

Disease of the Stomach

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I have no disclosures

I work for the Curators of the
University of Missouri

Disease of the Stomach

1. Neuromuscular disorders

Gastroparesis

Dumping syndrome and Rapid Gastric Emptying

2. Gastritis and Gastropathies

Autoimmune Metaplastic Atrophic Gastritis

Environmental Metaplastic Atrophic Gastritis

Disease of the Stomach (cont'd)

3. Peptic Ulcer Disease

Epidemiology

Risk Factors

Other Causes of Ulcer Disease

Gastrinoma with or without MEN Type 1

Systemic Mastocytosis

Miscellaneous Disorders

4. Upper GI Bleeding

5. Granulomatous Gastritides

Sarcoidosis

Xanthogranulomatous Gastritis

Disease of the Stomach (cont'd)

6. Distinctive Gastritides

Colagenous Gastritis

Lymphocytic Gastritis

Eosinophilic Gastritis

7. Miscellaneous Forms of Gastritis

IBD (Crohn's disease

Gastritis Cystica Profunda

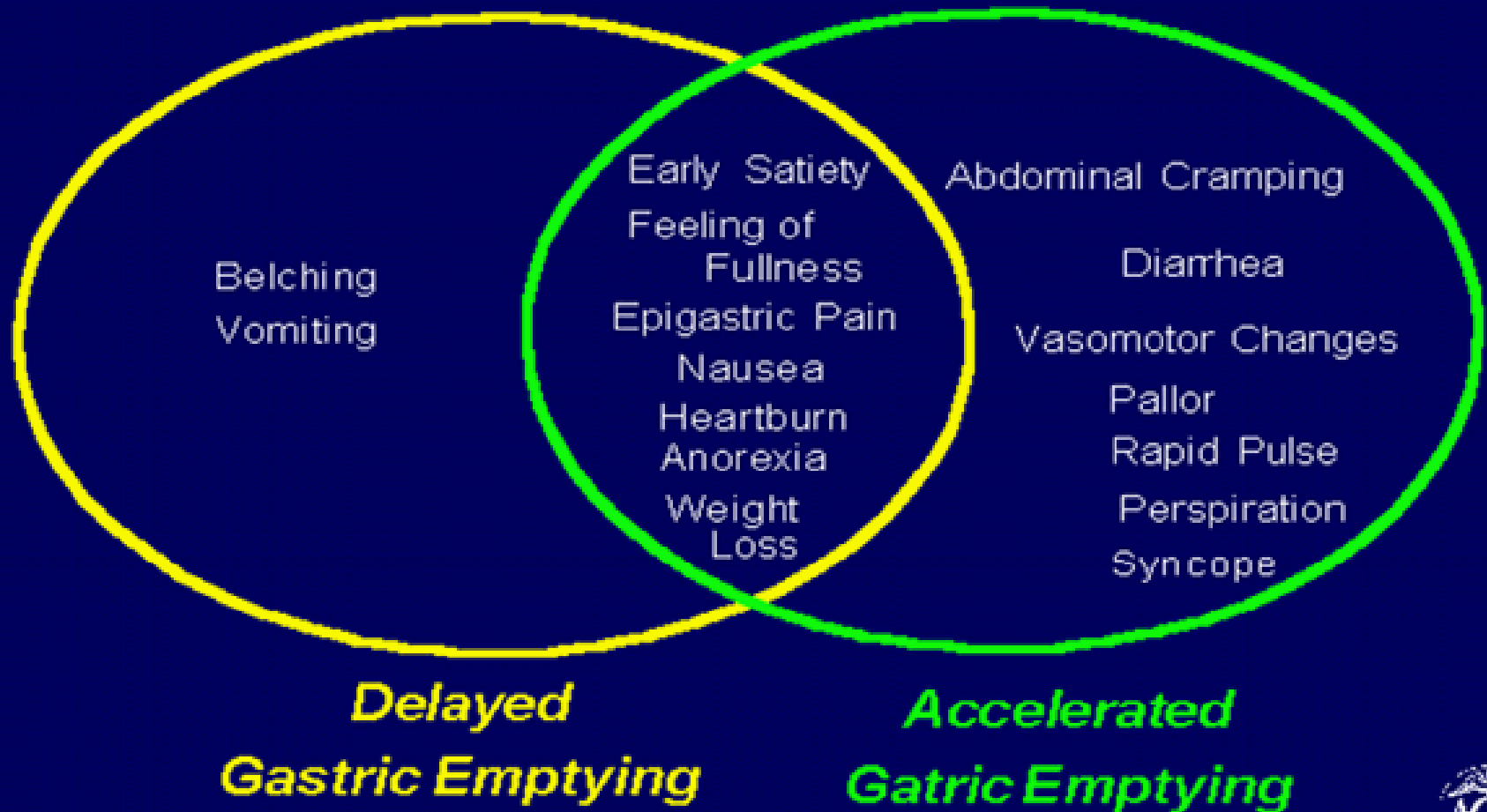
GVHD

8. Carcinoid Tumor in AMAG

Gastric & Intestinal Motility Disorders (*Classifications*)

- **Neuropathy**
 - Diabetic Gastroenteropathy
 - Post-Vagotomy
 - Neuropathic variety of intestinal pseudo-obstruction
- **Myopathy**
 - Scleroderma
 - Myopathic variety of intestinal pseudo-obstruction
- **Drugs/Humoral**
- **Undefined**
 - ?N.U.D.
 - ?I.B.S.

SOME OF THE SYMPTOMS OF DELAYED AND ACCELERATED GASTRIC EMPTYING OVERLAP



Diabetic Gastroenteropathy

A Wide Spectrum of Dysfunction and Symptomatology

- **Esophageal Dysfunction**
 - Dysphagia
- **Gastroparesis**
 - Nausea/Vomiting
 - Post-prandial fullness
 - Abdominal Pain
- **Accelerated Emptying**
 - “Dumping” syndrome
- **Delayed Intestinal Transit**
 - Constipation
 - Abdominal Pain
- **Rapid Intestinal Transit**
 - Diarrhea
- **Gallbladder Dysfunction**
 - Gallstones
- **Anal Sphincter Neuropathy**
 - Incontinence

Diabetic Gastropathy

Clinical Features

- **Common (50% of long-standing Type 1)**
- **Most prevalent in Type 1 but also occurs in Type 2**
- **Usually (50-70%) associated with autonomic neuropathy**
- **High blood sugar levels can exacerbate gastropathy**
- **Consequences may include:**
 - Delayed emptying of solids and indigestible particles
 - Rapid emptying of liquids
 - Bezoar formation
 - Poor blood sugar control (tendency to hypoglycemia)
 - Malnutrition/weight loss

Dumping Syndrome

- Occurs in patients after vagotomy and pyloroplasty
- Abnormal post-op anatomy causes rapid emptying of food into the duodenum
- Symptoms 1st hour
 - Pain, bloating, nausea, vomiting
- Symptoms 2 to 4 hours later
 - Sweating, lightheadedness, cramps, diarrhea
- (Later symptoms due to rapid absorption of carbs)

Rapid Gastric Emptying

- **Definition: When more than 30% of the meal leaves the stomach within 30 minutes or more than 70% at 60 minutes**
- **Causes:**
 - Idiopathic
 - Early Diabetes Mellitus Type 2
 - Zollinger-Ellison Syndrome
 - Surgeries

