STOMACH DYSPEPSIA. CHRONIC GASTRITIS. PEPTIC ULCERS OF STOMACH AND DUODENUM

Internal Medicine. Chapter Gastroenterology. Lecture # 4
Internal Medicine #2 with postgraduate trainining ONMedU
Performed by ass. professor Iablonska V.B.

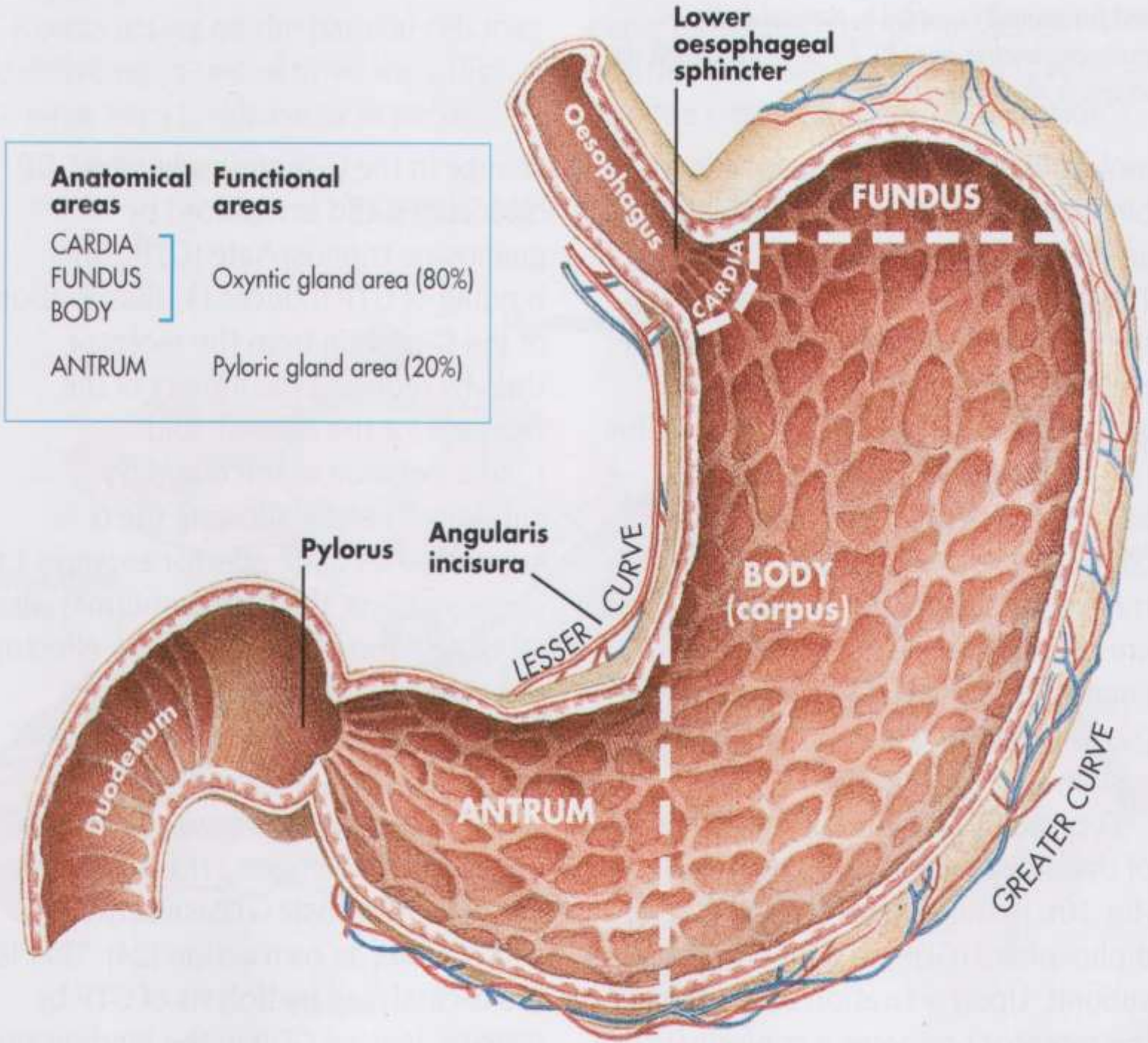


Fig. 3. Gross anatomical and functional areas of the stomach. Parietal cells are located in the oxyntic gland area, whereas gastrin cells are located in the pyloric gland area.

Stomach Dyspepsia

Functional dyspepsia subdivided:

- Postprandial distress syndrome
- Epigastric pain syndrome

according to Rome IV Criteria (2016)

Definition

Functional dyspepsia is a functional disorder characterized by the onset of dispeptic symptoms, epigastric pain or epigastric burning sensation immediately after a meal, with food and sometimes diminishes with food intake for epigastric pain syndrome

Epidemiology

It is known that 10-30 percent of the world's population suffers from functional dyspepsia.

Risks of developing functional dyspepsia:

- age,
- female,
- stress,
- low socio-economic status,
- Hp-infection,
- taking NSAID

Pathophysiology of FD

Causing factors of FD:

- delayed gastric emptying,

- deterioration of gastric accommodation degradation (accumulation of chyme in the antrum and decreased filling of the proximal stomach,

- gastric and duodenal hypersensitivity to stretching, acid and other stimuli distension,

- Hp – infection,

- low-intensity duodenal inflammatin, increased mucosal permeability, food antigens, duodenal eosinophilia,

- the impact of external factors (acute infections),

- psychosocial factors (anxiety, depression, neurotization).

Diagnostic criteria for functional dyspepsia

Postrandial distress syndrome
(minimum 3 times a week)
- postprandial feeling of overcrowding
- early satiety

Epigastric pain syndrome
(minimum 1 time a week)
- epigastric pain or burning
- nausea

Additional signs of functional dyspepsia
- postprandial epigastric distention
- belching

Symptoms are annoying and affect daily activity

Differential Diagnosis of Dyspepsia

- Peptic ulcer disease
- Gastroesophageal reflux
- Gastric malignancy
- Biliary pain
- Irritable bowel syndrome
- Drug induced dyspepsia
- Functional (non-ulcer) dyspepsia

Peptic ulcer disease

- Individual symptoms have **NOT** been useful in identifying organic from functional dyspepsia
- PUD found in 5-15% of pts with dyspepsia
  - *May be missed in pts receiving antisecretory therapy (Proton Pomp Inhibitor or Histamin 2 Receptor's Antagonist)*

  - Duodenal ulcer → *H pylori* 90%
  - Gastric Ulcer → *H pylori* 70%

GERD

- Most common symptoms are heartburn and regurgitation
- Clinical diagnosis
  - heartburn correlates poorly with 24-hr pH monitoring and esophagogastroduodenoscopy findings
- Reflux esophagitis found in 5-15% of pts with dyspepsia at endoscopy

Gastric Malignancy

- **Alarm Features in Dyspepsia**
  - Age older than 55 with new-onset dyspepsia
  - Family history of upper GI malignancy
  - Unintended weight loss
  - Progressive dysphagia
  - Odynophagia
  - Unexplained iron-deficiency anemia
  - Persistent vomiting
  - Palpable mass or lymphadenopathy
  - jaundice

