Peptic Ulcer Disease (PUD)

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Discussion outline

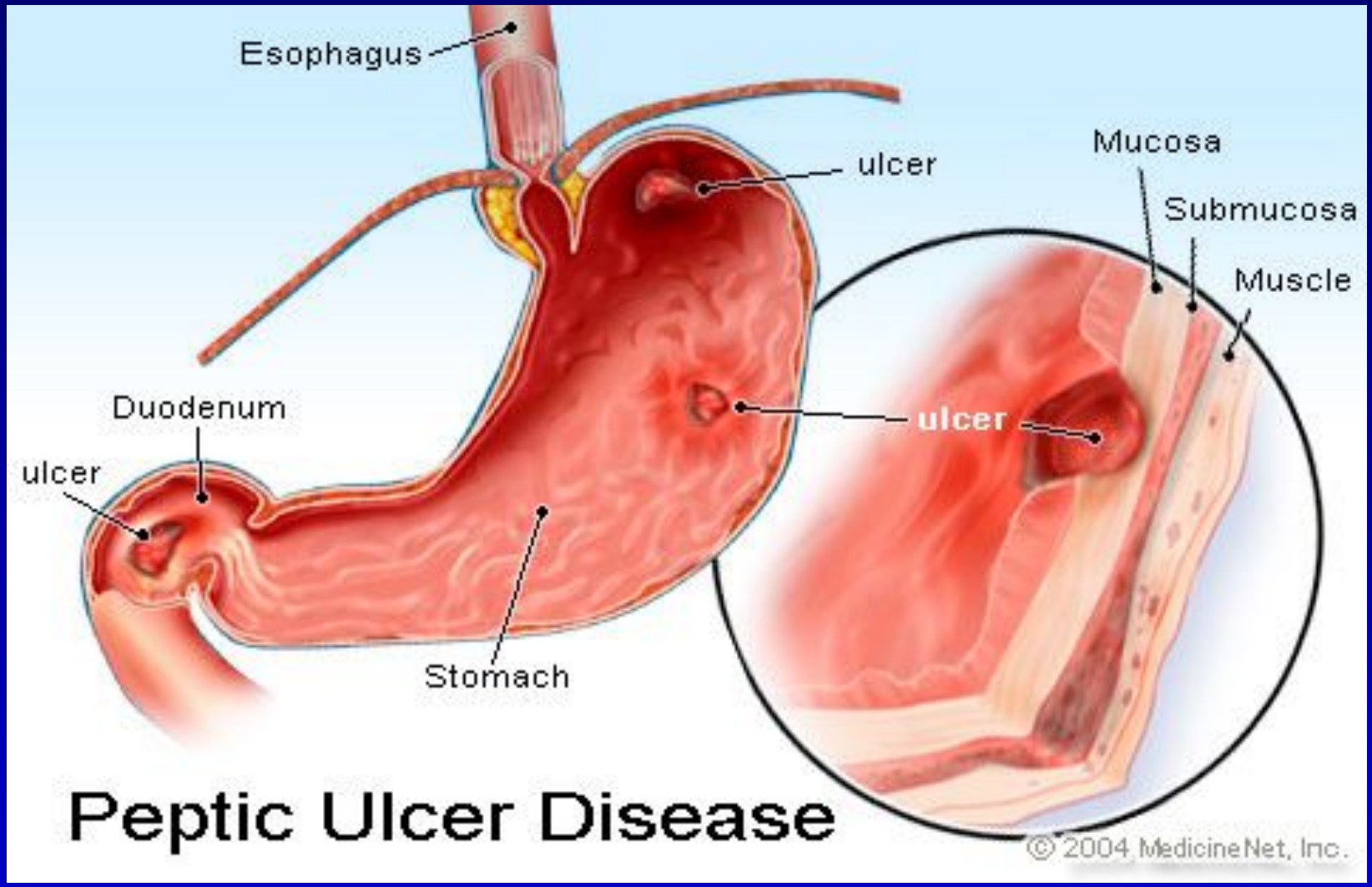
- Definitions
- Risk factors
- Complications
- Clinical presentation
- Management – HBP, NSAIDS
- Refractory PUD
- Prophylaxis

DEFINITION

- An **ulcer** in the gastrointestinal (GI) tract may be defined as a break in the lining of the mucosa, with appreciable depth at endoscopy or histologic evidence of involvement of the submucosa.

- **Erosions** are breaks in the surface epithelium that do not have perceptible depth.

- The term *peptic ulcer disease is used broadly to include ulcerations and erosions* in the stomach and duodenum from a number of causes.