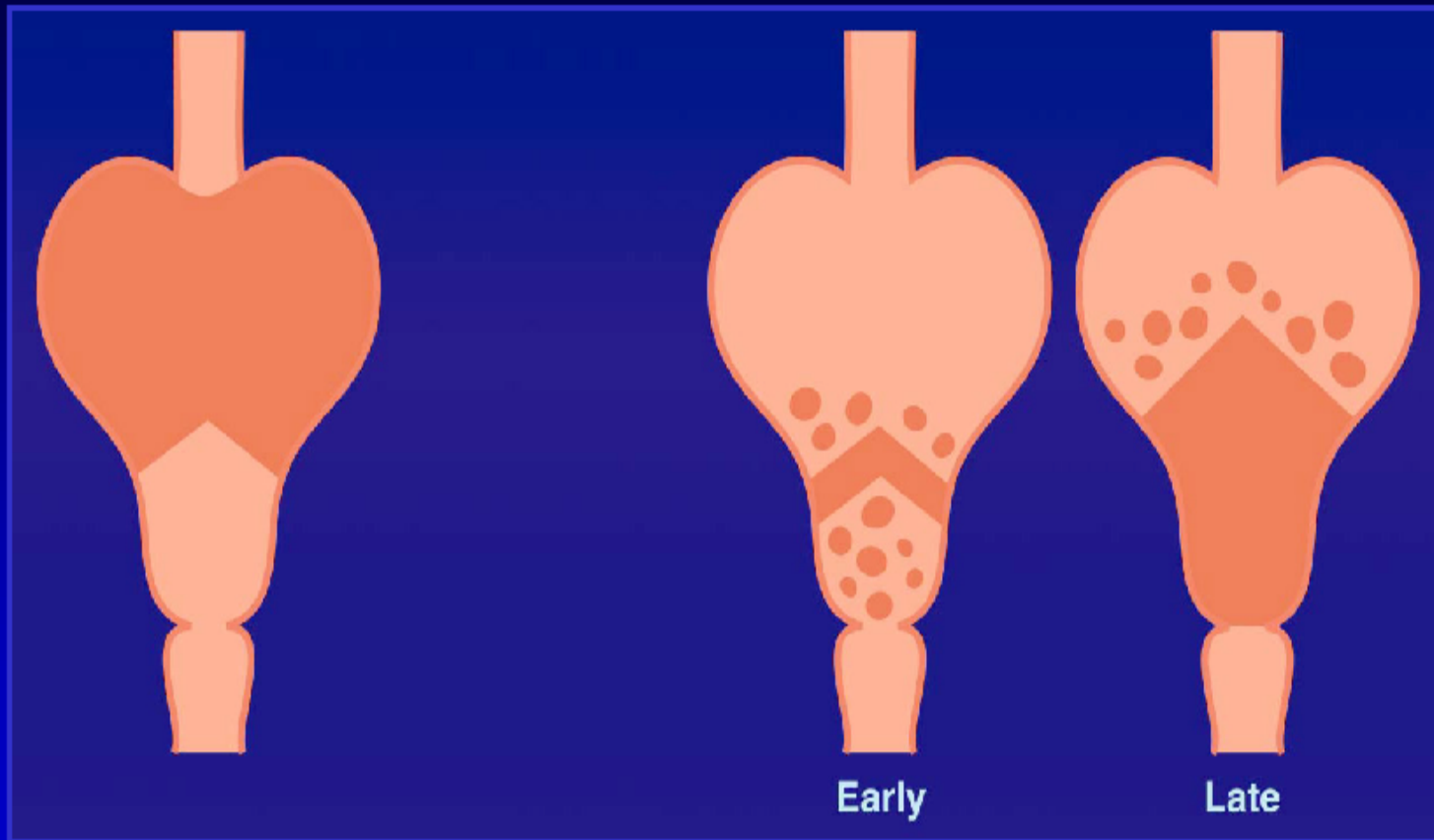
Gastropathy and Gastritis - Definitions

- **GASTROPATHY** - Literally, any gastric lesion
Used as substitute for “gastritis” when inflammation absent or minimal
- **GASTRITIS** - Leukocyte infiltration in stomach
 - **ACTIVE (=ACUTE) GASTRITIS** - Neutrophil infiltration present
- **CHRONIC GASTRITIS** - Mononuclear leukocytes increased
- **CHRONIC ACTIVE GASTRITIS** - Mixed chronic and active inflammation

Atrophic Gastritis: Clinical Features

Features	Autoimmune (Type A)	Environmental (Type B)
Causes	Autoimmunity Genetic?	Dietary Duodenal reflux?
Parietal Cell Ab's	All	None
Pernicious Anemia	Common	None
Serum Gastrin	High (often)	Low or Normal
HCl Secretion	Absent	Low
Gastric Ulcer	Rare	Increased
Gastric Cancer	? Increased	Increased

Metaplastic Atrophic Gastritis - Distributions of Autoimmune vs Environmental Types



Autoimmune

Environmental



Granulomas In Gastritis – Typical Causes

- **SYSTEMIC DISEASE-ASSOCIATED (non-infectious)**
 - Crohn's disease
 - Sarcoidosis
 - Wegener's granulomatosis (rare)
- **CONFINED TO STOMACH (non-infectious)**
 - Isolated (idiopathic) granulomatous gastritis
 - Foreign material
 - Tumor-associated (eg, MALT Lymphoma)
- **INFECTIOUS**
 - H pylori*
 - Tuberculous
 - Tertiary syphilis (gummatous)
 - Whipple's disease
 - Histoplasmosis



Lymphocytic Gastritis – Associated Conditions

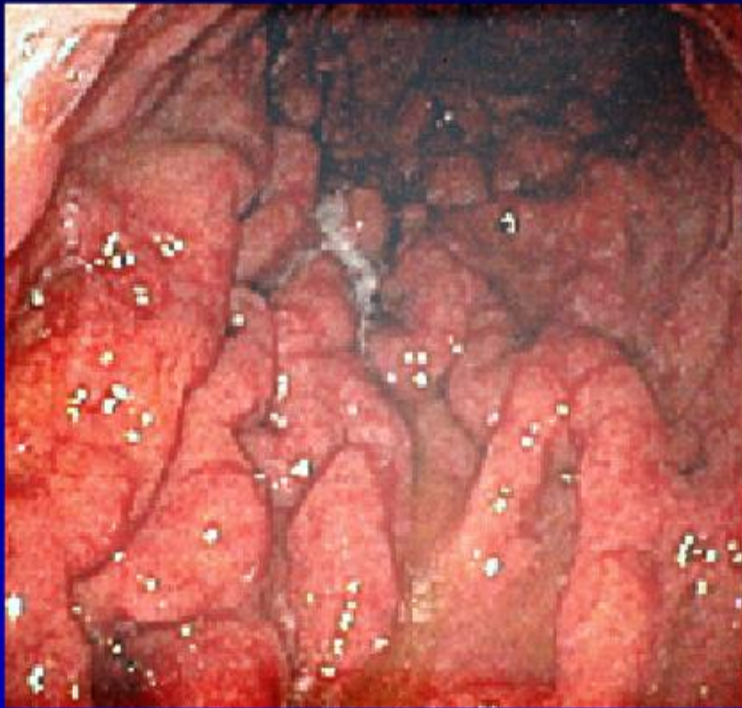
- Varioliform gastritis
- Celiac disease
- *H. pylori* gastritis
- Hypertrophic lymphocytic gastritis
- Ticlopidine administration
- Lymphocytic colitis
- Collagenous colitis



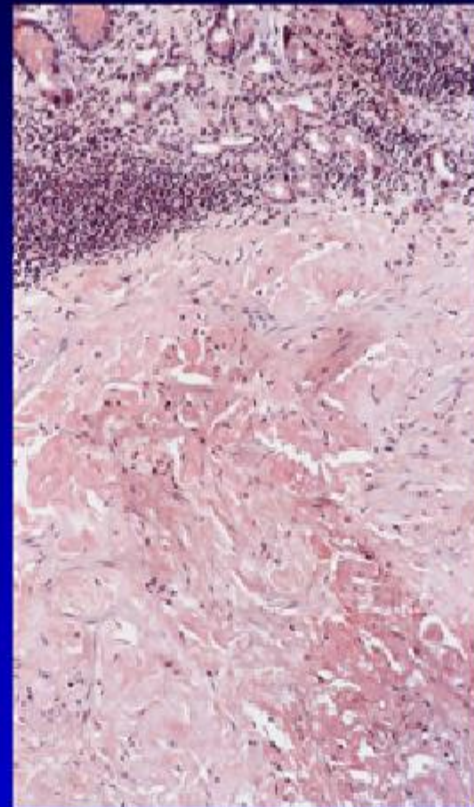
Large Gastric Folds: Classification

- **Gastrin-Stimulated Rugal Hypertrophy**
 - Z-E associated Some DU patients
- **Hypertrophic Hypersecretory Gastropathy**
 - Not gastrin-stimulated
 - Protein-losing gastropathy
- **Menetrier's Disease**
- **Miscellaneous Causes**
 - Hyperplastic polyps
 - Neoplasia (carcinoma, lymphoma)
 - Inflammatory (various)
 - Infiltrative (amyloid)