Biliary Pain

- "Classic" biliary pain characterized by
  - episodic acute and severe upper abdominal pain in epigastrium or right upper qudrant
  - lasting at least an hour (often several hours or more)
  - Pain may radiate to back or scapula
  - Often associated with restlessness, sweating or vomiting

Drug Induced Dyspepsia

- NSAID- related dyspepsia is common
  - 20% of pts taking NSAIDS
  - 10-20% may develop peptic ulcer disease detectable by endoscopy
- Other drugs
  - Calcium channel blockers
  - Methylxanthines
  - Bisphosphonates
  - Potassium supplements
  - Antibiotics (erythromycin, metranidazole)
  - Orlistat, acarbose

Functional (non-ulcer) Dyspepsia

- Definition
  - **At least 3 month history of dyspepsia in which there is no obvious structural explanation for the symptoms**
- Accounts for up to 60% of all pts presenting with dyspepsia
- **Pathophysiology** is unclear yet overlapping disorders of upper gastro-intestinal motor and sensory function are implicated
  - 25-40% have delayed gastric emptying
  - 30% have altered visceral sensation
  - 20-60% have *H-pylori* induced gastritis
    - No association between *H-pylori* and any specific symptom profile

Clinical examination of patients with FD

- anamnesis and identifying “alarming” symptoms and iatrogenic causes (for example, taking NSAIDS)

- gastroduodenoscopy

- determination of the presence of Hp-infection

If eradication therapy is not effective, the diagnosis of functional dyspepsia can be considered.
If eradication therapy (6-12 months) is effective, the diagnosis of Hp-infection associated dyspepsia can be determine.

Treatment of FD

- lifestyle modification (refusal to drink coffee, alcohol, smoking)
- diet (frequent fractional meals in small portions, refusal to eat fatty foods)
- avoid taking NSAIDS
- eradication of Hp-infection (strategy test and treat)
- psychotherapeutic treatment
- treatment of concomitant gastroesophageal reflux disease

Drug therapy for patients with FD

First line drugs

- Prokinetics (domperidone, itopridum)
- Proton pump inhibitors (omeprazole, pantoprazolum) and H_2-histamine blockers (ranitidine, famotidine)