Esophagus
ulcer
Mucosa
Submucosa
Muscle
Duodenum
ulcer
ulcer
Stomach
Peptic Ulcer Disease
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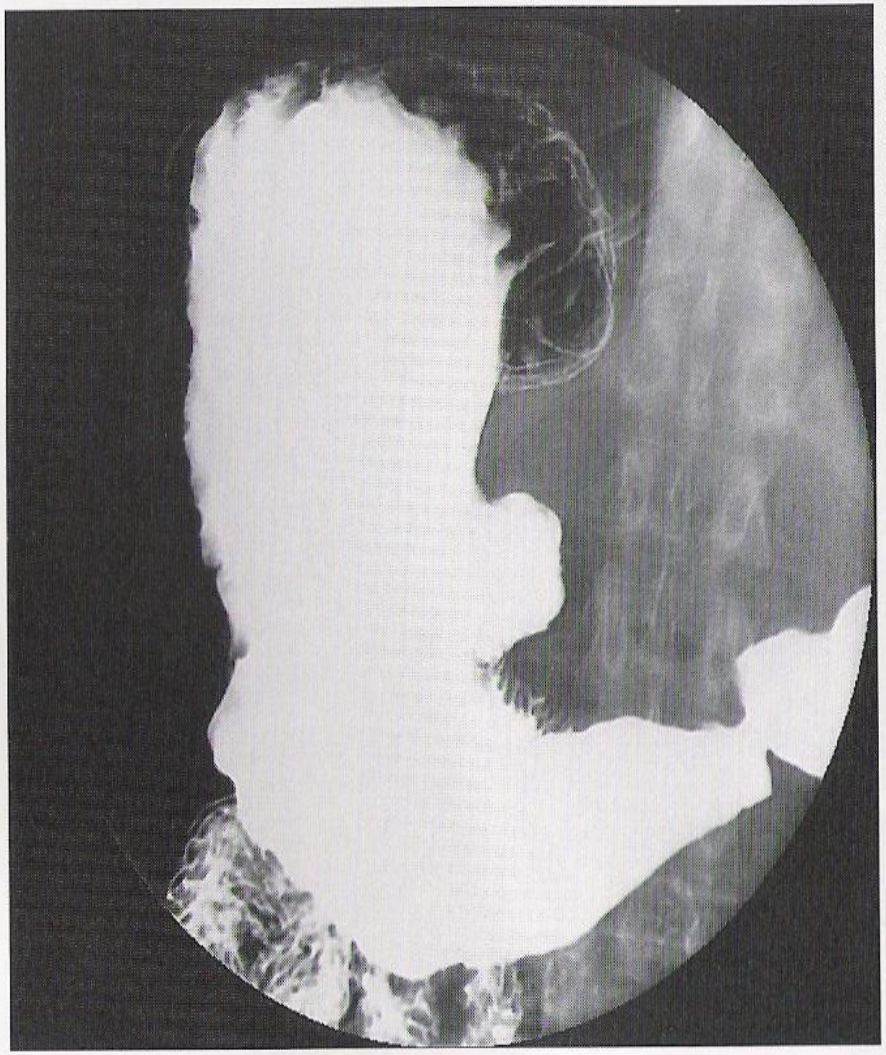
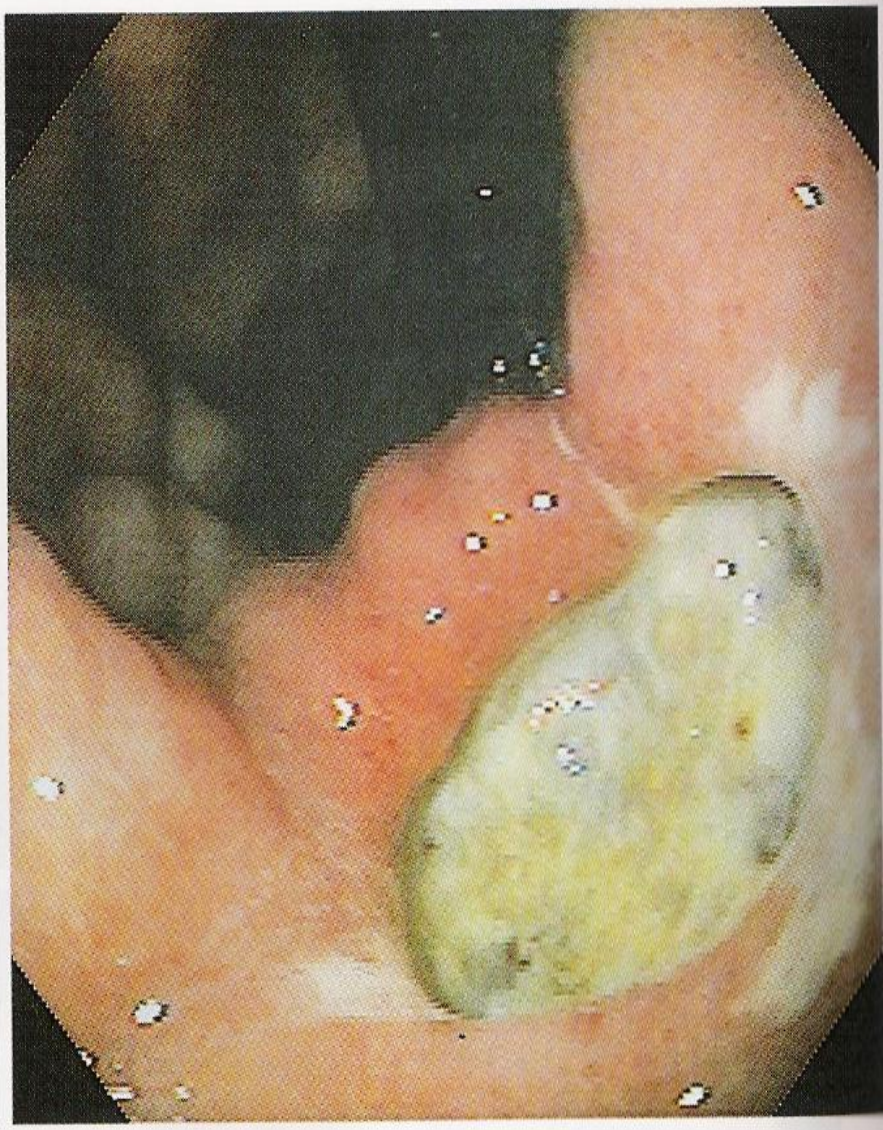




A

FIGURE 3.29 **Benign Gastric Ulcer**
A. Ulcer on the angularis projecting away from the gastric lumen, suggesting a benign lesion. **B.** Large benign-appearing ulcer on the angularis. Exudate covers the base. The ulcer has a symmetric punched-out appearance, and there are no abnormal-appearing rugal folds around the lesion.

