1. Gastrointestinal Tract Part 1

Gastrointestinal Tract
Part 1

Basic Human Pathology II, 2008

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2. Gastrointestinal Tract, Part 1

Gastrointestinal Tract, Part 1

- Stomach diseases
  - Gastritis
    - Acute
    - Chronic
      - Non-erosive
        - Type A
        - Type B
      - Reflux gastritis
  - Peptic ulcer disease
  - Carcinoma

- Diseases of the Small and Large Intestine
  - Infections
    - Bacterial
    - C. difficile
      (Pseudomembranous colitis)
    - Protozan
  - Malabsorption syndromes
    - Celiac Disease
    - Crohn's disease
    - Ulcerative Colitis (GI part 2)
3. Overview

Overview

• Anatomic Components
  • Extend from lips to anus
  • Single disease can vary from site to site
  • Sites
    ➢ Ear, Nose, Throat, Larynx
    ➢ Esophagus
    ➢ Stomach
    ➢ Small intestine
    ➢ Large intestine
    ➢ Rectum

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4. Stomach Anatomy

Stomach Anatomy

• Anatomy
  ➢ Cardia
    ▪ Adjacent to esophageal junction; mucous glands
  ➢ Body/fundus
    ▪ Long tubular
    ▪ Secretes hydrochloric acid (parietal cells) and intrinsic factor
  ➢ Pyloric antrum
    ▪ Gastrin secreting cells; mucous glands

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5. Stomach Anatomy

Stomach Anatomy

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6. Stomach – Normal

Stomach – Normal

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7. Acute Gastritis

Acute Gastritis

- Acute type
  - Ingestion of chemicals
  - Superficial acute inflammation
- Necrotizing, ulcerative type
  - Severe, suicidal ingestion of strong alkalis and acids
- Acute, erosive type
  - Etiology - shock, stress from severe burn (Curling ulcer) or brain injury (Cushing ulcer), NSAIDs, cigarette smoking, heavy alcohol intake
  - Focal damage to the superficial gastric epithelium, acute inflammation, necrosis, hemorrhage
  - Dyspepsia; vomit with blood sometimes
  - Sometimes acute gastric ulcer, often multiple

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8. Gastrointestinal Tract I: Slide 8

Acute Erosive Gastritis

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Chronic Gastritis

Chronic Gastritis

- Chronic (nons erosive) type
  - Chronic mucosal inflammation and atrophy of mucosal glands, fairly common
  - Three patterns:
    - Autoimmune - Type A gastritis
    - H. pylori pattern - Type B gastritis
    - Reflux pattern - reactive gastritis

Chronic Gastritis

- Chronic (nons erosive) type (cont’d)
  - Type A chronic gastritis - Autoimmune pattern (particularly affects body of stomach)
    - Elderly
      - Antibodies to gastric parietal cells and intrinsic factor → achlorhydria and pernicious anemia (megaloblastic, macrocytic anemia)
    - Severe atrophy due to ↓ HCL and Vit. B₁₂ absorption
    - Associated with autoimmune diseases, aging, partial gastrectomy, gastric ulcer, and gastric carcinoma
11. Chronic Gastritis

Chronic Gastritis

➢ Chronic (nonerosive) type (cont’d)
  ➢ Type B chronic gastritis - H. pylori pattern
    • Most common gastritis, onset at any age
    • Pyloric antrum most affected
    • H. pylori colonies on the surface epithelium beneath the
      thin mucus layer
      – Damage the epithelium with mixed inflammation
    • Associated with gastric and duodenal peptic ulcer; strong
      suspect to cause gastric carcinoma and lymphoma
      • Not associated with pernicious anemia, antibodies, or
        achlorhydria

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12. Type B Chronic Gastritis

