MECHANISMS OF HUMAN DISEASE: LABORATORY SESSIONS
GASTROINTESTINAL (GI) PATHOLOGY LAB #1

January 06, 2012

Faculty Copy

GOAL:

1. **Describe the basis morphologic and pathophysiologic changes which occur in various conditions of the gastrointestinal tract.**

2. **Define (Describe) and correlate symptoms and signs of diseases with structural changes of diseased organs.**

OBJECTIVE:

1. **Review the normal gross and histologic anatomy of the gastrointestinal tract.**

2. **Describe the morphologic changes which characterize esophagitis and Barrett esophagus.**

3. **Describe the morphologic changes which characterize esophageal carcinoma.**

4. **Describe the morphologic changes which characterize peptic ulcer disease.**

CASE 1
CHIEF COMPLAINT:
"I feel like my stomach is burning after I drink coffee or eat."

HISTORY:
A 54 year-old male presents with burning epigastric pain radiating to the chest. The pain is worse post-prandially or in a supine position. He says he frequently has a "sour" taste in his mouth and feels better after taking an antacid.

PHYSICAL EXAMINATION:
BP 130/90, HR 90/min, RR 18/min, T 98°F
The patient is an obese male, alert and in no apparent distress, who uses an open hand to indicate the area of burning pain in his upper abdomen. The abdomen is soft and non-tender with no palpable masses or organomegaly. Rectal exam is done – stool is brown and occult blood negative.

1. What is the major clinical problem?

   Epigastric pain radiating to the chest

2. Develop a differential diagnosis for this problem.

Gastroesophageal reflux disease (GERD), biliary colic ("dyspepsia" due to gall stones), esophageal/gastric ulcer
Rarely chronic symptoms are punctuated by attacks of severe chest pain that can be mistaken for "heart attack"

3. Which diagnosis do you favor?

GERD

4. What are the potential complications of this problem?

- **Esophageal stricture**
- **Ulcer (esophageal)**
- **Development of Barrett Esophagus**
- **Hoarseness, pulmonary aspiration if reflux is severe enough**

5. Describe/identify organ in slides.
   - **Esophagus**

   - **Slide shows a section of esophagus with a predominantly mononuclear cell infiltrate of the submucosa. Sheets of lymphocytes and plasma cells infiltrate the muscularis propria. The squamous epithelium is thickened and demonstrates inflammatory changes: necrosis of surface cells, reactive changes of the squamous cells, and infiltration of the squamous epithelium by inflammatory cells, including neutrophils. There is increased vascularity and a prominent band of inflammatory cells in the lamina propria, adjacent to the basal epithelial layer.**

   - **HISTOLOGIC HALLMARKS OF CHRONIC ESOPHAGITIS**
     - **Inflammatory cells, including eosinophils, neutrophils and excessive numbers of lymphocytes in the epithelial layer.**
     - **Basal zone hyperplasia exceeding 20% of the epithelial thickness**
     - **Elongation of lamina propria papillae with congestion, extending into the top third of the epithelial layer.**

   - **Slide A shows a section of esophagus with islands of glandular epithelium interspersed between areas of non-keratinizing stratified squamous epithelium. The lamina propria and submucosa contains an infiltrate of mononuclear inflammatory cells.**

     - **"Metaplasia" of squamous mucosa to glandular mucosa. Occurs in up to 11% of symptomatic patients.**

6 What is your diagnosis?

- **Reflux → chronic esophagitis → Barrett esophagus**

- **Barrett esophagus → columnar epithelium replaces normal squamous epithelium of distal**

esophagus; "metaplasia"

7 What complication(s) can occur with the diagnosis in slide A?

- **Low, high grade dysplasia (clinical intervention required in high grade dysplasia)**
- **Adenocarcinoma (30-40 fold increased rate over general population, usually in patients with > 2 cm of Barrett's mucosa)**

CASE 2

CHIEF COMPLAINT:
"Food sticks in my throat when I swallow."

HISTORY:
72 year-old male has dysphagia which gradually progressed from solids to soft foods then to liquids. He has fatigue and a 20 lb weight loss over 6 months.
He has a 30 pack year smoking history and a history of heavy alcohol use. He has been abstinent for the past 10 years.

PHYSICAL EXAMINATION:
BP 140/80, HR 85/min, RR 19/min, T 98°F
Alert, extremely thin male in no apparent distress who has enlarged (palpable), firm, fixed cervical lymph nodes.
The remainder of the physical examination is unremarkable.