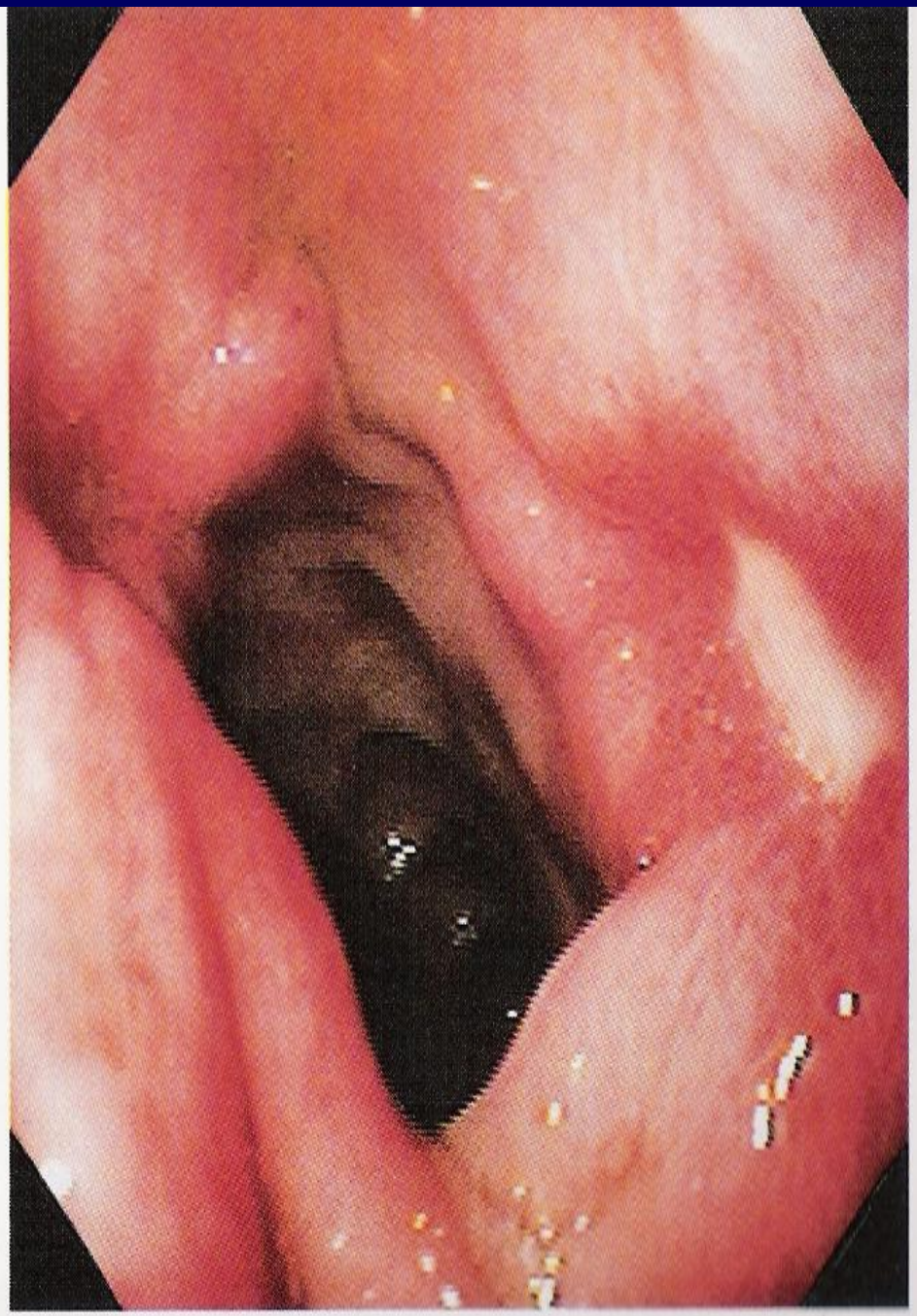
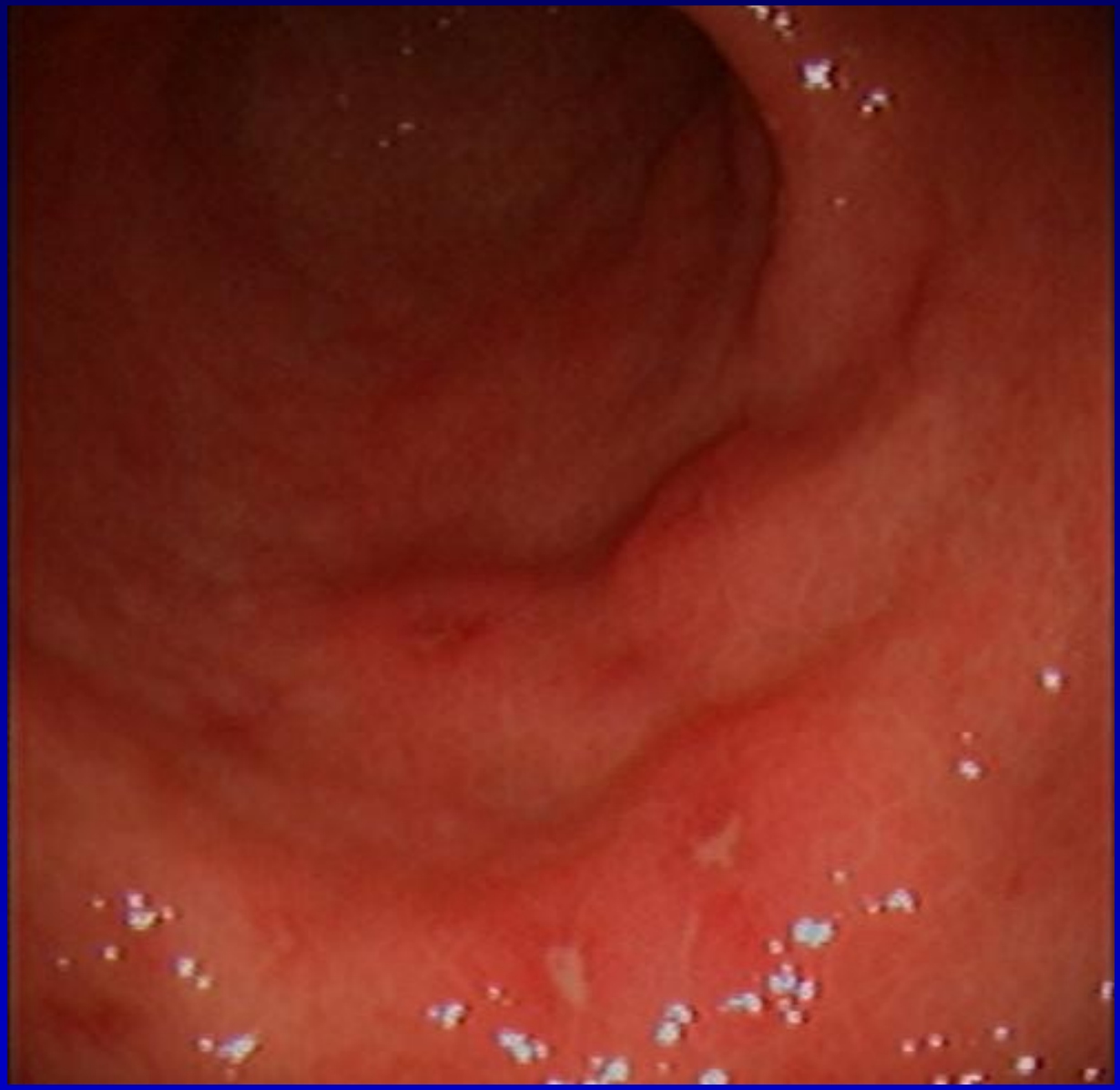


FIGURE 4.12 **Duodenal Ulcer**
A. A persistent collection of barium with radiating folds in the duodenal bulb, highly suggestive of an ulcer. **B.** Posterior duodenal ulcer with a clean base. There is marked edema of the bulb, with folds radiating from the ulcer. Subepithelial hemorrhage is seen surrounding the ulcer as well as in the remainder of the bulb. A small ulcerative lesion is also seen anteriorly.



- Which one of the factors below does not predispose for peptic ulcer disease?

1. Treatment with NSAIDs.
2. Infection with Helicobacter Pylori.
3. Gastrinoma.
4. Treatment with glucocorticosteroids.
5. Treatment with low dose aspirin.