Type B Chronic Gastritis

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13. Chronic Gastritis

**Chronic Gastritis**

- **Reflux gastritis - (reactive gastritis) pattern**
  - Alkaline duodenal fluid (bile) refluxes into lower part of stomach
  - **Etiology**
    - NSAIDs direct toxic damage to the mucus layer
    - Previous pyloric gastric surgery patients
    - Pyloric sphincter incompetence OR
    - Pyloric sphincter incompetence with no history of surgery

14. Complications of Chronic Gastritis

**Complications of Chronic Gastritis**

1. **Intestinal metaplasia**
   - Normal gastric epithelium replaced by:
     - Goblet cell pattern (similar to small intestine)
     - Mucous cell pattern (similar to pyloric antrum)
   - Premalignant change \(\longrightarrow\) squamous cell carcinoma or adenocarcinoma
   - Management
     - Repeated endoscopic biopsies

2. **Peptic ulceration**
   - NOT a precursor of stomach carcinoma
   - Most often at the lesser curvature
15. Peptic Ulcer Disease

Peptic Ulcer Disease

- **Etiology**
  - Damage by gastric secretions, especially HCL and pepsin \(\rightarrow\) mucosal breakdown
  - Precipitators (aggravators)
    - Rupturated bile
    - H. pylori infection
      - Ureases and proteases destroy glycoproteins in the mucus layer \(\rightarrow\) interfere with epithelial protection
    - NSAIDs and aspirin
    - Cigarettes and alcohol
    - Chronic gastritis
    - Genetics

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16. Peptic Ulcer Disease

Peptic Ulcer Disease

- **Acute type**
  - Less frequent than chronic type
  - Esophagus, stomach, proximal duodenum
  - Develops from areas of erosive gastritis
  - Etiology
    - Stress or shock (burns, major trauma) with hypotension
  - Pathogenesis
    - Acute hypoxia of surface epithelium
  - Three outcomes:
    - Causes severe bleeding or
    - Heal with no scarring or
    - Chronic peptic ulcer

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17. Peptic Ulcer Disease

Peptic Ulcer Disease

➤ Chronic – more common form

❖ Lower esophagus

❖ Due to gastric reflux

❖ Stomach, and duodenum

❖ Most common; due to HCl

❖ Gross morphology

❖ Usually 1-7 cm, sharply defined (punched out) with nonelevated margins and a smooth base

❖ Histology

❖ Floor of fibrous scar with overlay of granulation tissue, inflammation and necrotic slough

❖ Depth into muscularis propria

– Complete healing results in replacement of muscle with fibrous tissue and surface scar

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18. Peptic Ulcer Disease

Peptic Ulcer Disease

• Chronic

– Complications

❖ Hemorrhage

❖ Penetration of stomach or duodenum into pancreas or liver

❖ Perforation - - - -> peritonitis

❖ Fibrous stricture of esophagus - - - -> scarring, obstruction

❖ Pyloric stenosis in stomach

❖ Malignant change – very rare

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19. Peptic Ulcer Disease

Peptic Ulcer Disease

NORMAL

Aggressive Forces:
- Gastric acidity
- Peptic activity

Defensive Forces:
- Surface mucus secretion
- Bicarbonate secretion into mucus
- Mucosal blood flow
- Apical surface membrane transport
- Epithelial regenerative capacity
- Elaboration of prostaglandins

INCREASED AGGRESSION

Aggravating Causes:
- Helicobacter infection
- NSAIDs, aspirin
- Cigarettes, alcohol
- Impaired regulation of acid-pepsin secretion

IMPAIRED DEFENSE

Impaired Defense:
- Ischemia, shock
- Delayed gastric emptying
- Duodenal-gastric reflux

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20. Gastric Ulcers

Gastric Ulcers

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21. Stomach Ulcers

Stomach Ulcers

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22. Chronic Peptic Ulcer of the Pylorus

Chronic Peptic Ulcer of the Pylorus

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23. Chronic Peptic Ulcer of the Duodenum