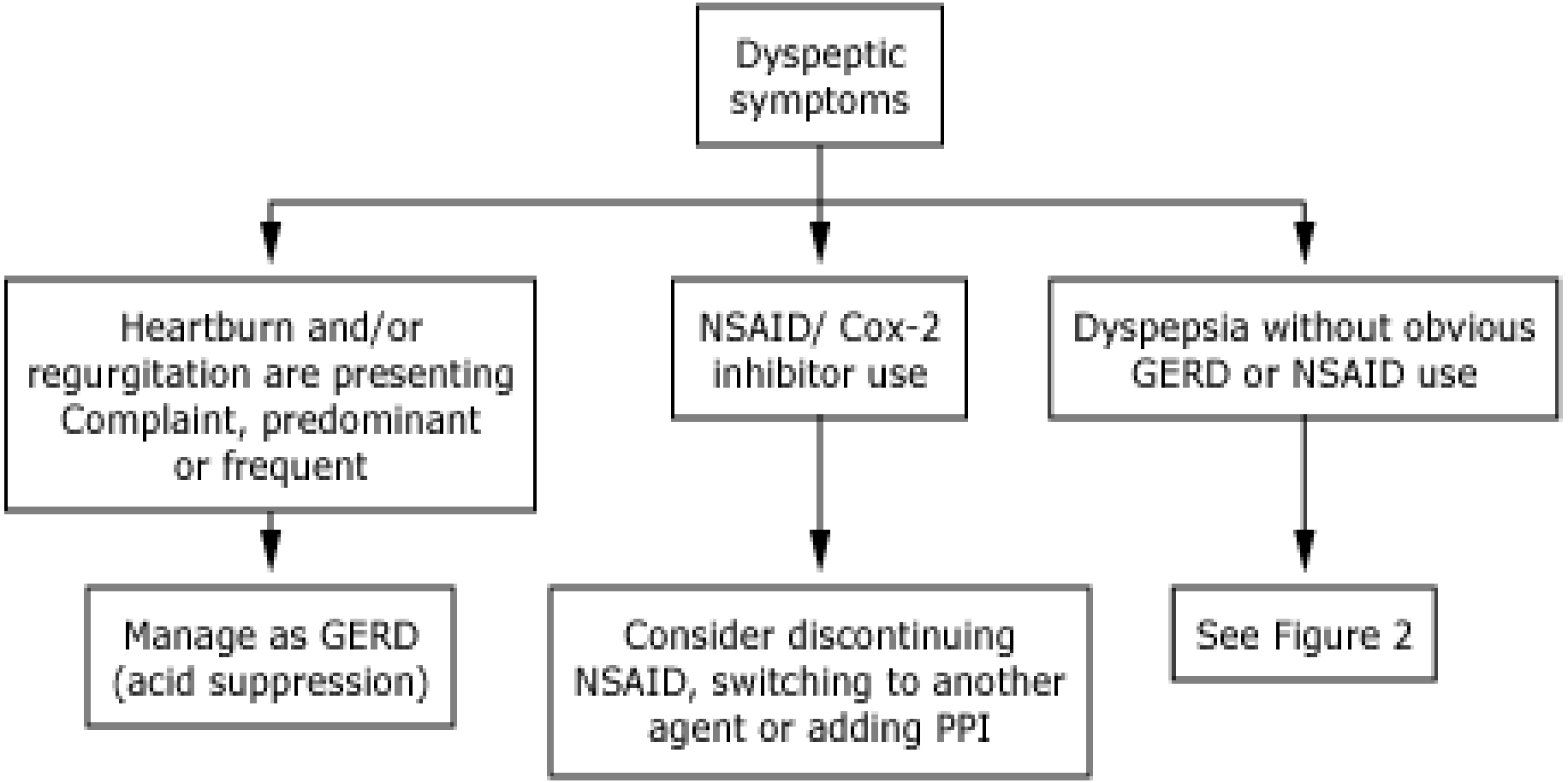
Second line drugs

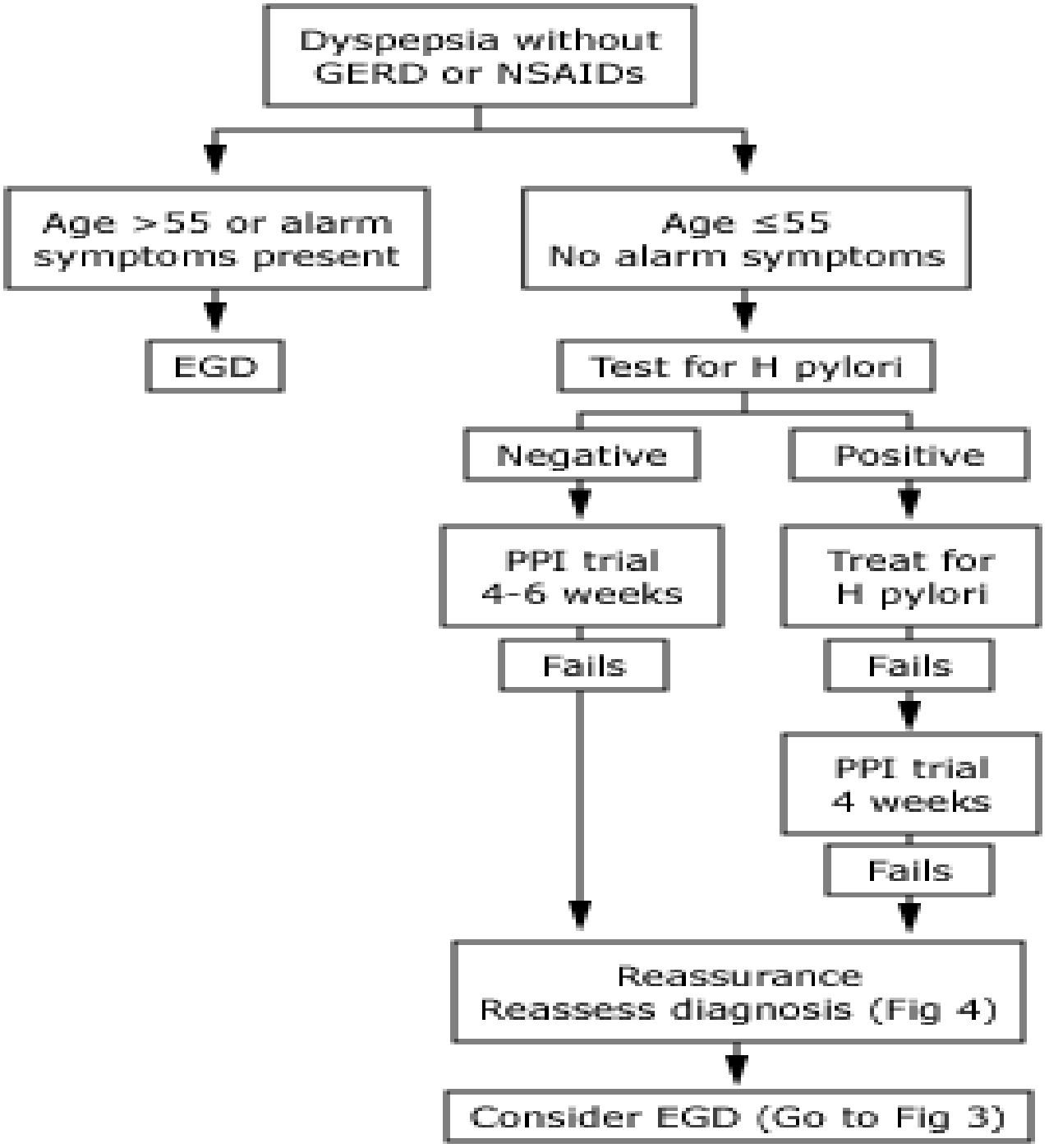
- Antidepressants (amitriptyline, paroxenus)
- Other psychotropic drugs with sedative and prokinetic properties (levosulpiride)
- Fundic reloxants (acotiamide, buspiron)
- Montelukast and H_1-histamine blockers
- Phytotherapy

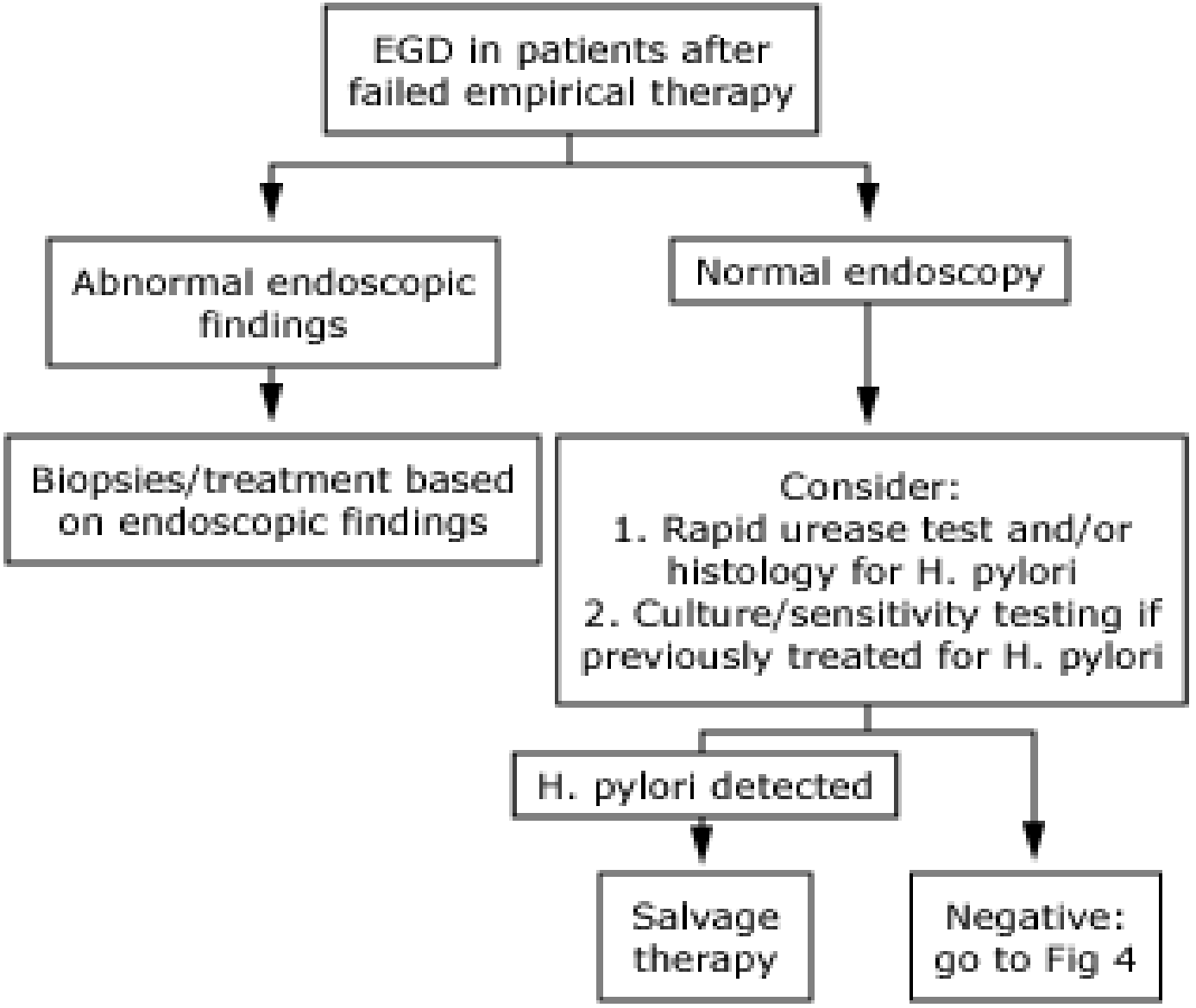
Diagnostic Strategies for the Evaluation of Dyspepsia