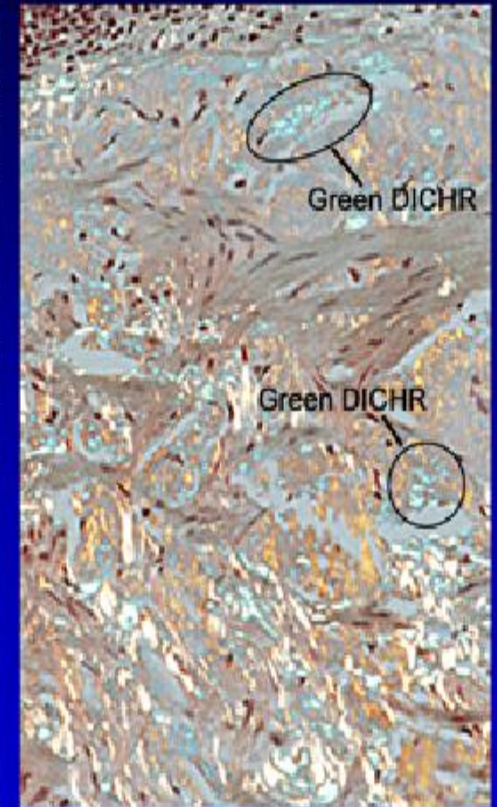
Gastric Amyloidosis with Large Rugal Folds – Endoscopy and Histology (Congo Red)