24. The Base of a Non-perforated Chronic Peptic Ulcer

Necrosis (N)
Inflammation (I)
Granulation tissue (G)
Scar (S)
(Top - luminal surface,
Bottom - muscular wall)
25. Carcinoma of the Stomach

Carcinoma of the Stomach

- Most important tumor of the stomach
  - Histology almost always adenocarcinoma
- Etiologic factors
  - Chronic atrophic gastritis w/ or w/o pernicious anemia
  - H. pylori is highly suspect
  - Nitrosamines (smoked fish, meat, pickled vegetables)
  - Excessive salt intake and low intake of fresh vegetables and fruit
  - Gastric adenomatous polyps
  - Not peptic ulcer!

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26. Carcinoma of the Stomach

Carcinoma of the Stomach

- More in men; > 30 years old, especially > 50 years old
- More common in Far East, Scandinavia, South America
  - Decreasing incidence in U.S.
- More common in blood group A
- Most common site is distal stomach along the lesser curvature of the antrum or prepyloric region; rare in fundus

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27. Carcinoma of the Stomach

Carcinoma of the Stomach

- **At-risk groups**
  - Chronic gastritis and intestinal metaplasia
  - Post-gastrectomy with persistent inflammation
  - Gastric cancer families

- **Pathogenesis of fundus and antrum**
  - Normal $\longrightarrow$ chronic gastritis $\longrightarrow$ intestinal metaplasia $\longrightarrow$ dysplasia and intramucosal carcinoma $\longrightarrow$ invasive carcinoma

- **Pathogenesis of cardiac region**
  - Unknown or (rarely) chronic gastritis

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28. Carcinoma of the Stomach – Three Growth Patterns

Carcinoma of the Stomach – Three Growth Patterns

1. **Polypoid (intestinal type)**
   - High degree of assoc. with H. pylori infection
   - Gastric discomfort
   - Protrudes into lumen and traumatized
   - Best prognosis since confined to mucosa and submucosa

2. **Ulcerative**
   - Transforms from polypoid type
   - Most common
   - Firm, raised margins with irregular necrotic base; shaggy, unlike peptic ulcer

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29. Carcinoma of the Stomach – Growth Patterns

Carcinoma of the Stomach – Growth Patterns

3. Diffuse, infiltrative
   - Not associated with \textit{H. pylori} infection
   - Creates ‘\textit{litium plastica}’ or leather bottle stomach (shrinkage)
     - Thickened rigid stomach wall due to diffuse infiltration of tumor cells with fibrosis
   - Observed very late since symptoms are nonspecific loss of appetite and food intolerance (stomach distension hindered)
     - Surface ulceration not a prominent feature so hematemesis delayed
     - Metastasis to liver and lymph nodes when clinically discovered -> worst prognosis

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30. Carcinoma of the Stomach – Three Growth Patterns

Carcinoma of the Stomach – Three Growth Patterns

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31. Adenocarcinoma of the Stomach

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32. Adenocarcinoma of the Stomach

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33. Adenocarcinoma of the Stomach

Adenocarcinoma of the Stomach

- **Histology**
  - Intestinal Pattern
    - Gland formation by malignant cells invading the muscular wall of the stomach
  - Diffuse Infiltrative Pattern
    - Sheets of anaplastic cells, many with a single vacuole of mucin displacing the nucleus to one side (signet-ring cell)

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34. Carcinoma of the Stomach

Carcinoma of the Stomach

- **Four main routes of metastastic spread**
  1. Direct invasion
     - Through wall to adjacent viscera
  2. Lymphatic spread
     - Main route: nodes of greater or lesser curvature of stomach
     - Virchow’s node (Treisier’s sign) – supraclavicular node
  3. Hematogenous spread
     - Liver, lungs, brain
     - Krukenberg tumor – bilateral to ovaries
  4. Transeuclear spread
     - Through peritoneum resulting in malignant ascites

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35. Carcinoma of the Stomach