LAB TESTS: Hgb 11gm/dl, Hct 33%, MCV 82
Stool hemoccult is positive

1. What are the major clinical problems?

   Dysphagia (weight loss, lymphadenopathy, occult blood positive stool)

2. Formulate a differential diagnosis for the problems?

   Esophageal stricture/diverticula/tracheoesophageal fistula, carcinoma, esophageal motility problems, reflux dysphagia can occur after hiatal hernia repair, achalasia

3. Identify/describe organ in the virtual microscopy section.

   - **Esophagus**
   - **Sections show a well-differentiated squamous cell carcinoma. In this section the neoplasm replaces the normal epithelium and infiltrates the muscularis propria. Keratin pearls and inflammatory cells are present. The surface of the neoplasm is necrotic.**

4. What is your diagnosis?

Squamous cell carcinoma; three morphologic patterns according to Robbins – protruded/polypoid 60%, diffuse infiltrative/thickened wall 15%, and excavated/necrotic ulcer 25%.

5. Correlate the clinical findings with the pathology.

- **Bulky neoplasms obstruct lumen of esophagus causing solid food to pass with difficulty.**
- **Cervical lymphadenopathy due to metastasis of tumor to lymph nodes**
- **Weight loss from impaired nutrition and effects of tumor itself (cancer cachexia)**

6. What are risk factors, including genetic, for development of this lesion?

- **Lifestyle**
  - **Tobacco, alcohol**
    - **In the United States and western Europe, cigarette smoking and alcohol consumption are major risk factors for esophageal squamous cell cancer**
- **Dietary factors**
  - **High nitrosamines/nitrites, betal nut chewing, ingestion of very hot foods and beverages (such as tea), Vitamin A deficiency**
- **Esophageal disorders**
  - **Esophagitis, achalasia, Plummer-Vinson syndrome**
- **Genetic predisposition**
  - **Long-standing celiac disease, racial predisposition**
  - **Tylosis – a rare disease associated with hyperkeratosis of the palms of the hands and soles of the feet and a high rate of esophageal squamous cancers**

CASE 3

CHIEF COMPLAINT:
"My stomach hurts unless I eat something."

HISTORY:
37 year-old male truck driver presents with epigastric pain, which is relieved by eating. His social history is significant for a 20-pack year smoking habit. He notes that he is extremely tired lately and that he has noticed intermittent passage of black tarry stool.

PHYSICAL EXAMINATION:
BP 145/90, HR 80/min, RR 18/min, T 98°F
Alert and oriented male in no apparent distress. The abdomen is soft with mild epigastric tenderness. No palpable masses or organomegaly are noted. Rectal exam shows black stool which is hemoccult positive

LAB TESTS: Hgb 10g/dl Hct 35% MCV 78

1. What is the main clinical problem?

   Epigastric pain, (abdominal tenderness, fatigue, melena, anemia)

2. What is the differential diagnosis of the clinical problem?

   GERD, dyspepsia, gastric or duodenal ulcer, Zollinger – Ellison syndrome, biliary colic

3. Identify the organ in the slide and describe pathologic changes.

   Duodenum (Brunner's glands)

   Sections show a chronic peptic ulcer extending through the muscularis propria. The floor of the ulcer is composed of granulation tissue on an area of fibrosis. The edges of the ulcer are sharp. Suture is present.

4. What is your diagnosis?

   Chronic peptic ulcer disease of duodenum; peptic ulcers are chronic lesions occurring anywhere in the GI tract exposed to the aggressive action of acid-peptic juices.

5. What are associated risk factors?

   ***H.pylori* is present in virtually all patients with duodenal ulcer and 70% of those with gastric ulcer; chronic NSAID use, cigarette smoking, alcoholic cirrhosis associated with peptic ulcer, high dose corticosteroids**

6. List and describe methods to diagnose infection with H. pylori.

- **Histology**
  - **H&E, Giemsa stains**
- **Biopsy Urease Testing**
  - **CLO (Campylobacter-like Organism) test**
    - **Biopsied gastric tissue placed in agar well containing urea and a pH reagent**
    - **Urease cleaves urea to liberate ammonia, producing an alkaline pH and resultant color change**
- **Urea breath test**
  - **Based upon hydrolysis of urea by *H. pylori* to produce CO2 and ammonia**
    - **Labeled carbon isotope is given by mouth**
    - **H. pylori liberates tagged CO2, which can be detected in breath samples**
- **Stool antigen detection**

7. What are potential complications related to the disease process?

- **GI Bleeding**
- **Gastric outlet obstruction**
- **Perforation with penetration into pancreas/peritonitis**
- **Intractability to medical therapy/intractable pain**