Endoscopy

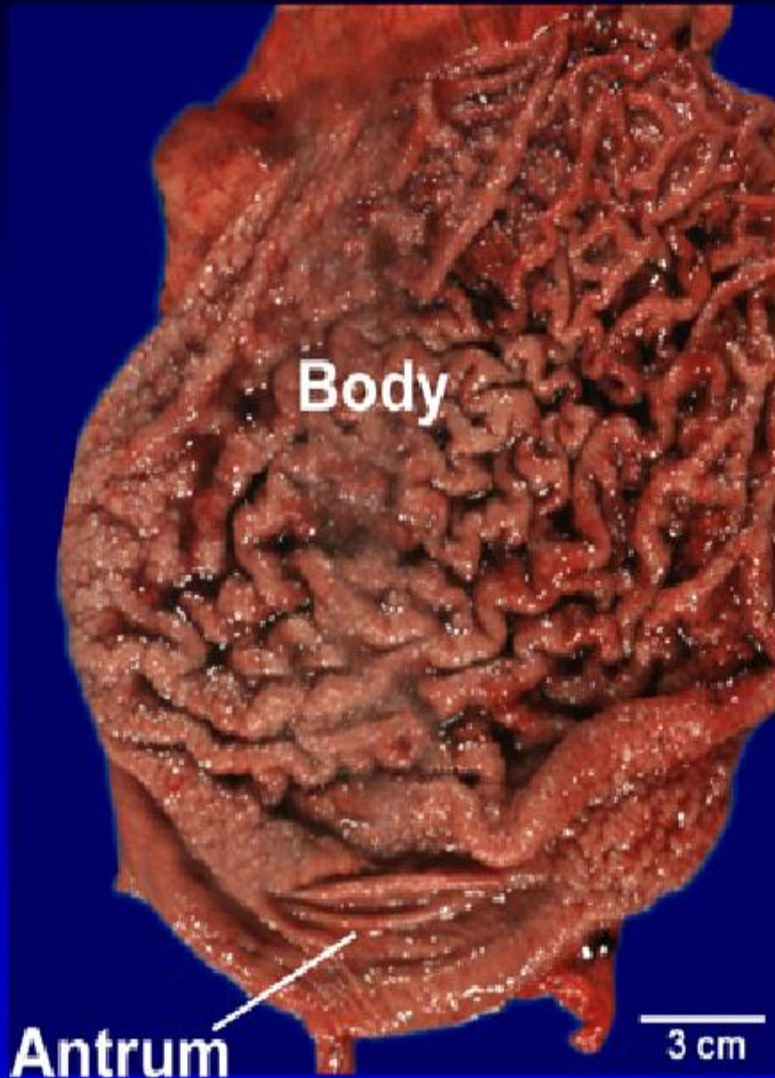


Congo Red

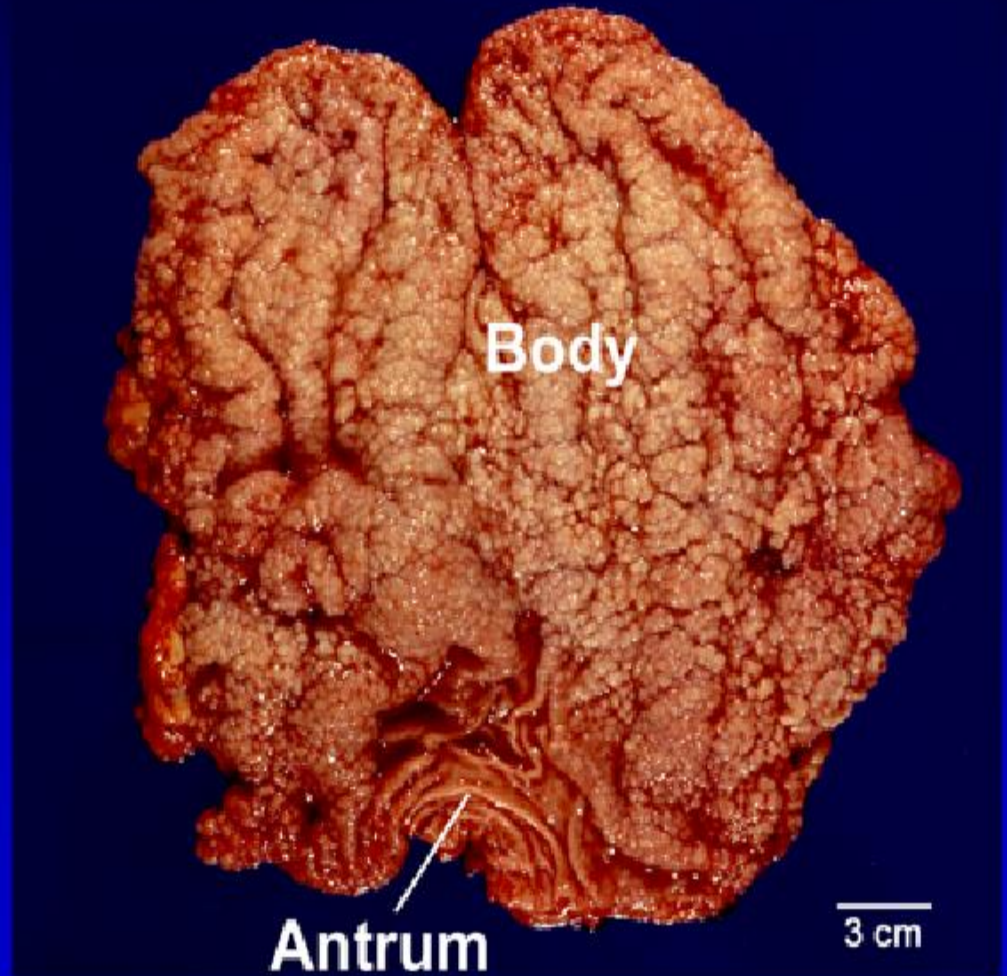


Polarized

Hyperplastic Gastropathies - Gross



Zollinger-Ellison

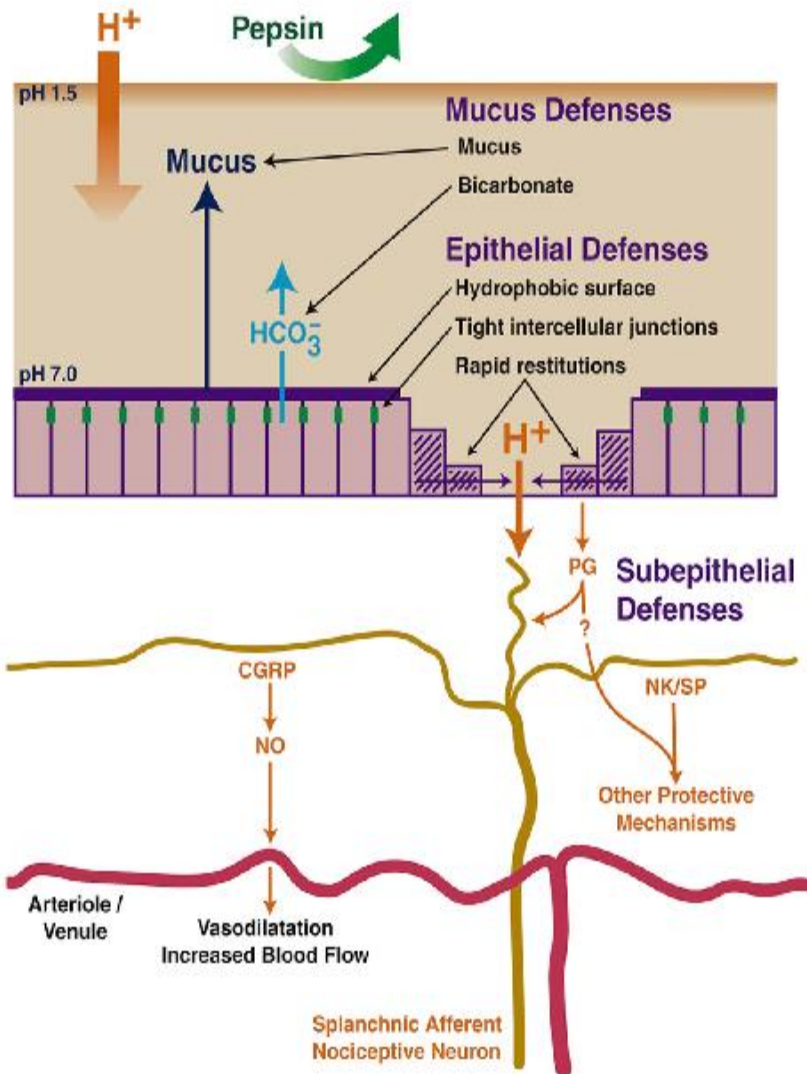


Ménétrier's

Non-Ulcer Dyspepsia

- *H. pylori* frequency about the same as in asymptomatic population
- Prospective clinical trials of anti-*H. pylori* therapy generally have had disappointing results
- As yet unable to identify subpopulation that achieves long term symptomatic benefit from *H. pylori* therapy

The Gastric Mucosa is Protected by a Multi-layered Defense



Causes of Peptic Ulcer

- *Helicobacter pylori* infection
- NSAID use
- Rare causes
 - Pathologic hypersecretory states
 - Herpes simplex infection
 - Crohn's disease, etc.
 - Systemic Mastocytosis



Ulcers May Be Caused by Non-acid/peptic Disorders

Esophagus

- herpes simplex
- tablet induced
tetracycline
KCl
others
- cytomegalovirus

Stomach

- carcinoma
- Kaposi's
- lymphoma
- pancreatic rest
- syphilis
- candida

Duodenum

- Crohn's disease
- pancreatic carcinoma



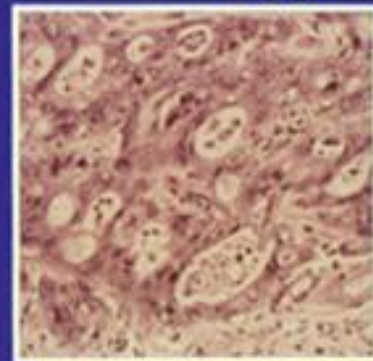
Gastric Cancers May Ulcerate and Resemble Gastric Ulcers

X-Ray

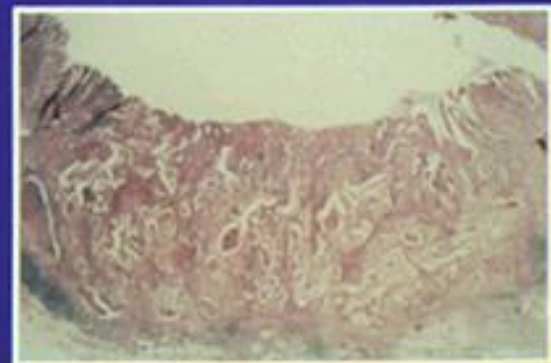
Endoscopy

Histology

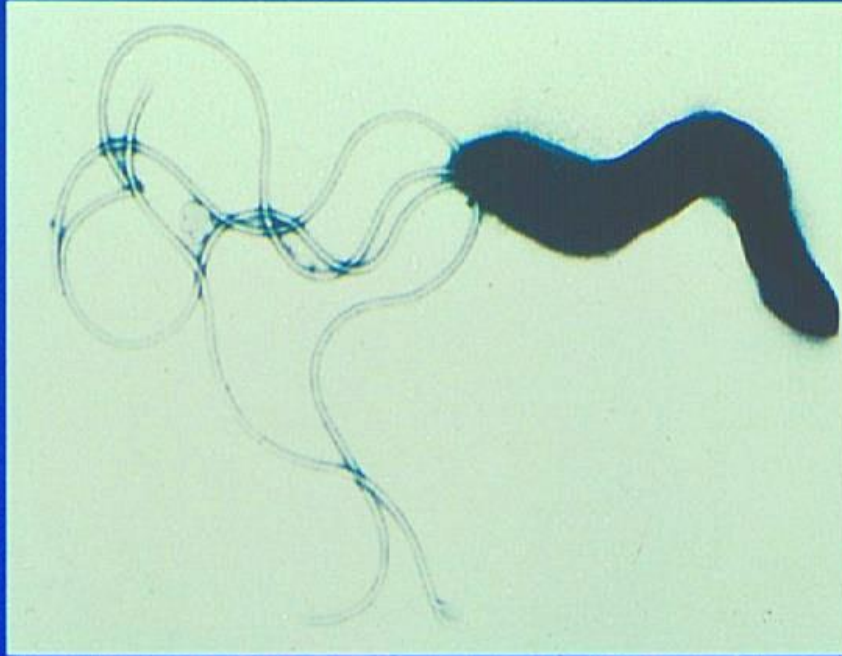
Gastric Cancer



Gastric Ulcer



EM of spiral flagellated *H. pylori*



J. A. J. van Laauws & G. Tytgat *Campylobacter pylori*: 1989



Helicobacter Pylori

- **Gram-negative**
- **Spiral rod**
- **Fastidious**
- **Microaerophilic**
- **Urease-positive**
- **Unipolar flagella**