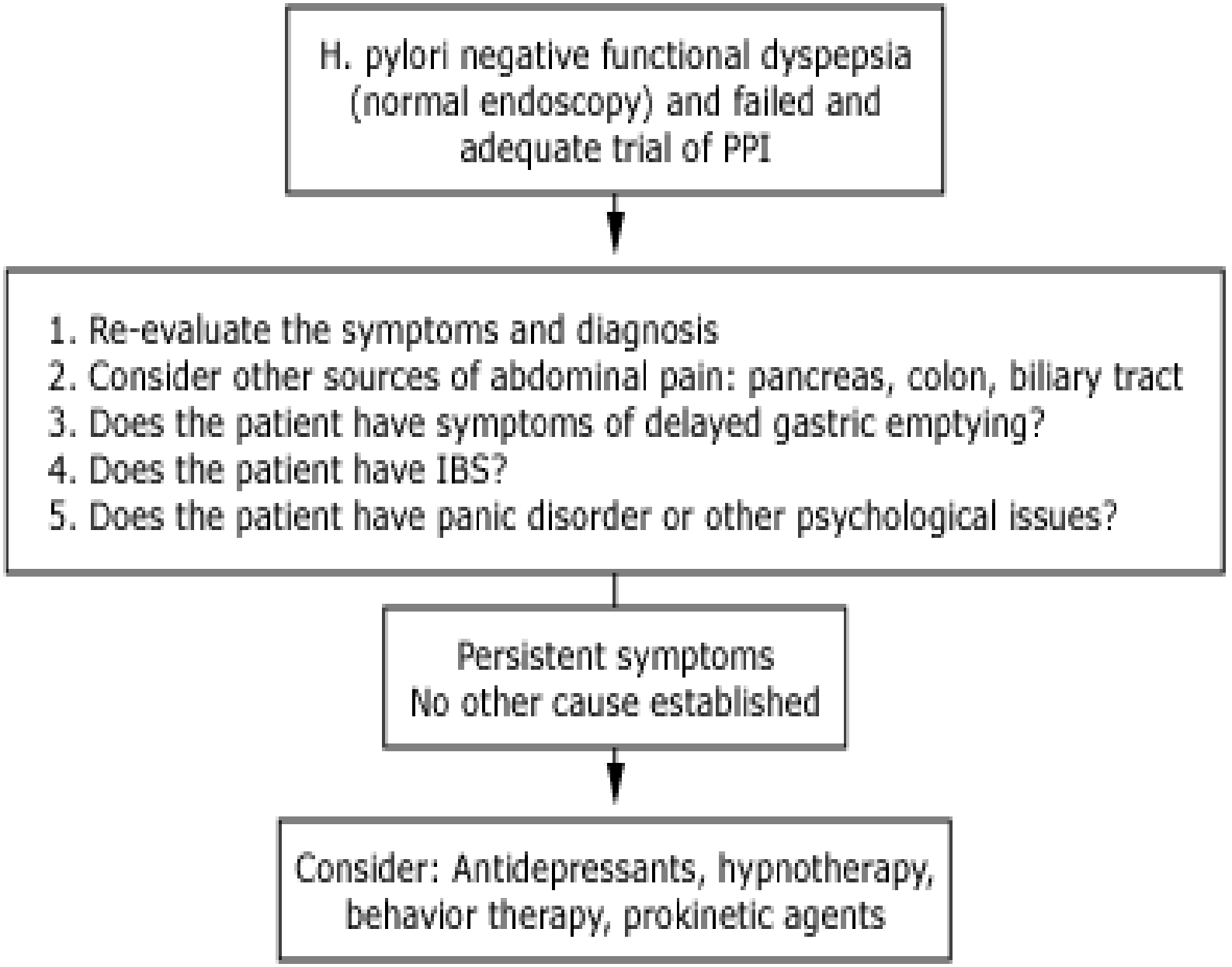
- Empiric Treatment with acid suppression
- Endoscopy in all patients
- Test for H-pylori and treat if positive

American Gastroenterological Association (AGA) guidelines for the management of Dyspepsia




Dyspepsia without GERD or NSAIDs
Age >55 or alarm symptoms present
EGD
Age ≤55 No alarm symptoms
Test for H pylori
Negative
Positive
PPI trial 4-6 weeks
Fails
Treat for H pylori
Fails
PPI trial 4 weeks
Fails
Reassurance Reassess diagnosis (Fig 4)
Consider EGD (Go to Fig 3)


EGD in patients after failed empirical therapy
Abnormal endoscopic findings
Normal endoscopy
Biopsies/treatment based on endoscopic findings
Consider:
1. Rapid urease test and/or histology for H. pylori
2. Culture/sensitivity testing if previously treated for H. pylori
H. pylori detected
Salvage therapy
Negative: go to Fig 4


H. pylori negative functional dyspepsia (normal endoscopy) and failed and adequate trial of PPI
1. Re-evaluate the symptoms and diagnosis
2. Consider other sources of abdominal pain: pancreas, colon, biliary tract
3. Does the patient have symptoms of delayed gastric emptying?
4. Does the patient have IBS?
5. Does the patient have panic disorder or other psychological issues?
Persistent symptoms
No other cause established
Consider: Antidepressants, hypnotherapy, behavior therapy, prokinetic agents

Case Presentation

- 34 year old patient - security guard
- 5 years of intermittent epigastric discomfort
- Bloating, postprandial nausea
- Smokes, drinks 3 beers/day,
- 4 coffees/day
- Ranitidine prescribed one year ago
  - Initially beneficial, not now
- Family history of peptic ulcer
- Examination is normal

Case Presentation

- You suspect functional dyspepsia
- The patient requests investigation (worried about cancer or infection)

What investigations would you do?

What management suggestions would you make?

Would you suggest any medication?

- The term ***gastritis*** is used to denote inflammation associated with mucosal injury
- Gastritis is mostly a histological term that needs biopsy to be confirmed
- Gastritis is usually due to infectious agents (such as Helicobacter pylori) and autoimmune and hypersensitivity reactions.

- Epithelial cell damage and regeneration without associated inflammation is properly referred to as "***gastropathy***."
- Gastropathy may be referred without histological evidence and just according to gross appearance in endoscopy or radiology
- Gastropathy is usually caused by irritants such as drugs (eg, nonsteroidal antiinflammatory agents and alcohol), bile reflux, hypovolemia, and chronic congestion.

Definition of Chronic gastritis (CG)

CG – chronic, inflammatory-dystrophic process in the gastric mucosa, which is accompanied by a violation of the processes of cell regeneration and progressive atrophy of the glandular epithelium.

Diagnosis of CG can be established only by:
- at endoscopic observations,
- histological evaluation of biopsy specimens.

Etiology

- **auto-immunologic factor**
  - high positive rate (90%) of serum anti-parietal cell antibody (APCA)
  - animal model: gastritis induced by injecting APCA repeatedly
  - high positive rate (75%) of serum anti-intrinsic factor antibody

Other factors

- H. pylori, other bacteria, viruses, fungi, parasites
- reflux of duodenal juice
  incompetence of pyloric sphincter
  post operate stomach
- chemical substances, medicines, heavy salty foods, food allergy, alcohol aging, environmental factors portal hypertension,sarcoidosis radiation damage, foreign bodies idiopathic factors, etc.