Conditions associated with PUD

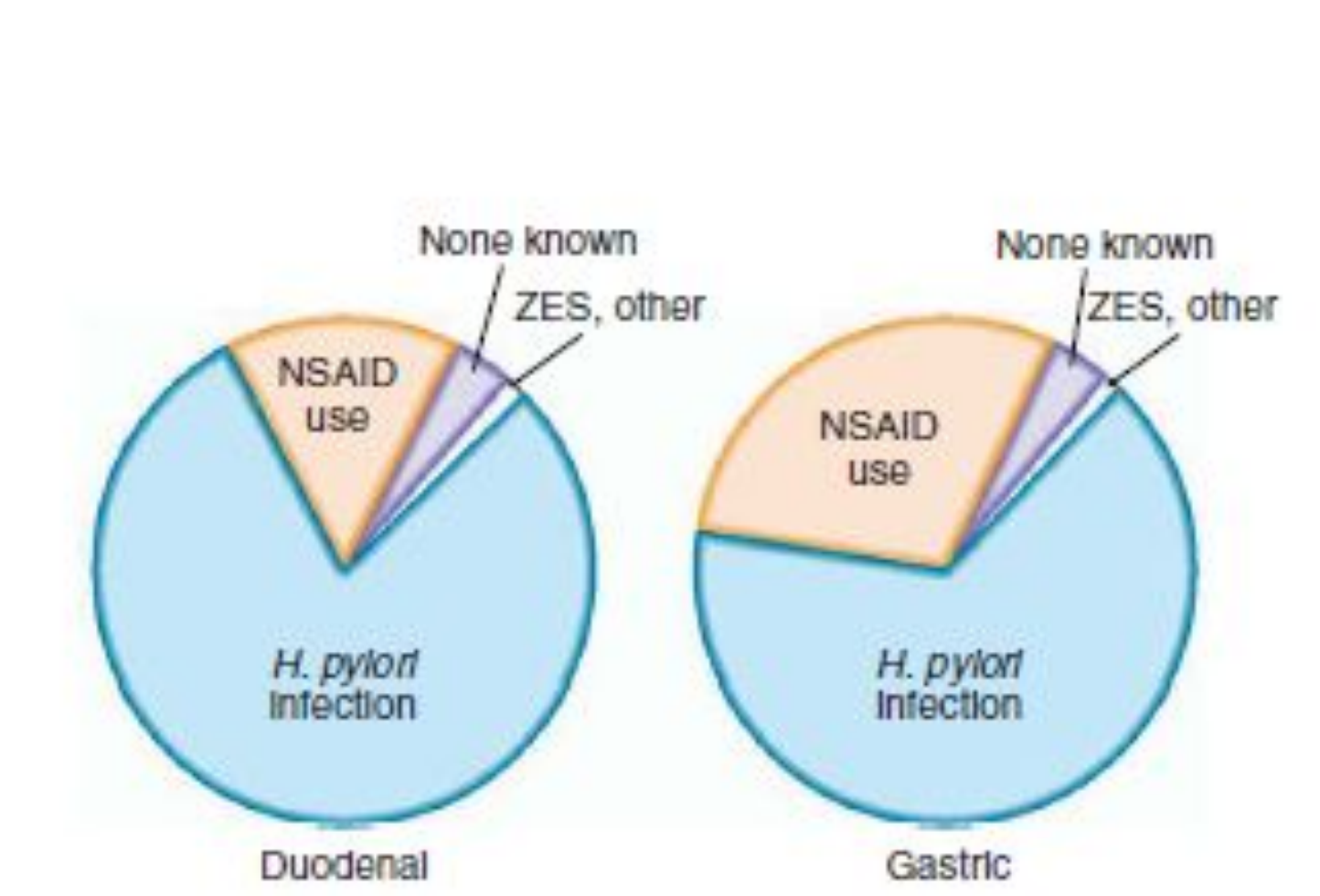


Table 293-1 Causes of Ulcers Not Caused by *Helicobacter Pylori* and NSAIDs
Pathogenesis of Non-Hp and Non-NSAID Ulcer Disease
Infection
Cytomegalovirus
Herpes simplex virus
H. heilmannii
Drug/Toxin
Bisphosphonates
Chemotherapy
Clopidogrel
Crack cocaine
Glucocorticoids (when combined with NSAIDs)
Mycophenolate mofetil
Potassium chloride
Miscellaneous
Basophilia in myeloproliferative disease
Duodenal obstruction (e.g., annular pancreas)
Infiltrating disease
Ischemia
Radiation therapy
Sarcoidosis
Crohn's disease
Idiopathic hypersecretory state

Divergent mucosal and secretory responses to *H. pylori* infection

Chronic *H. pylori* Infection

10-15%

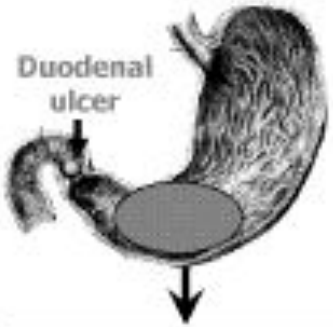
~80%

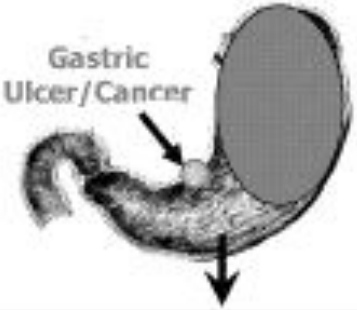
2-5%

Antral-predominant diffuse Gastritis
⇧ Acid, ⇧ Gastrin, little or no atrophy
low risk of Gastric Carcinoma

Corpus-predominant Multifocal Atrophic Gastritis (MAG), ⇩ Acid, ⇧ Gastrin
high risk of Gastric Carcinoma

Mild/Mixed Chronic Gastritis





Normal or Reduced Acid

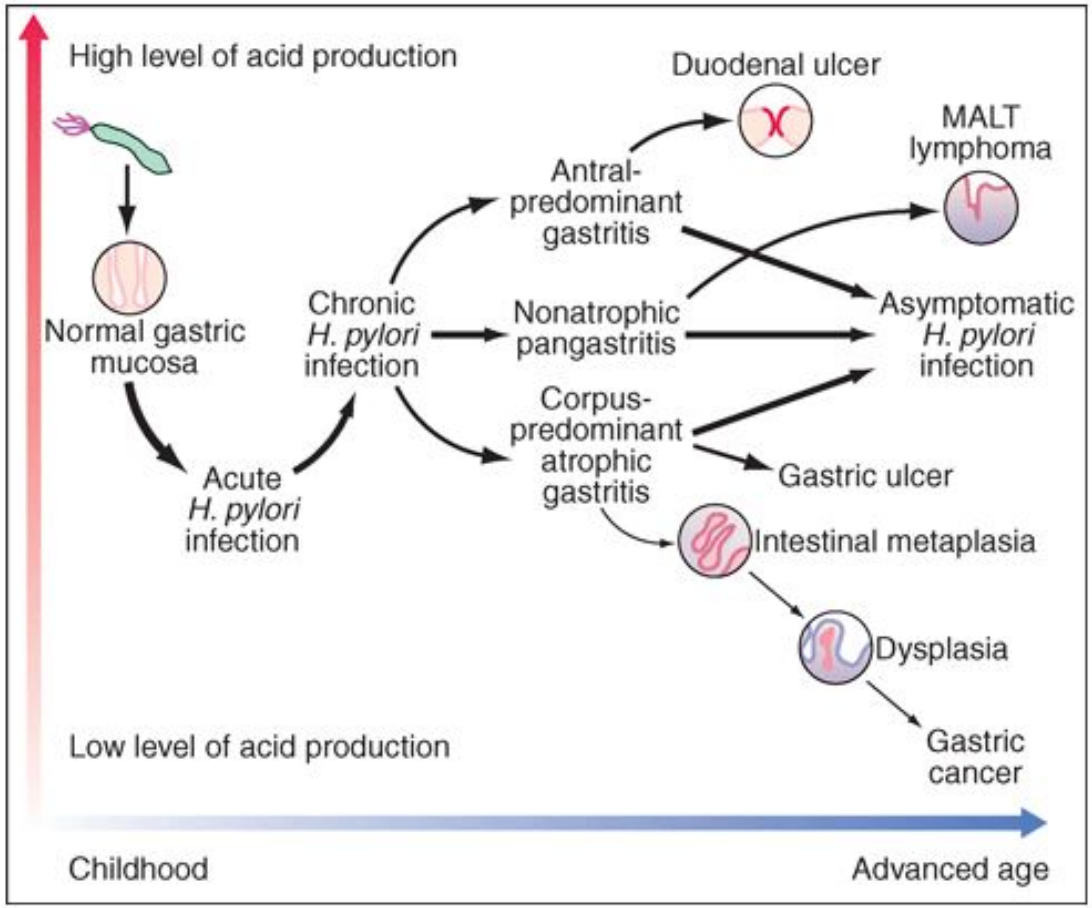
Duodenal ulcer

Gastric Ulcer/Cancer

No significant disease

? Bacterial ? Environment ? Host

Figure 293-8



Natural history of *H. pylori*-infection. *(Used with permission from S Suerbaum, P Michetti: N Engl J Med 347:1175, 2002.)*