Pathophysiology

Postulated Steps in Infection

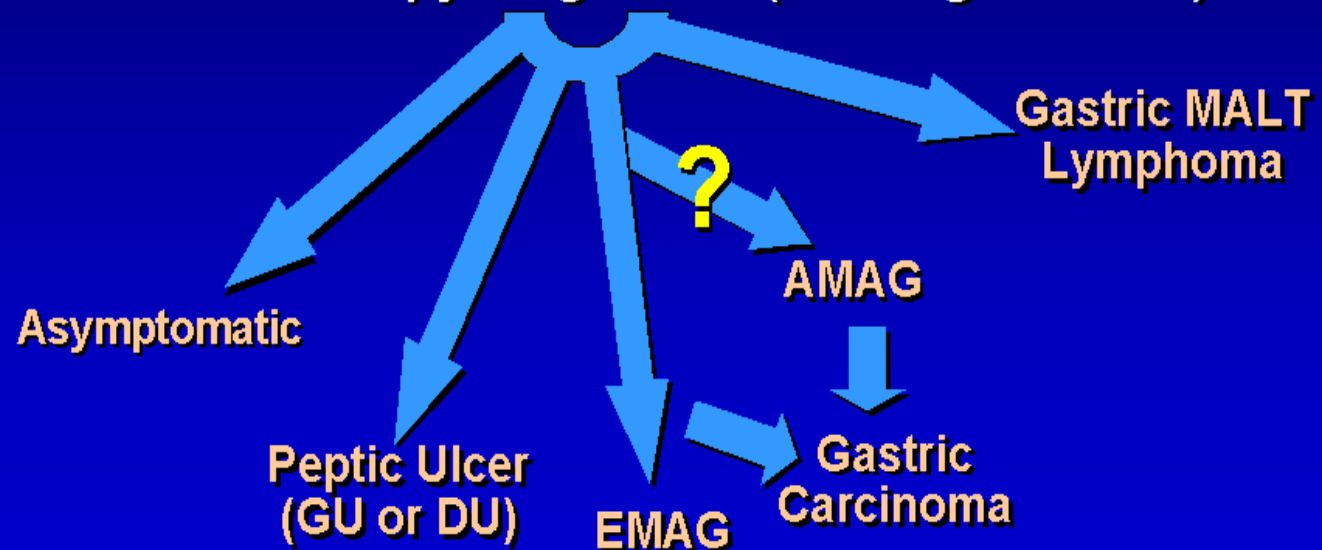
- Ingestion of *H. pylori*
- 'Swim' through mucus
- Attach to mucosa
- Multiply
- Damage tissue
- Internalization into epithelium?

Clinical Outcomes & Sequelae of *Helicobacter pylori* Infection

Acute infection (usually unrecognized)

Acute gastritis (transient hypochlorhydria)

Chronic Active *H. pylori* gastritis (life-long infection)



Pathophysiology

Duodenal Abnormalities

- **Alterations in duodenal structure and function**
 - Damage to surface cells
 - Increase in proportion of surface covered by gastric metaplasia; some with ability to make acid
 - Scarred, deformed smaller bulb (altered motility?)
 - Abnormal bicarbonate secretion

Diagnostic Tests

- **Non-invasive**
 - Antibody tests
 - Urea Breath Tests
 - Stool antigen
- **Invasive**
 - Rapid Urease Tests
 - Histology
 - Culture

Antibody Tests

- **Used for initial diagnosis**
- **FDA approved tests are for serum IgG, antibody tests and are sensitive, specific, and cost effective**
- **IgA or IgM tests: unapproved and poor**
- **Titers decline slowly, limiting use for follow-up**
- **Saliva and urine tests are experimental**

Urea Breath Tests

Diagnose Active Infection

- **[13C] - urea**
 - stable isotope
 - non-radioactive
- **[14C]- urea**
 - radioactive isotope
 - special handling and disposal

World Health Organization

International Agency for Research on Cancer

Working Group Meeting - June 1994

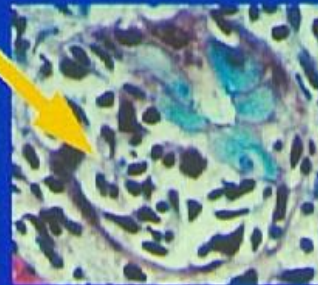
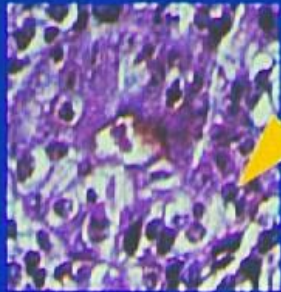
- **Conclusions:**

- There is sufficient evidence in humans for the carcinogenicity of infection with *H. pylori*.
- *H. pylori* is a Group 1 or definite carcinogen

GASTRIC MALT LYMPHOMA

MALT: Mucosa-Associated Lymphoid Tissue
- a benign reactive process consisting of lymphoid follicles

MALT LYMPHOMA: monoclonal proliferation of neoplastic B-lymphocytes infiltrating gastric glands (lymphoepithelial lesions)



Gastric Malt Lymphoma

Presentation

- **Clinical**

- **Asymptomatic!**
- **Dyspepsia**
- **Weight Loss**
- **Ulcer**

- **Endoscopic**

- **Mucosa appears normal**
- **Thick folds**
- **Ulcerations**

Gastric Malt Lymphoma

Effect of Treatment of *Hp*

- Cure of *H. pylori* infection results in remission of approx. 75% of gastric MALT lymphomas
- Regression usually occurs within 6 months, but may take longer
- No features predict unresponsiveness
- Recurrence of MALT lymphomas associated with reinfection

Antimicrobial Drugs

Used for *H. pylori*

- **Amoxicillin**
- **Bismuth**
- **Clarithromycin (macrolides)**
- **Metronidazole**
- **Tetracycline**
- **Proton pump inhibitors**

