroke (NINDS) - Est. 1950
The mission of the NINDS is to reduce the burden of neurological diseases -- a burden born of disease and disability; the promotion of healthy lifestyles; the promotion of quality care; and families within a community context, and it also focuses on the special needs of at-risk and underserved populations.

National Institute of Nursing Research (NINR) - Est. 1986
NINR supports clinical and basic research to establish a scientific basis for the care of individuals with neurological disorders and disabilities. The promotion of quality care and families within a community context, and it also focuses on the special needs of at-risk and underserved populations.

National Library of Medicine (NLM) - Est. 1956
NLM collects, organizes, and makes available biomedical science information to scientists, health professionals, and the public. NLM conducts and supports research in environmental health; and provides grant and contract support for training, medical library...