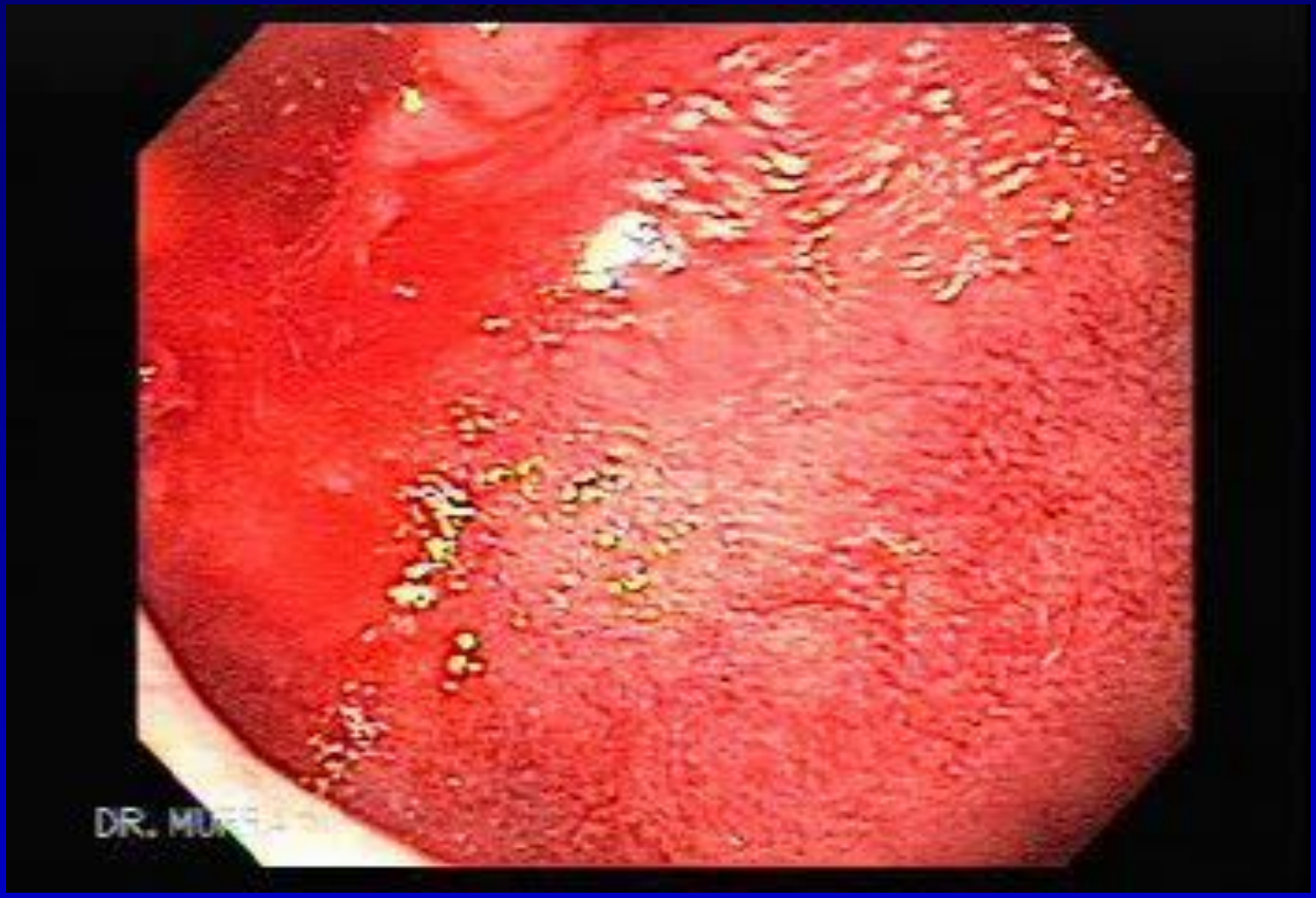
Which one is the most common complication of PUD?

1. infection
2. bleeding
3. perforation
4. obstruction
5. penetration

Complications

- Bleeding ~ 15% (More in >60 yrs –NSAID)
  10-20% - no warning sign

- Perforation 6-7%
  Free: Into the peritoneal cavity
  Penetration: DU posterior to pancreas
  GU into Lt hepatic lobe
  Gastrocolic fistula


DR. MU

Complications

- Outlet obstruction 1-2%
  Inflammatory – reversible by Tx
  Scar tissue – balloon dilatation, surgery

- Healthy male, 38 years old. During the last year he is complaining of burning epigastric pain, that appears about half an hour after a meal and continues approximately 2 hours. He does not take any medications. His physical examination is normal.

  What would you suggest for this patient?

  1. gastroscopy
  2. Empirical treatment with proton pump inhibitors
  3. Breath test for Helicobacter Pylori
  4. US of the upper abdomen
  5. Barium swallow

- Dyspepsia:
  - A medical condition characterized by chronic or recurrent pain in the upper abdomen, upper abdominal fullness and feeling full earlier than expected when eating.
  - It can be accompanied by bloating, belching, nausea, or heartburn

Clinical Presentation

- Dyspepsia
- Abdominal Pain, poor predictive value:

  Epigastric dull “hunger pain”
  DU- 1.5 –3 hrs postprandial relieved by food
  GU – May occur with meals
  NSAID: 10% asymptomatic

- Physical examination: Poor predictive value, not specific. Pain may occur in RUQ ~ 20%

- Rule out complications and signs of malignancy!

Alarm Features in Patients with Suspected Peptic Ulcer Disease

Age older than 55 years with new-onset dyspepsia

Family history of upper gastrointestinal cancer

Gastrointestinal bleeding, acute or chronic, including unexplained iron deficiency