**Carcinoma of the Stomach**

- **Prognosis**
  - Poor in most cases
  - 5-year survival rate
    - Low
    - Depends on staging
  - 10-year survival
    - 90%, if confined to mucosa and submucosa
      (ex. a small polypoid type)
  - 10-yr. survival
    - 20%, if advanced at diagnosis

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36. Digestive Tract Anatomic Review and Nomenclature

**Digestive Tract Anatomic Review and Nomenclature**

Source: [http://digestive.niddk.nih.gov](http://digestive.niddk.nih.gov)

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Diseases of the Small and Large Intestine

- Infective disorders – common
  - Viruses
    - Rotavirus, Norwalk
  - Bacteria
    - Campylobacter jejuni (direct damage, colon)
    - Salmonella typhi (direct damage)
    - Enterotoxin producers (salmonellosis, E. coli)
    - Mycobacteria spp. (terminal ileum)
    - Yersinia (ileitis)
  - Protozoa
    - Giardia (small intestine, malabsorption)
    - Cryptosporidia and microsporidia spp.
  - Fungi
    - Only in immunosuppressed
      - premed: ex. – Candida albicans
  - Helminths
    - Widespread, especially in tropics

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Diseases of the Small and Large Intestine

- Bacterial infections WITH invasion
  - Bacterial dysentery – diarrhea, blood and pus in the stools
    - Campylobacter
      - Jejunum and ileum and colon, ulceration and acute inflammation
    - Salmonella typhi and S. paratyphi
      - Contaminated food and water by feces, urine of carrier
      - Reticuloendothelial system --> ulcerated Peyer’s patches, fever, diarrhea, splenomegaly, skin rash with rose spots
    - Shigella
      - Especially sigmoid and rectum and distal ileum
      - --> mucosal ulceration

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39. Diseases of the Small and Large Intestine

Diseases of the Small and Large Intestine

- **Bacterial infections WITHOUT invasion**
  - Two types of enterotoxins cause disease:
    1. Formed in food before eaten (vomiting and diarrhea 12 hours later)
      - Example: Staphylococcal food poisoning
    2. Formed after ingestion (24 hr. delay in symptoms)
      - *Salmonella spp.*
        - 24 - 48 hr. incubation
        - *Enterocolitis* – profuse diarrhea and vomiting for 48 hours
      - *Vibrio cholerae*
        - Water contamination with feces
        - Grow in small intestine and colon
        - Toxin -> severe watery diarrhea

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40. Diseases of the Small and Large Intestine

Diseases of the Small and Large Intestine

- **Pseudomembranous colitis**
  - *Clostridium difficile* overgrowth
  - Enterotoxin -> superficial, gray mucosal exudate, fibrinous necrosis and loosely adherent mucosal debris (pseudomembrane) -> fever, toxicity, abdominal pain and diarrhea
  - Main predisposer: associated with broad-spectrum antibiotic therapy
  - Other predisposers
    - Gastrointestinal surgery
    - Ischemia
    - Burn

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41. Pseudomembranous Colitis

Pseudomembranous Colitis

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42. Diseases of the Small and Large Intestine

Diseases of the Small and Large Intestine

- Protozoan infections
  - Giardia lamblia
    - Flagellate
    - Contaminated water
    - Duodenum and upper jejunum
    - Diarrhea, abdominal pain, weight loss, malabsorption
  - Cryptosporidium parvum
    - Contaminated water
    - Self-limiting diarrhea
  - Entamoeba histolytica
    - Acquired from cysts in contaminated water or food
    - Amebic colitis – may be life-threatening; colon
Malabsorption Syndromes - Overview

- Four main elements of normal small intestine absorption
  1. Pancreas secretes digestive enzymes into the gut lumen \[\rightarrow\] macromolecules
  2. Liver secretes bile acids \[\rightarrow\] fats
  3. Transverse mucosal folds and villi provide vast absorptive surface area
  4. Brush border enzymes of mucosa \[\rightarrow\] complex sugars
- Malabsorption exists if one of the above is missing