***H. PYLORI* Treatment**

PPI Therapies X 14 days

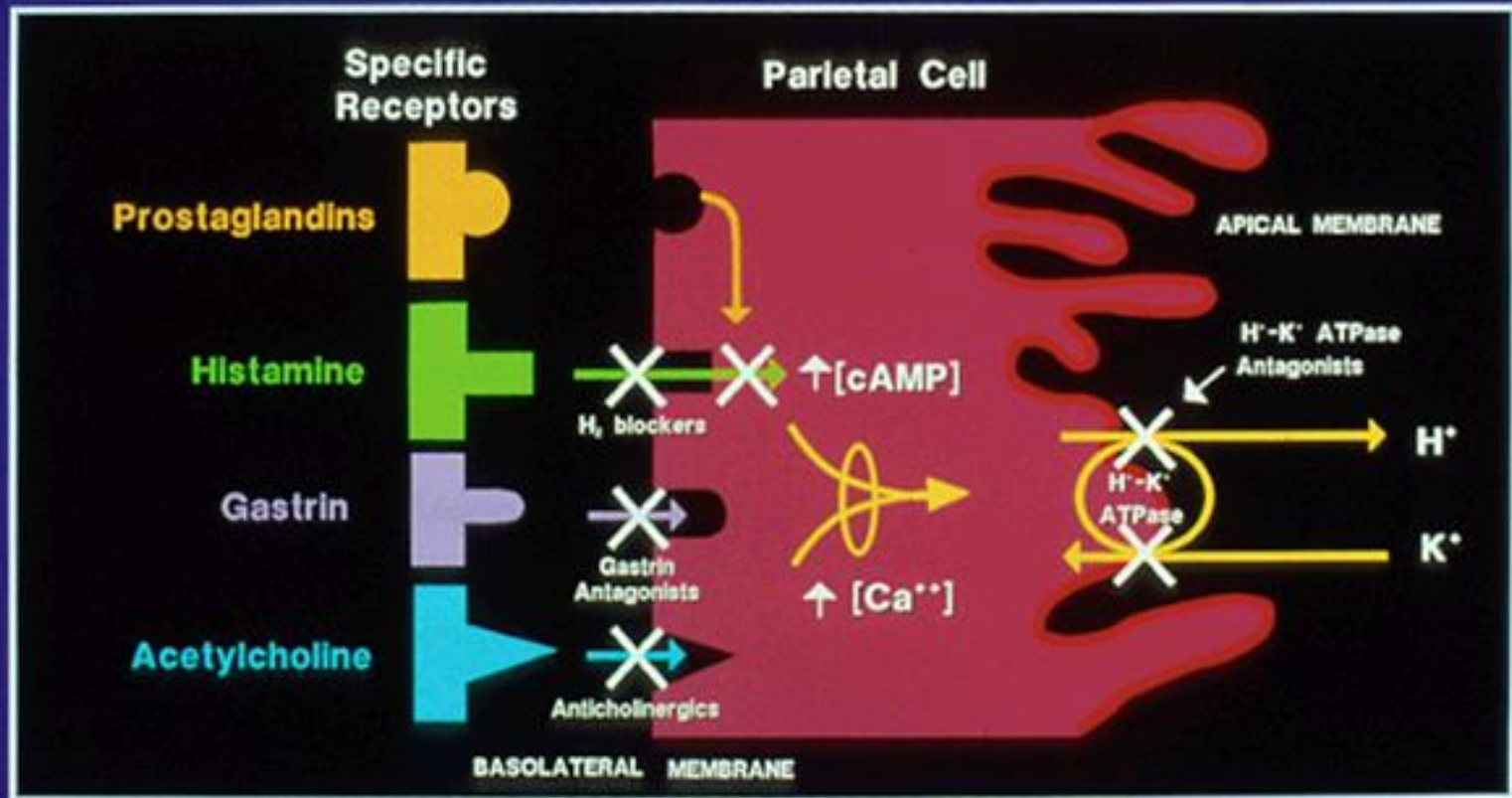
- **TRIPLE THERAPY (OAC)**

- Omeprazole 20 mg b.i.d.
- Amoxicillin 1000 mg b.i.d.
- Clarithromycin 500 mg b.i.d.

- **Lansoprazole can substitute for Omeprazole**



Parietal Cell Secretion is Regulated by Site-Specific Agonists and Antagonists

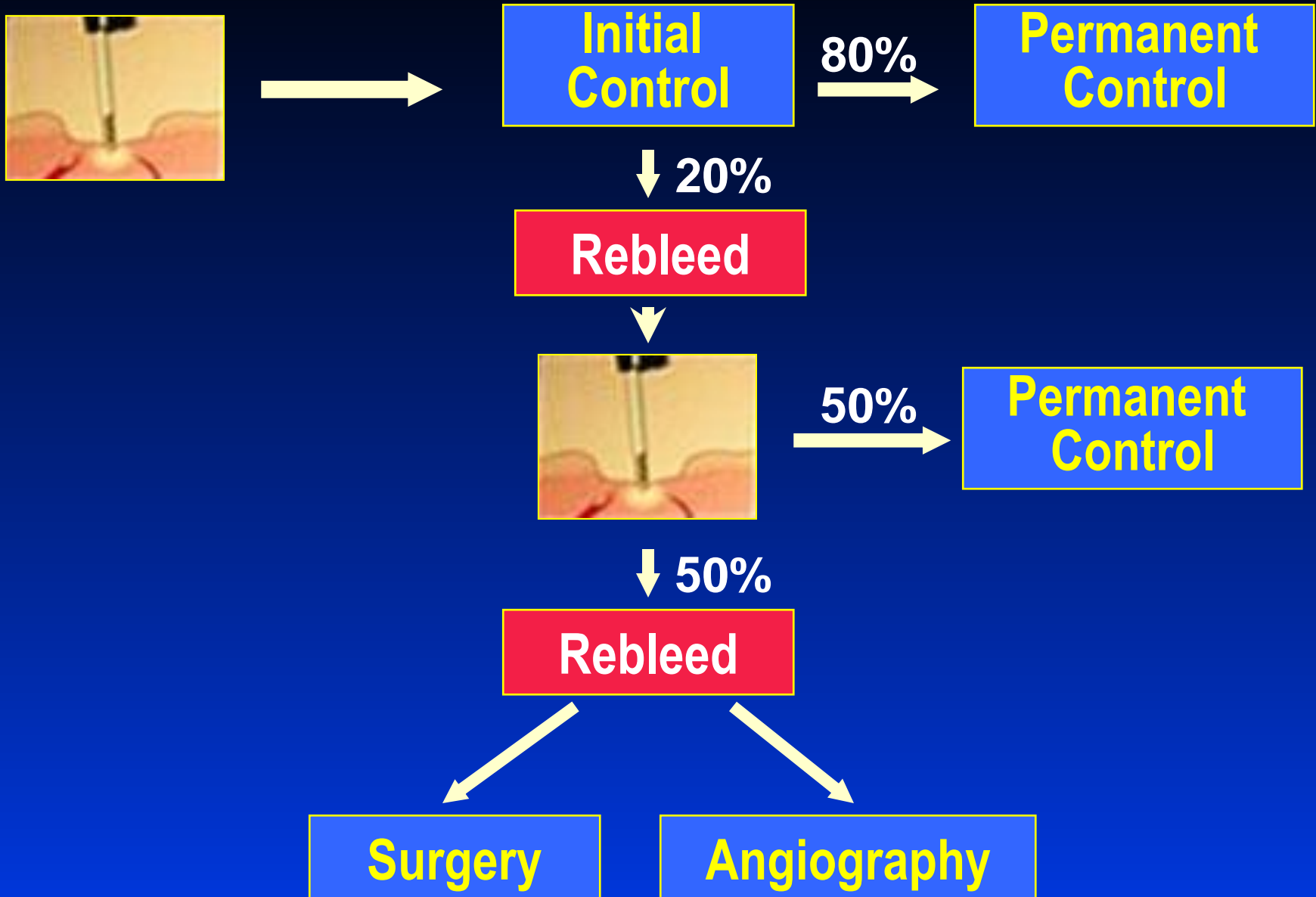


NSAID ULCER

Clues

- **History**
 - NSAID use, arthritis
- **Location**
 - Greater curve GU
 - Giant DU
- **Presentation**
 - UGI Bleeding
- ***H. pylori* tests**
 - neg. for *H. pylori*
- **Clinical Course**
 - Difficult to heal