Jaundice

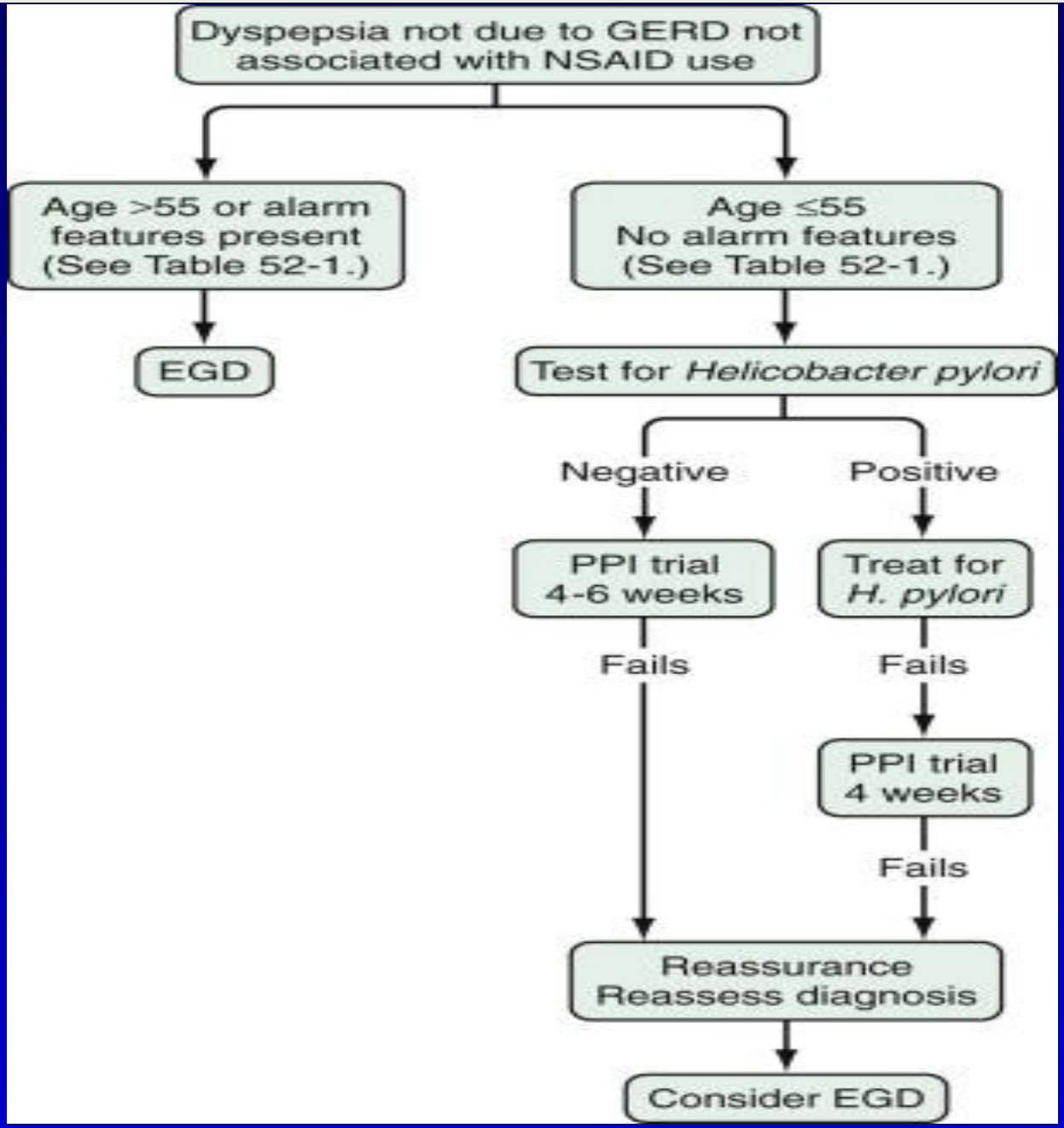
Left supraclavicular lymphadenopathy (Virchow's node)

Palpable abdominal mass

Persistent vomiting

Progressive dysphagia

Unintended weight loss


Dyspepsia not due to GERD not associated with NSAID use
Age >55 or alarm features present (See Table 52-1.)
Age ≤55 No alarm features (See Table 52-1.)
EGD
Test for Helicobacter pylori
Negative
Positive
PPI trial 4-6 weeks
Treat for H. pylori
Fails
Fails
PPI trial 4 weeks
Fails
Reassurance Reassess diagnosis
Consider EGD

- Healthy male, 38 years old. During the last year he is complaining of burning epigastric pain, that appears about half an hour after a meal and continues approximately 2 hours. He does not take any medications. His physical examination is normal.

  What would you suggest for this patient?

  1. gastroscopy
  2. Empirical treatment with proton pump inhibitors
  3. Breath test for Helicobacter Pylori
  4. US of the upper abdomen
  5. Barium swallow

- Whish of the following diagnostic tests is the most suitable for diagnosis of H. Pylori in this patient?
  1. Urease breath test
  2. Antigen in stool
  3. Bacterial culture
  4. Serology in blood
  5. Rapid urease test

Table 50-2 Diagnostic Tests for *Helicobacter pylori*

NONENDOSCOPIC TESTS	ADVANTAGES	DISADVANTAGES
Serology (qualitative or quantitative immunoglobulin G [IgG])	Widely available, inexpensive, good NPV	Poor PPV if HP prevalence is low, not useful after treatment
Urea breath test (^{13}C or ^{14}C)	Identifies active infection, accuracy (PPV, NPV) not affected by *H. pylori* prevalence, useful both before and after treatment	Availability and reimbursement inconsistent, accuracy affected by PPI and antibiotic use, small radiation dose with ^{14}C test
Stool antigen test	Identifies active infection; accuracy (PPV, NPV) not affected by *H. pylori* prevalence; useful both before and after treatment (monoclonal test)	Fewer data available for polyclonal test, accuracy affected by PPI and antibiotic use
ENDOSCOPIC TESTS	**ADVANTAGES**	**DISADVANTAGES**
Histology	Excellent sensitivity and specificity, especially with special and immune stains; provides additional information about gastric mucosa	Expensive (endoscopy and histopathology costs), interobserver variability, accuracy affected by PPI and antibiotic use
Rapid urease test	Rapid results, accurate in patients not using PPIs or antibiotics, no added histopathology cost	Requires endoscopy, less accurate after treatment or in patients using PPIs
Culture	Specificity 100%, allows antibiotic sensitivity testing	Difficult and tedious to perform; not widely available; expensive
Polymerase chain reaction (PCR) assay	Excellent sensitivity and specificity, permits detection of antibiotic resistance	Not widely available; technique not standardized; expensive

NPV, negative predictive value; PPI, proton pump inhibitor (see Table 50-3); PPV, positive predictive value.
Adapted from Chey WD, Wong BC. American College of Gastroenterology guideline on the management of *Helicobacter pylori* infection. Am J Gastroenterol 2007; 102:1808-25.