Etiological Classification of Chronic Gastritis

Kyoto Global International Consensus (2015)

I. Autoimmune CG (etiology unknown, autoimmune pathogenesis)
II. Infections CG
    1. Helicobacter pylori (Hp)-induced CG
    2. Bacterial non-Hp CG
        a) caused by enterococci
        b) caused by mycobacteria
        c) caused by pallid treponema (lues), secondary syphilitic CG
    3. Viral CG
        a) enteroviral CG
        b) cytomegaloviral CG

Etiological Classification of Chronic Gastritis

Kyoto Global International Consensus (2015)

4. Fungal CG
   a) CG with gastric mucomycosis
   b) CG with gastric pandidiasis
   c) CG with gastric histoplasmosis
5. Parasitis CG
   a)cryptosporidium-induced CG
   b) gastric strongylondosis
   c) gastric anisakiasis

III. CG due to external factors

1. Medicinal CG
2. Alcoholic CG
3. Radiation CG
4. Chemical CG
5. CG due to duodenal reflux

Etiological Classification of Chronic Gastritis

Kyoto Global International Consensus (2015)

IV. CG due to specific causes
    1. Lymphoblastic CG
    2. Menetrier's Disease
    3. Allergic CG
    4. Eozinophilic CG
V. CG due to other causes
    1. CG due to sarcoidosis
    2. CG due to vasculitis
    3. CG due to Crohn's Disease

Classification of Chronic Gastritis

(Sydney 1990, modified in Houston 1994)

Sydney Classification System includes 3 sectious

1. Topography

A) antral (type B)

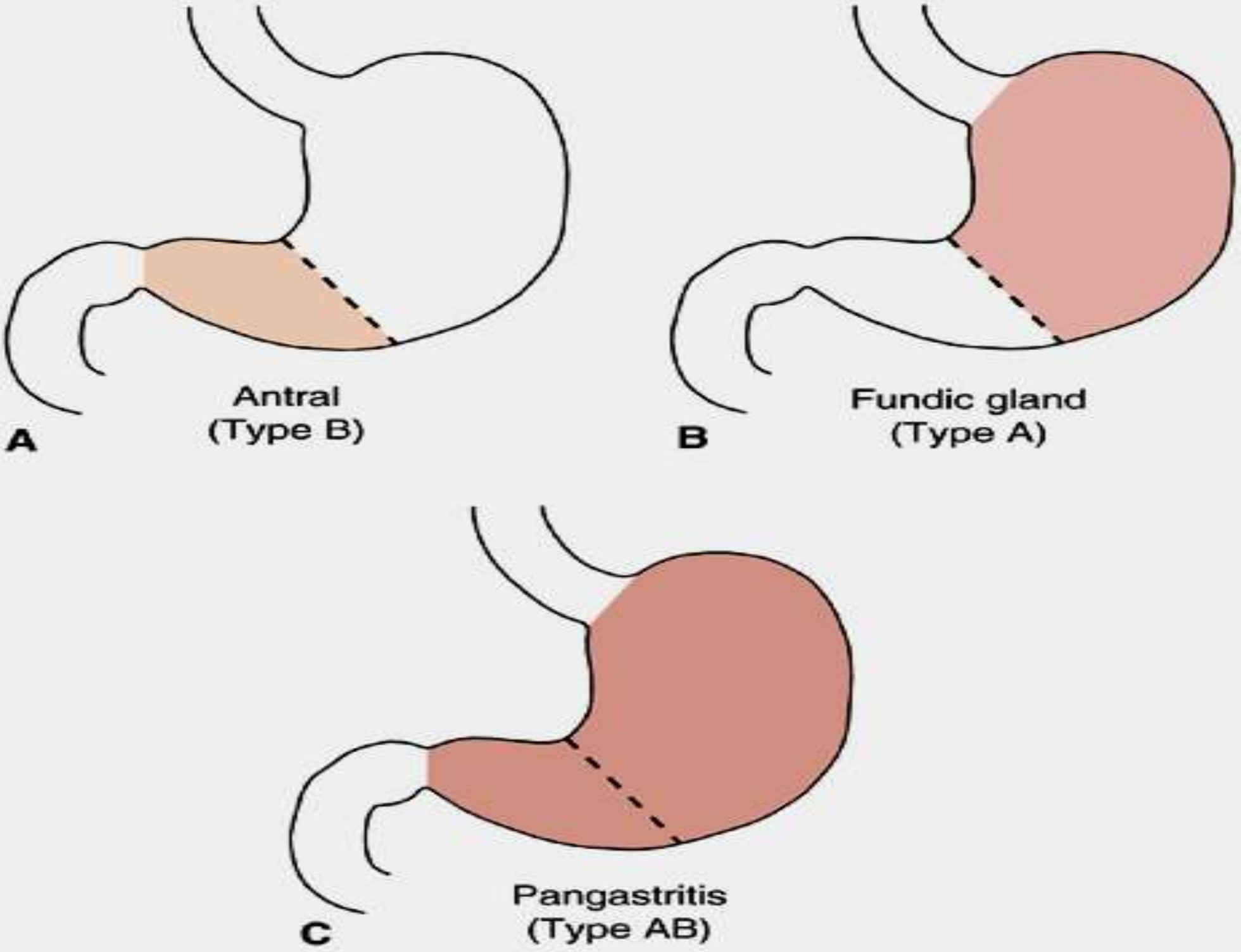
B) fundic gland (type A)

C) pangastritis (type AB)

2. Histology

- chronic superficial gastritis
- chronic atrophic gastritis

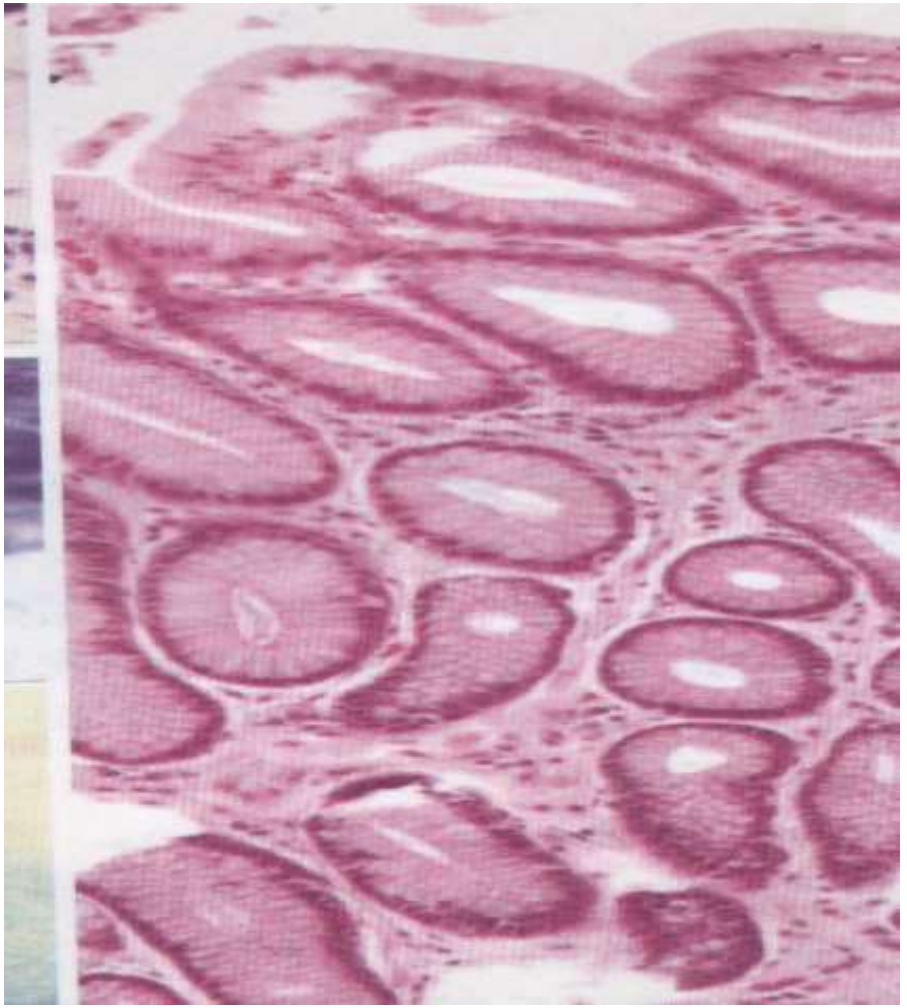
3. Etiology


A
Antral
(Type B)
B
Fundic gland
(Type A)
C
Pangastritis
(Type AB)