Peptic Ulcer -Therapeutic Endoscopy

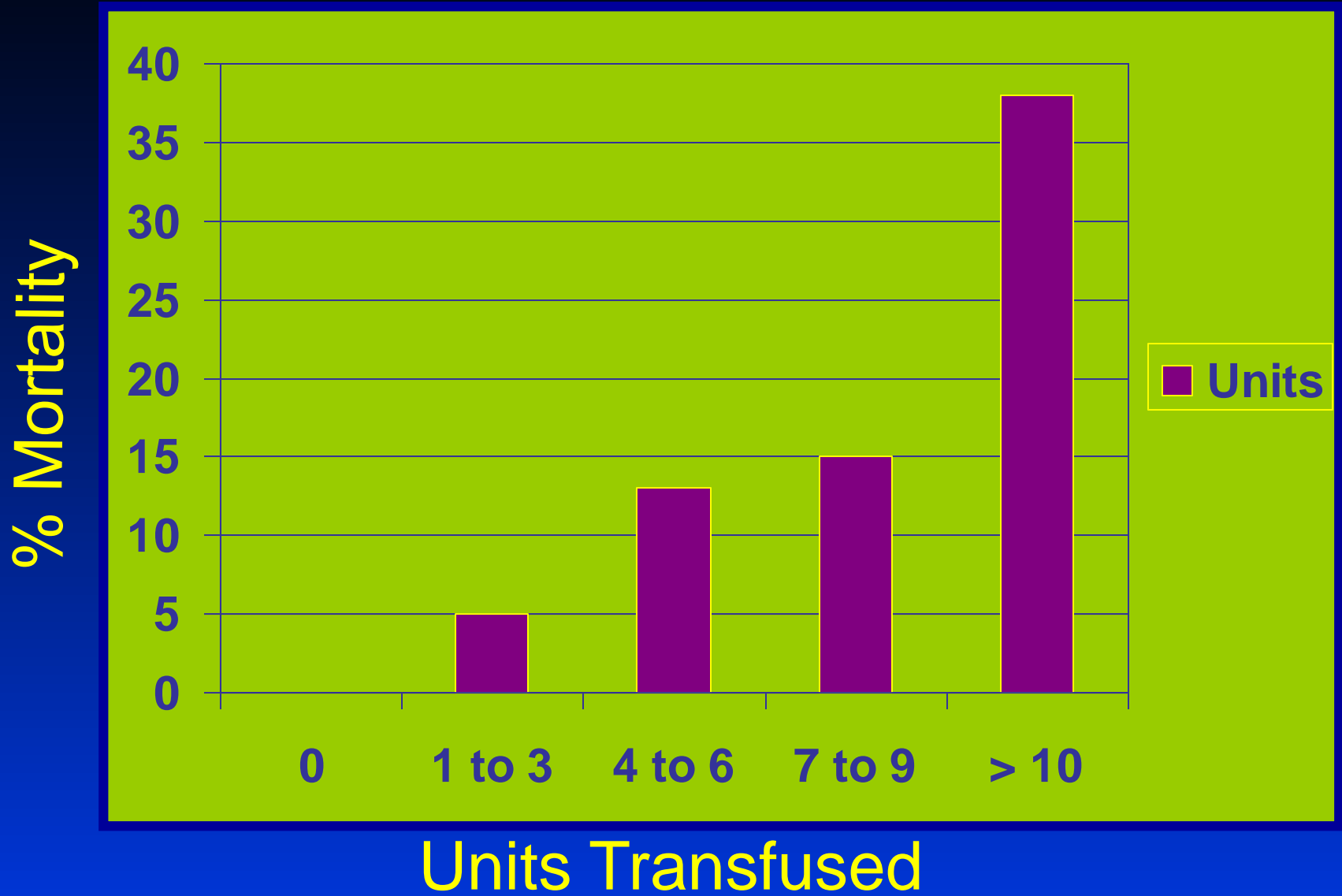


UGI BLEEDING

Adverse Clinical Prognostic Factors

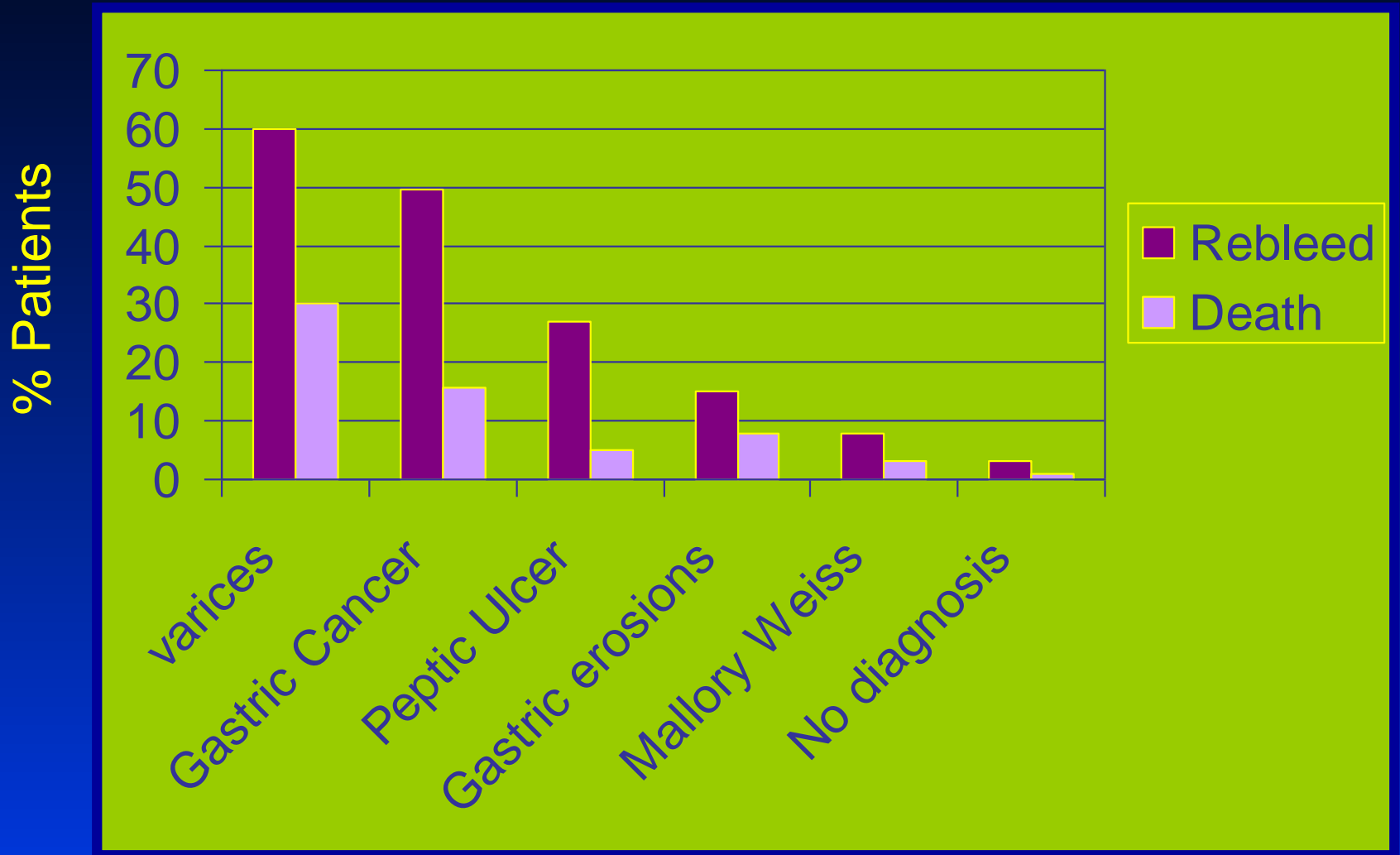
- **Shock, red blood**
- **Cause of bleeding
(varices or cancer)**
- **Comorbid disease**
- **Older age**
- **Onset in hospital**
- **Recurrent bleeding**

UGI Bleeding



UGI Bleeding

Outcome



UGI Bleeding – Stress Ulcer

Indications for Prophylaxis

- **Critical illness**
 - ventilator dependent > 48 hours
 - coagulopathy
- **Burns**
 - > 30% surface area
- **Head injury**
 - Neurosurgical patients