The principle of the ^{13}C- or ^{14}C-urea breath test

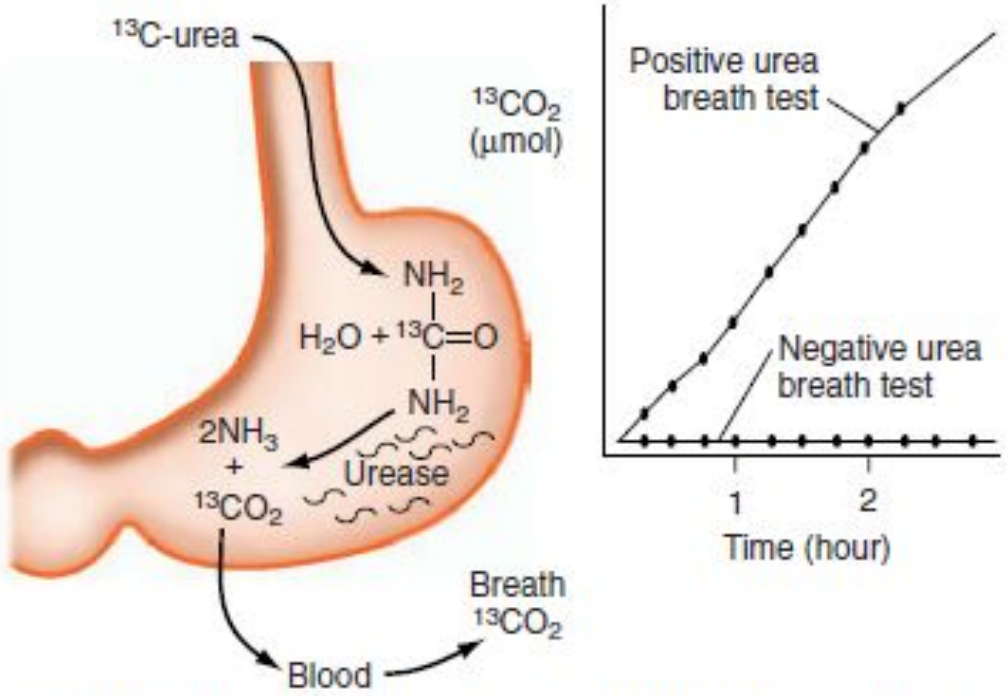
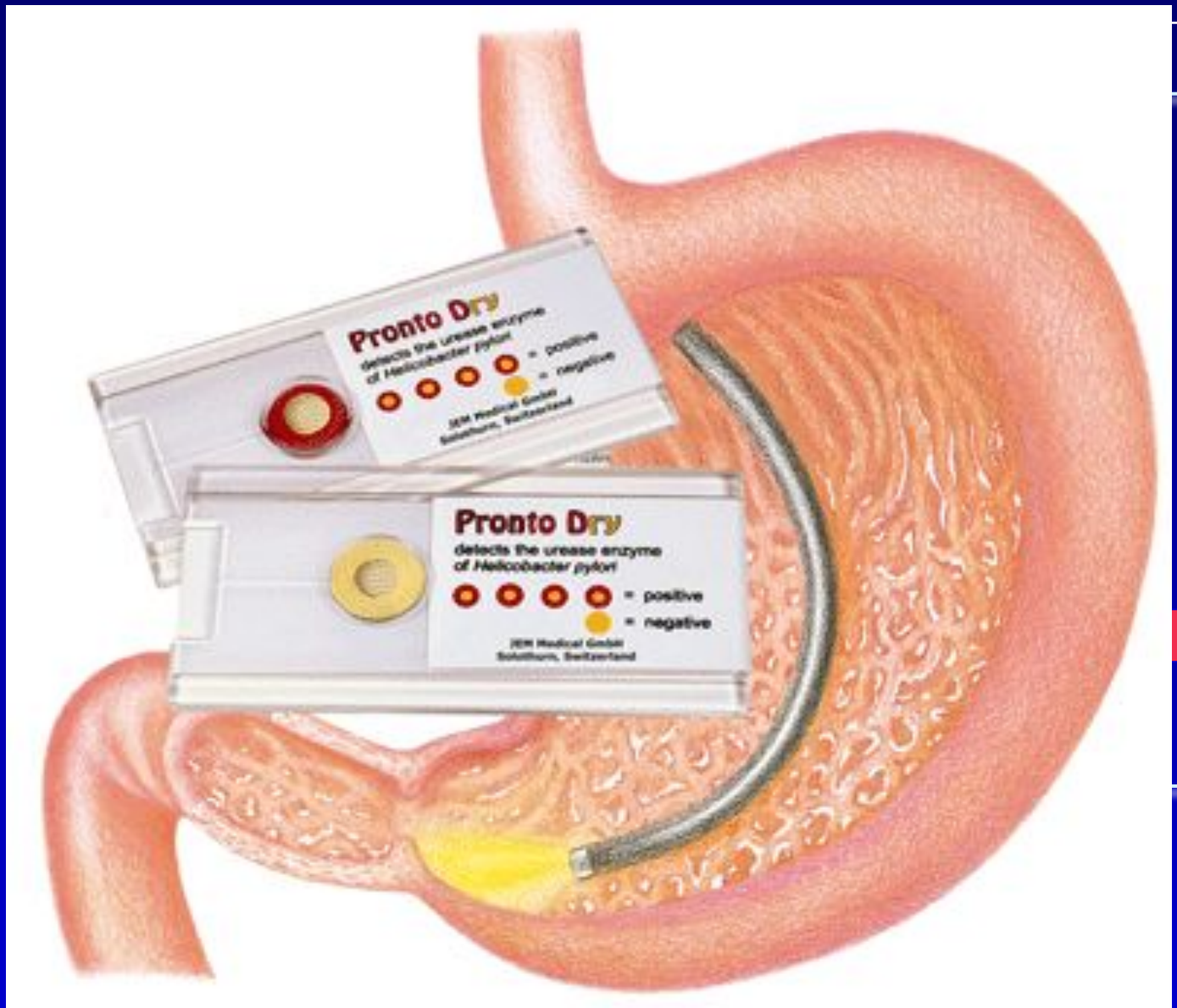


Figure 50-2. The urea breath test. (From Walsh JH, Peterson WL. Drug therapy: The treatment of *Helicobacter pylori* infection in the management of peptic ulcer disease. N Engl J Med 1995; 333:984.)

The principle of the rapid urease test



+ HCO_3^-

What is the preferred first-line combination treatment for ?patient with dyspepsia and positive H Pylori test

1. Amoxicillin, clarithromycin and PPI for 10 days.
2. Bismuth salicylate, metronidazole and clarithromycine for 10 days.
3. Tetracycline and PPI for 10 days.
4. Tetracycline, ceftriaxone for 10 days and PPI for 2 months.

Table 50-3 First-Line Treatment of *Helicobacter pylori* Infection*

TREATMENT REGIMEN*	DURATION	ERADICATION RATE	COMMENTS
PPI†, clarithromycin 500 mg, amoxicillin 1000 mg (each twice daily)	10-14 days	70%-85%	Macrolide resistance affects eradication success; not appropriate for penicillin allergic individuals or those who have received a clarithromycin regimen in the past
PPI†, clarithromycin 500 mg, metronidazole 500 mg (each twice daily)	10-14 days	70%-85%	Appropriate for penicillin-allergic individuals who have not received a clarithromycin-containing regimen in the past
PPI†, amoxicillin 1000 mg (each twice daily) **followed by** PPI†, clarithromycin 500 mg, tinidazole 500 mg (each twice daily)	5 days 5 days	90%	Appears highly effective despite clarithromycin resistance; limited experience to date in the United States
Bismuth subsalicylate 525 mg, metronidazole 500 mg, tetracycline 500 mg (each four times daily) **plus** PPI† or H_2RA (twice daily)	10-14 days	75%-90%	Inexpensive but complicated regimen; consider in penicillin allergic individual or if clarithromycin resistance is suspected; can be used for retreatment (see Table 50-4)

*Note that not all of these regimens are currently approved by the U.S. Food and Drug Administration (FDA).
†Lansoprazole 30 mg, pantoprazole 40 mg, rabeprazole 20 mg, omeprazole 20 mg, or esomeprazole 40 mg (esomeprazole can be taken once daily).
H_2RA, histamine H_2-receptor antagonist; PPI, proton pump inhibitor.
Adapted from references 131, 150, and 151.

A 68 year old male is admitted due to "coffee ground" vomiting. After initial hemodynamic stabilization and treatment with IV PPI, he underwent gastroscopy that showed 1 cm clear ulcer at the stomach body. Biopsies are positive for H Pylori, without evidence of malignancy. After treatment for eradication of H Pylori and PPIs for two months he is feeling well. What is your recommendation for this patient?

1. Breath test to confirm eradication of H Pylori.
2. Long term treatment with PPI.
3. Second-look gastroscopy 8-12 weeks after the first one.
4. Blood test for gastrin level.
5. No further evaluation is needed.