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Malabsorption Syndromes

- Weight loss and abdominal distension
- Loose bulky stools
  - Pale, foul-smelling, float in water (fat not being absorbed, remains in stool)
- Most common cause in western hemisphere is due to celiac disease
- Most common cause in developing world is parasitic and worm infestation

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Malabsorption Syndromes

- Pancreatic enzymes missing in several conditions
  - Cystic fibrosis
  - Chronic pancreatitis
  - Carcinoma
  - Surgery

- Bile secretion impaired
  - Solubilization of fats and fat soluble vitamins does not occur

- Loss of absorptive surface is common
  - Due to infarction and Crohn’s disease

- Brush border function is compromised
  - Lack of disaccharidase enzyme
  - Whipple’s disease

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Malabsorption Syndromes

- Etiology – Comparative Incidence
  - Common conditions
    - Pancreatic insufficiency
    - Celiac disease
    - Resection of ileum
    - Parasitic infection of the gut
  - Frequent (less than common) conditions
    - Resection of stomach
    - Crohn’s disease
    - Liver disease causing failure of bile secretion
  - Rare conditions
    - Whipple’s
    - Abetalipoproteinemia
    - Giardiasis
    - A-chain disease, tropical sprue, disaccharidase deficiency

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Celiac Disease

- Atrophy of small intestinal villi due to an abnormal sensitivity to gluten in cereal products
  - Protein in wheat flour (gluten enteropathy)
- Occurs at any age
- Etiology – genetic and immune-mediated
  - Immune response to gliadin, a glycoprotein component of gluten; serum antibodies also observed
  - Familial linkage with certain HLA groups (e.g., HLA-B8)

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Celiac Disease

- Symptoms
  - Weight loss, weakness, diarrhea
  - Pale, bulky, frothy, foul-smelling stools
  - Growth retardation, failure to thrive
- Diagnosis
  - Biopsy of small intestine mucosa
  - Loss of villous architecture and crypts
    - -> flattened, mosaic pattern
- Complications – malignancy
  - Most often primary T-cell lymphoma of small intestine

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Celiac Disease

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51. Chronic Inflammatory Bowel Disease

Chronic Inflammatory Bowel Disease

❖ Crohn’s disease

- Chronic, non-caseating granulomatous inflammation of unknown etiology
- More common in women; most common in the second and third decades of life
- Most common in terminal ileum, but any part of digestive tract (including oral cavity, colon, and anus)
- Affects all layers of the intestinal wall
- Discontinuous pattern – ‘skip’ lesions
- Abdominal pain, diarrhea, malabsorption, fever, intestinal obstruction
- Remission and relapses with complications

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52. Crohn’s Disease

Crohn’s Disease

❖ Gross appearance

- Early
  • Marked swelling (edema)
  • Loss of transverse folds and creation of ulcers → fissures
- Established
  ❖ Cobblestone pattern (submucosal edema) [M] and fissured ulcers [U]
  ❖ Stricture formation
  ❖ Regional nodes enlarged
  ❖ “Skip” lesions since areas of normal bowel

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53. Crohn’s Disease

Crohn’s Disease

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54. Crohn’s Disease

Crohn’s Disease

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Crohn's Disease

Crohn’s Disease

- Histology
  - Transmural inflammation with submucosal edema
  - Ulcers that extend deep into the bowel and form fissures
  - Fibrous scarring
  - Non-caseating granulomas (G)

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Complications

- Serosal involvement --> adhesions to other loops of bowel, bladder, abdominal wall
- Deep fissure ulcers --> fistulae and sinuses
- Stricture formation
- Fibrous adhesions
- Perforation of the bowel
- Perianal fistulae, fissures and abscesses
- Increased incidence of bowel cancer
- Sometimes significant bleeding from ulcers
- Systemic complications (similar to ulcerative colitis)
  - Skin, eye, joints, and liver

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