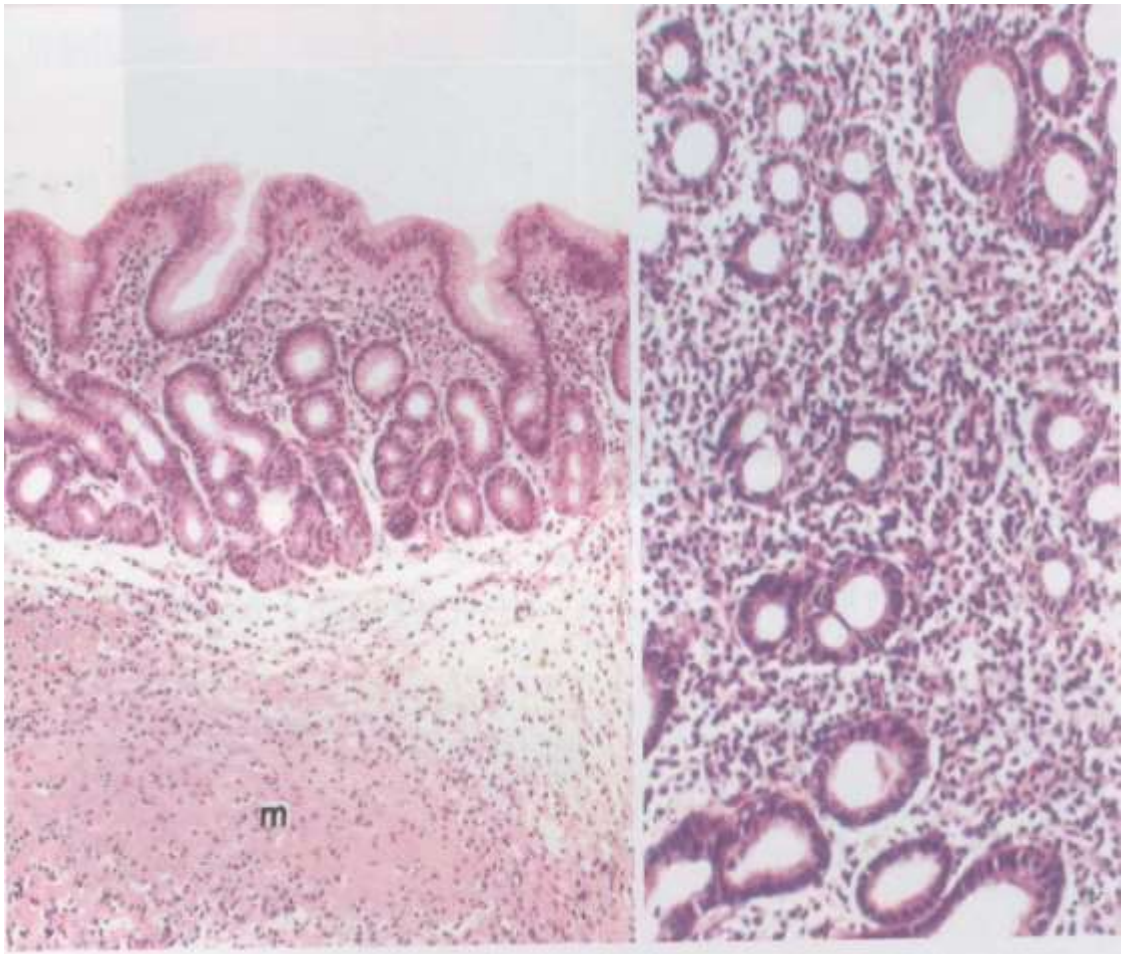
Histology

Chronic superficial gastritis

Chronic inflammation without glandular atrophy



Chronic atrophic gastritis



Chronic inflammation
with glandular atrophy

Classification of Chronic Gastritis (Sydney / Houston)

1. Chronic Atrophic Gastritis (autoimmune,diffuse gastritis of stomach corpus, associated with pernicious anemia, chronic multifocal gastritis, type A), present in 15-18% cases of CG.

2. Chronic Nonatrophic Gastritis (Helicobacteric antrial gastritis, type B), which represents almost 70% of all gastritis types.

3. Special forms of chronic gastritis:

- Chemical (reactive chronic gastritis, which occurs in case of bile, duodenum-stomach reflux (about 15%), after NSAID therapy (about 10%),
- Granulomatous (in case of Crohn's disease,Sarkoidosis, Tuberculosis),
- Eozinophilic (in case of Bronchial Asthma, food allergy),
- Lymphocytic (with manifested lymphocytic infiltration of epithelium),
- Gigant Hypertrophic Gastritis (Menetrier's disease),
- Radiation Gastritis

Clinical Manifestations

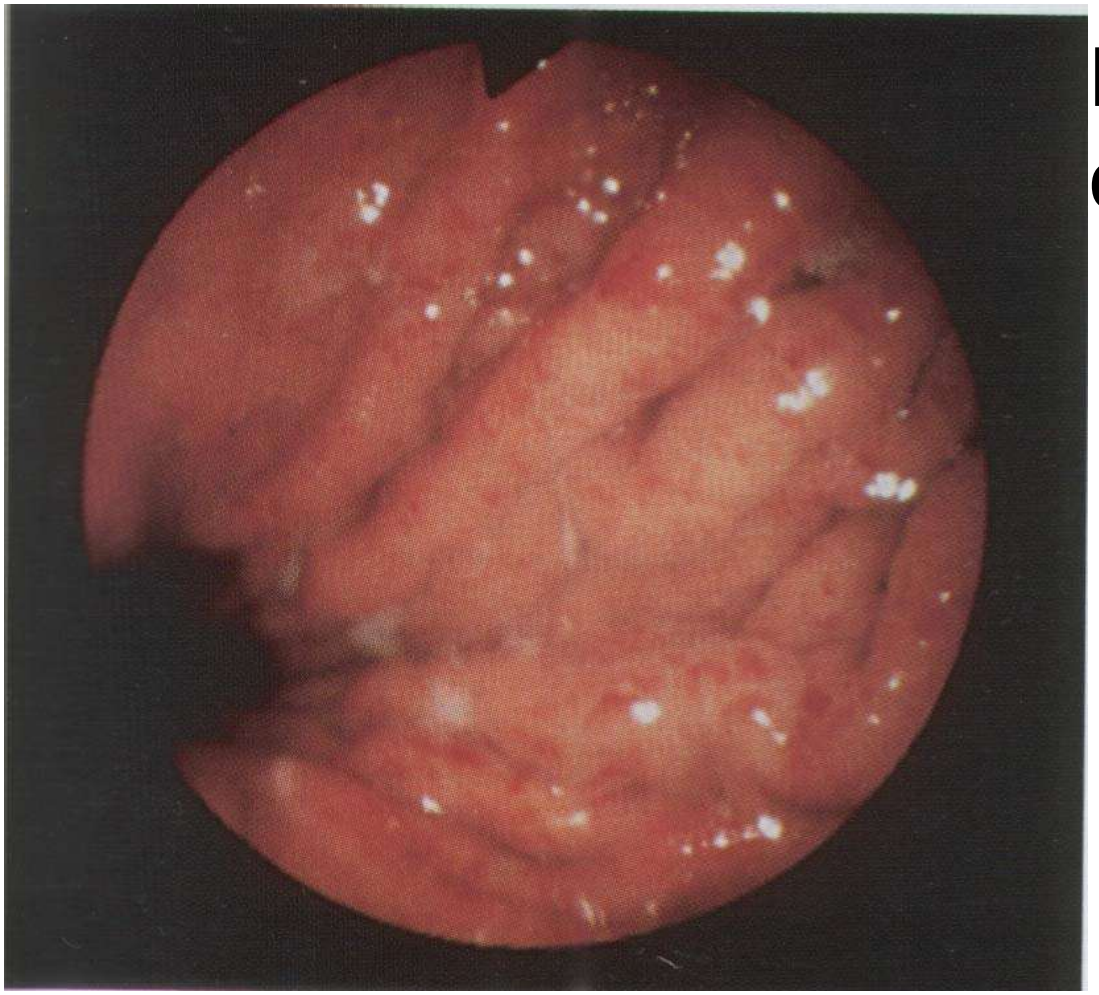
- Most of patients are asymptomatic
- Dyspepsia: upper abdominal pain or discomfort (bloating, belching, nausea,vomiting,diarrhea)
- Symptoms of anemia
- The symptoms are not specific
- No typical physical sign found