UGI Bleeding

Vascular Anomalies

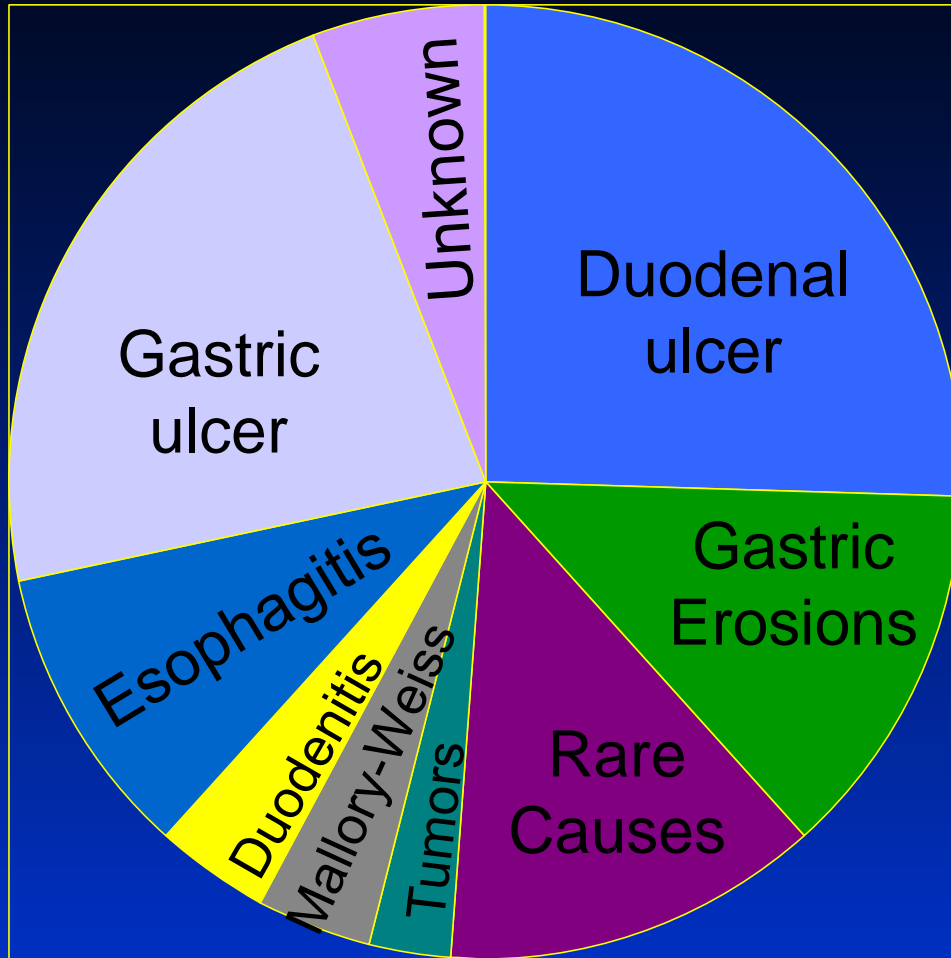
GUT

- **Vascular ectasia**
 - angiodysplasia
 - watermelon stomach
 - congestive gastropathy
- **Vascular tumor**
- **Dieulafoy's lesion**
- **AVM**

GUT + skin

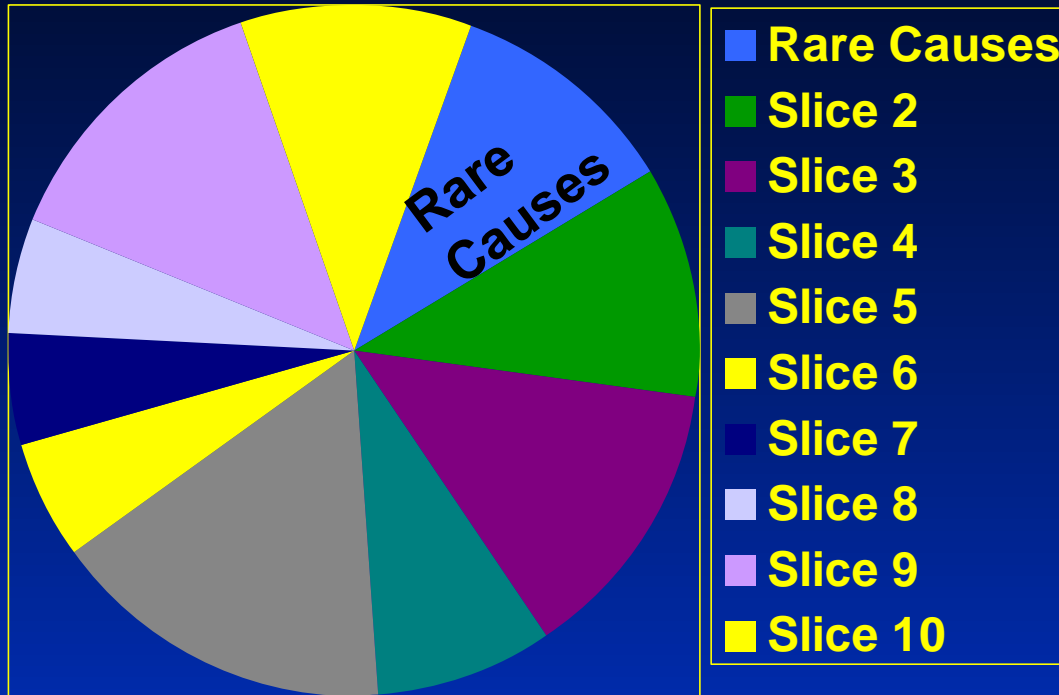
- **Olser-Weber-Reneu**
- **CRST**
- **Blue rubber bleb**
- **Ehlers-Danlos**

UGI Bleeding



- Duodenal ulcer
- Gastric erosions
- Rare causes
- Tumors
- Mallory-Weiss
- Duodenitis
- Esophagitis
- Gastric Ulcer
- Unknown

UGI Bleeding



- AVMs
- Stomal ulcer
- Dieulafoy's lesion
- Watermelon stomach
- Hemobilia
- Connective tissue disorder
- Kaposi's sarcoma
- Aorto-enteric fistula
- Benign tumors
- Others

Zollinger-Ellison Syndrome

Is a Clinical Triad Consisting of:

- Gastric acid hypersecretion
- Severe peptic ulcer disease
- Non-beta islet cell tumors of the pancreas

- The tumors produce gastrin (G17 & G34); referred to as “gastrinomas”
- Tumors localized usually to head of pancreas, duodenal wall or regional lymph nodes
- About 1/2 of gastrinomas are multiple and 2/3 are malignant
- About 1/4 have multiple endocrine neoplasia syndrome (MEN I) - tumors of parathyroid, pituitary, and pancreatic islets

Clinical Features that Distinguish ZE Syndrome from DU

- Diarrhea
- Weight loss/steatorrhea
- Large gastric folds
- Large amounts of gastric secretions
- Family history of endocrine tumor
- Intractable or post-surgical recurrence of ulcer disease
- Increased gastric acid secretion, decreased duodenal/jejunal pH
- Inactivation of lipase
- Mucosal Inflammation
- Trophic effect of gastrin
- Secretory effect of gastrin
- MEM I - parathyroid tumor/hyperplasia
- Acid hypersecretion due to gastrin-secreting tumor

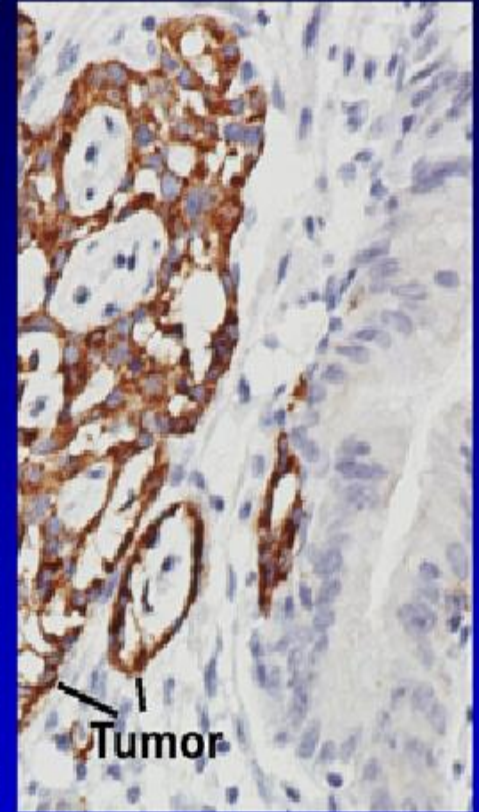
Carcinoid Tumor in Autoimmune Metaplastic Atrophic Gastritis With Infiltrating Tumor



Polyps & Atrophic Mucosa



Carcinoid Tumor



Infiltrating Tumor

Gastric Carcinoid Tumors: Main Features

Precursor State	Serum Gastrin	Primary Cell Type	Percent of Gastric Carcinoids	Percent of Gastric Potential
Autoimmune Metaplastic Atrophic Gastritis	↑	ECL	60-80	Low
MEN 1 (Z-E)	↑	ECL	15-20	Intermediate
Sporadic	NL	Mixed	~5	High