Peptic disease: epidemiology

- DU: 6-15% of the population
  - >95% in first duodenal part
  - mostly benign
  - Increased acid secretion

- GU: Peak in sixth decade
  - May be malignant
  - Most benign ulcers are distal to antral junction
  - Normal-reduced acid secretion

Table 293-7 When to Obtain a Fasting Serum Gastrin Level
Multiple ulcers
Ulcers in unusual locations; associated with severe esophagitis; resistant to therapy with frequent recurrences; in the absence of NSAID ingestion or *H. pylori* infection
Ulcer patients awaiting surgery
Extensive family history for peptic ulcer disease
Postoperative ulcer recurrence
Basal hyperchlorhydria
Unexplained diarrhea or steatorrhea
Hypercalcemia
Family history of pancreatic islet, pituitary, or parathyroid tumor
Prominent gastric or duodenal folds

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4. Blood test for gastrin level.
5. No further evaluation is needed.

Refractory Ulcers

- Consider refractory after 8-12 wks of Tx
- Ensure that refractory symptoms = refractory ulcer (endoscopy)
- Consider “silent” refractory ulcer in high risk pts (~25% of refractory ulcers)

Refractory Ulcers - causes

- Persistent HP infection
- Persistent NSAID use
- Poor compliance
- Giant ulcers (healing at 3 mm/wk)
- Smoking
- Underlying pathology (ZE, lymphoma, Crohn's disease ,infections I.e. TB syphilis, sarcoidosis)

Refractory Ulcers - Approach

1. Compliance?
2. Persistant HP infection?
3. Is the patient still taking an NSAID?
4. Does the patient smoke cigarettes?
5. Has the duration of ulcer treatment been adequate (large ulcers)?
6. Is there evidence of a hypersecretory condition?
   - Family history of gastrinoma or multiple endocrine neoplasia type 1
   - Personal history of chronic diarrhea, hypercalcemia due to hyperparathyroidism, or ulcers involving the postbulbar duodenum
7. Is the ulcer penetrating the pancreas, liver, or other organ?
8. Is the ulcer indeed peptic?

- A 70 year old woman with rheumatoid arthritis is treated constantly with NSAIDs. She complains of epigastric pain and on gastroscopy a duodenal ulcer is found. Rapid urease test is negative for H Pylori. Which of the following is the best option for this patient?

1. Stop NSAIDs and start misoprostol.
2. Continue NSAIDs and add H2 blockers.
3. Continue NSAIDs and add PPI.
4. Switch to COX2 inhibitors.
5. Stop NSAIDs and add sucralfate.

NSAIDS

- In the USA :30 mil OTC, 20 mil prescriptions
- 3-4% ulcerations, 1.5% complicated
- 20,000 die of NSAID complications
- 80% have no preceding dyspepsia
- Important to identify at risk populations

  Previous gastritis/ulcer
  Elderly
  Concomitant GC, anticoagulants

Table 293-3 Drugs Used in the Treatment of Peptic Ulcer Disease		
Drug Type/Mechanism	**Examples**	**Dose**
Acid-suppressing drugs		
Antacids	Mylanta, Maalox, Tums, Gaviscon	100–140 meq/L 1 and 3 h after meals and hs
H_2 receptor antagonists	Cimetidine	400 mg bid
	Ranitidine	300 mg hs
	Famotidine	40 mg hs
	Nizatidine	300 mg hs
Proton pump inhibitors	Omeprazole	20 mg/d
	Lansoprazole	30 mg/d
	Rabeprazole	20 mg/d
	Pantoprazole	40 mg/d
	Esomeprazole	20 mg/d
Mucosal protective agents		
Sucralfate	Sucralfate	1 g qid
Prostaglandin analogue	Misoprostol	200 μg qid
Bismuth-containing compounds	Bismuth subsalicylate (BSS)	See anti- regimens (Table 293-4)

Recommendations: NSAIDs induced PUD

- NSAIDs should be discontinued if possible.
- PPIs are more effective than H2 receptor antagonists, sucralfate, and misoprostol in **healing** NSAID-associated ulcers when continuous NSAID treatment is required.
- When NSAIDs can be discontinued, an H2 receptor antagonist is an effective alternative.
- Treatment with COX-2 inhibitors in patients with active ulcers who continue to require antiinflammatory therapy is not recommended.

- A 70 year old woman with rheumatoid arthritis is treated constantly with NSAIDs. She complains of epigastric pain and on gastroscopy a duodenal ulcer is found. Rapid urease test is negative for H Pylori. Which of the following is the best option for this patient?

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5. Stop NSAIDs and add sucralfate.

A 75 year old man with ischemic heart disease is treated with aspirin. He has a prior history of PUD. Because of severe osteoarthritis he is planned to start NSAIDs. Besides performing breath test for H Pylori, what else yould you suggest?

.Gastroscopy to ensure there is no active ulcer .1

.Treatment with COX2 inhibitors .2

Combination of COX2 inhibitors with PPI or misoprostol .3

.Combination of NSAIDs and PPI or misoprostol .4

Not to start NSAIDs or COX2 .5

ULCER PROPHYLAXIS

Table 53-1 Risk Ratios for the Various Risk Factors for Ulcer Complications Induced by NSAIDs*

RISK FACTOR	RISK RATIO
History of complicated ulcer	13.5
Use of multiple NSAIDs (including aspirin), cyclooxygenase-2 [COX-2] inhibitor)	9
High doses of NSAIDs	7
Use of an anticoagulant	6.4
History of uncomplicated ulcer	6.1
Age > 70 years	5.6
Helicobacter pylori infection	3.5
Use of a glucocorticoid	2.2

Table 53-2 Recommendations for Reducing the Risk of Ulcers Associated with Nonsteroidal Anti-inflammatory Drugs (NSAIDs) as a Function of Gastrointestinal and Cardiovascular Risk

	GI Risk		
	LOW*	**MODERATE***	**HIGH***
Low CV risk	Use the least ulcerogenic NSAID at the lowest effective dose	NSAID plus either a PPI or misoprostol	COX-2 inhibitor plus a PPI, or misoprostol
High CV risk†	Naproxen plus either a PPI or misoprostol	Naproxen plus either a PPI or misoprostol	Avoid NSAIDs or COX-2 inhibitors; use alternative therapy.

**Low GI risk* denotes absence of any risk factors (see Table 53-1); *moderate GI risk* denotes presence of one or two risk factors; *high GI risk* denotes presence of three or more risk factors, prior complicated ulcer, or concomitant use of low-dose aspirin or anticoagulants. All patients with a history of ulcer who require NSAIDs should be tested for *H. pylori*, and if infection is present, eradication therapy should be given (see Chapter 50).

†*High CV risk* denotes the requirement for prophylactic low-dose aspirin for primary or secondary prevention of serious cardiovascular events.

COX-2, cyclooxygenase-2; CV, cardiovascular; GI, gastrointestinal; PPI, proton pump inhibitor.

What is the best treatment to prevent ?stress ulcers in intubated patients

1. PPI
2. H2B
3. SULCRAFATE
4. MISOPROSTOL

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- Clinical presentation
- Management – HBP, NSAIDS
- Refractory PUD
- Prophylaxis