Laboratory and other examinations

- Endoscopy examination with mucosal biopsy - the most reliable method for diagnosis

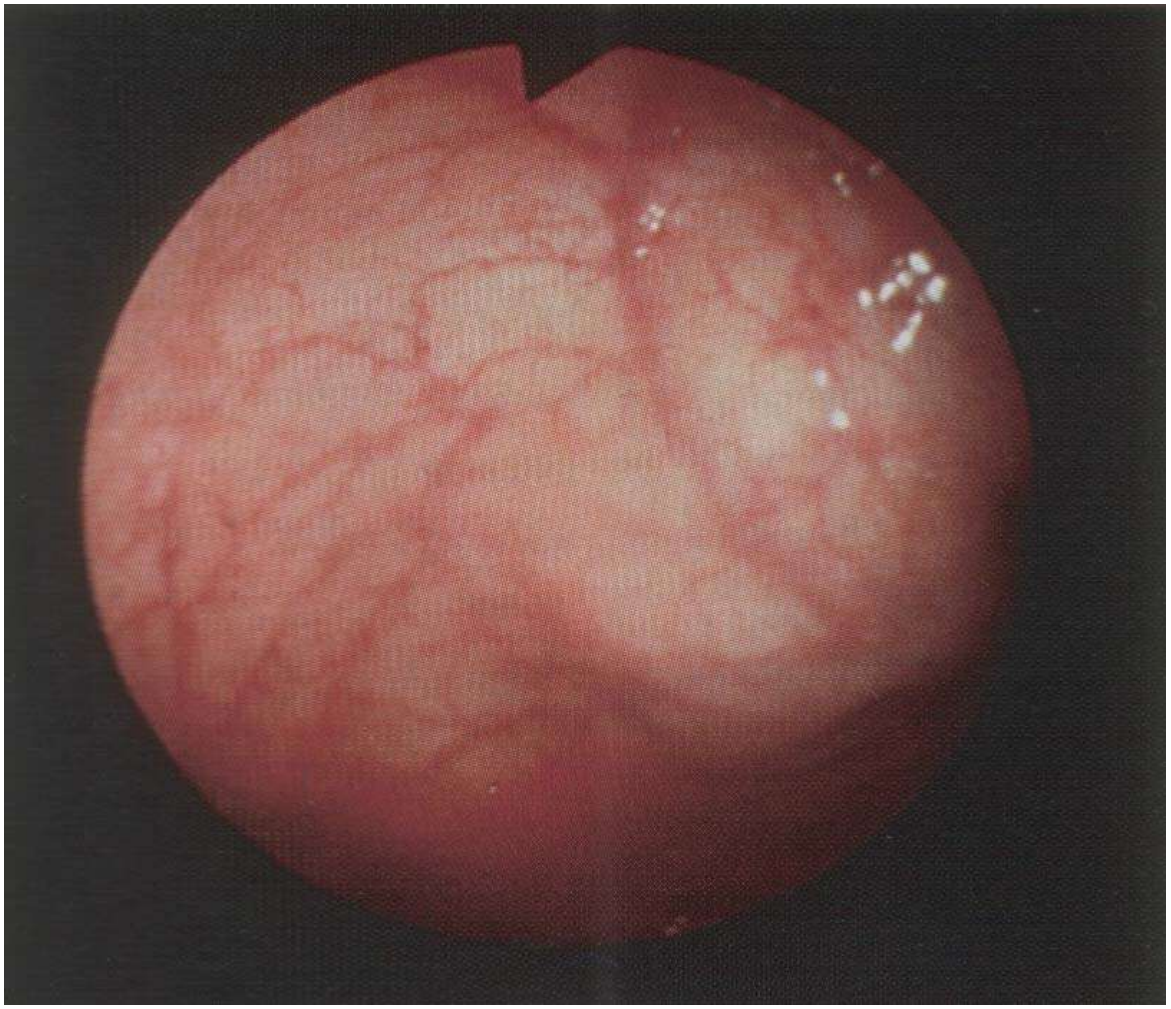
Endoscopy examination

- **superficial gastritis** edema, erythema, exudate, erosion



Edema
erythema

❖ **Atrophic gastritis**: grey, reduced mucosa folds, submucosal visible vessels



Visible vessels

Gastric biopsy protocol to diagnose gastritis

Biopsy specimens (circles) should be obtained from

- the greater and lesser curvatures of the autrum – 2 biopsies
- the greater and lesser curvatures of the body - 2 biopsies
- the incisura -1 biopsy

Note

imperfect co-relations between endoscopic appearances and histological classification, the final diagnosis should be made by histological examination.

Chronic Gastritis: Autoimmune Gastritis

Characterized by:

- **Antibodies mediated parietal cells damage, decrease intrinsic factor and acid production, increase serum gastrin levels**
- **Reduced serum pepsinogen I concentration**
- **Antral endocrine cell hyperplasia**
- **Vitamin B12 deficiency**
- **Defective gastric acid secretion**
- **Association with Hashimote thyroiditis, Addison's disease**
- **Patient at risk of developing gastric carcinoma/carcinoid tumos**

Hypertrophic Gastropathies: Menetrier's Disease

- **Rare; due to excessive secretion of tumor grouth factor (TGF-α)**
- **Diffuse hyperplasia of foveolar epithelium of the body and fundus**
- **Protein-losing enteropathy: hypoproteinemia**
- **Increased risk of gastric adenocarcinoma in adults**
- **Characteristic feature: hyperplasia of foveolar mucous cells**

Menetrier's Disease

- Epigastric pain – 65 percent
- Asthenia – 60 percent
- Anorexia – 45 percent
- Weight loss – 45 percent
- Edema – 38 percent
- Vomiting – 38 percent

- *80 percent of patients had hypoalbuminemia*

Treatment of Chronic Gastritis

- Individual diet
- Eradication of Hp-infection
- Proton pump inhibitors (omeprazole, antoprazolum) and H2-histamine blockers (ranitidine, famotidine) in case of increased gastric secretory function
- Substitution therapy (natural gastric juice, hydrochloric acid, acidin-pepsin) in case of decrease gastric secretory function
- Enveloping agents
- Vitamin B12 in case of megaloblastic anemia
- Prokinetics (domperidone, itopridum) in case of reflux gastritis
- Antihistamines in case of eosinophilic gastritis

Recommended Treatment Strategy for the Eradication of Helicobacter pylori

Fist-line therapy (10-14 days)

PPI (standard dose 2 times/d)
Clarithromycin (0.5g 2 times/d)
Amoxicillin (1g 2 times/d)

PPI (standard dose 2 times/d)
Clarithromycin (0.5g 2 times/d)
Metronidazole (0.5g 2 times/d)

Second-line therapy (10-14 days)

PPI (standard dose 2 t/d)
Bismuth (120mg 4 t/d)
Metronidazole (0.5g 3 t/d)
Tetracycline (0.5g 4 t/d)

PPI (standard dose 2 t/d)
Metronidazole (0.5g 2 t/d)
Tetracycline (0.5g 4 t/d)

PPI (standard dose 2 t/d)
Metronidazole (0.5g 2 t/d)
Amoxicillin (1g 2 t/d)

Third-line therapy (10-14 days)

PPI (standard dose 2 times/d)
Amoxicillin (1g 2 times/d)
Levofloxacin (0.5g 3 t/d)

Empiric rescue therapy

Treatment tallored to individual antibiotic sensitivity

Risk factors of peptic ulcer

You’re at risk for peptic ulcer disease if you:

- Are 50 years old or older.
- Diabetes may increase your risk of having *H. pylori*
- Drink alcohol excessively
- Smoke cigarettes or use tobacco.
- Have a family history of ulcer disease.

You’re at risk for NSAID-induced ulcers if you:

- Are age 60 or older (your stomach lining becomes more fragile with age).
- Have had past experiences with ulcers and internal bleeding
- Take steroid medications, such as prednisone.
- Take blood thinners, such as warfarin.
- Consume alcohol or use tobacco on a regular basis.
- Experience certain side effects after taking NSAIDs, such as upset stomach and heartburn.
- Take NSAIDs in amounts higher than recommended
- Take NSAIDs for long periods of time
- Stress does not cause an ulcer, but may be a contributing factor
- Chronic disorders such as liver disease, emphysema, rheumatoid arthritis may increase vulnerability to ulcers
- Improper diet, irregular or skipped meals
- Type O blood (for duodenal ulcers)

Classification of the Peptic Ulcers

1. Depending on the etiology:

a) Hp-positive

b) Hp-negative

- medicinal
- symptomatic (stressful, with Zollinger-Ellison syndrome, with hyperparathyroidism, with brain damage,shock conditions, cirrhosis of the liver, tenal failure,Crohn’s disease, other infections

Medicines with an ulcerogenic effect

- Non-steroidal anti-inflammatory drugs
- corticosteroids
- cytostatics
- antibiotics
- digoxin
- teophylline
- diazolin
- potassium and iron preparations

Classification of the Peptic Ulcers

2. Depending on the localization:

- Stomach ulcer (cardiac, subcardial portion, little big curvature, pyloric region),
- Duodenum ulcer (bulbus, post bulbar region),
- Combined (ulcers of the stomach and duodenum)

3. Depending on the number of ulcers:

- singl,
- multiple

Classification of the Peptic Ulcers

4. Depending on the diameter of the ulcer:

- small (no more than 0.5 cm),
- medium (0.5-1 cm),
- large (more than 1 cm),
- giant (more than 3 cm for stomach, more than 2 cm for duodenum),

5. Depending on the level of gastric secretion:

- with decreased acidic secretion,
- with increased acidic secretion,
- with preserved acidic secretion,

6. Phase:

- exacerbation,
- remission.

Complication of the Peptic Ulcer

- Penetration in pancreas, gall bladder, liver, colon, hepatoduodenal legomentum,

- Acute bleeding,

- Perforation,

- Stenosis (compensated, subcompensated, decompensated, reflux-esophagitis),

- Malignisation

Clinical Manifestations

- As a rule, the patient with an ulcer complains of dull, gnawing pain or a burning sensation in the midepigastrium or in the back. It is believed that the pain occurs when the increased acid content of the stomach and duodenum erodes the lesion and stimulates the exposed nerve endings.

- pyrosis (heartburn), vomiting, constipation or diarrhea, and bleeding. Pyrosis is a burning sensation in the esophagus and stomach that moves up to the mouth. Heartburn is often accompanied by sour eructation, or burping, which is common when the patient's stomach is empty. Fifteen percent of patients with gastric ulcers experience bleeding.

Assessment and Diagnostic Findings

- A physical examination may reveal pain, epigastric tenderness, or abdominal distention.
- A barium study of the upper GI tract may show an ulcer; however, endoscopy is the preferred diagnostic procedure because it allows direct visualization of inflammatory changes, ulcers, and lesions-biopsy.
- Stools may be tested periodically until they are negative for occult blood. Gastric secretory studies are of value in diagnosing achlorhydria. *H. pylori* infection may be determined by biopsy and histology with culture.
- There is also a breath test that detects *H. pylori,* as well as a serologic test for antibodies to the *H. pylori* antigen.

Comparing Duodenal and Gastric Ulcers

- **DUODENAL ULCER**
- Age 30–60
- Male: female 2–3:1
- 80% of peptic ulcers are duodenal
- Hypersecretion of stomach acid (HCl)
- May have weight gain
- Pain occurs 2–3 hours after a meal; often awakened between 1–2 AM;
- ingestion of food relieves pain
- Vomiting uncommon

GASTRIC ULCER

- Usually 50 and over
- Male: female 1:1
- 15% of peptic ulcers are gastric
- Normal—hyposecretion of stomach acid (HCl)
- Weight loss may occur
- Pain occurs 1/2 to 1 hour after a meal; rarely occurs at night; may be relieved by vomiting;
- ingestion of food does not help, sometimes increases pain
- Vomiting common

Differential Diagnosis

- Neoplasm of the stomach
- Pancreatitis
- Pancreatic cancer
- Diverticulitis
- Nonulcer dyspepsia (also called functional dyspepsia)
- Cholecystitis
- Gastritis
- GERD
- MI—not to be missed if having chest pain

Most helpful diagnostic examining

- Endoscopy

- X-ray (not obedient for non-complicated cases)

- Examining of secretory function (increasing of basal and stimulating secretion fraction) – is helpful to define functional disorders but not ulcer itself

- Helicobacter pyloric contamination

Gastric analysis includes measurement of:

Basal acid output (BAO)

- ✓ **Acid output of gastric juice collected via NGT over a 1-hour period on an empty stomach**
- ✓ **Normal = < 5 mEq/hr**

Maximal acid output (MAO)

- ✓ **Acid output of gastric juice that is collected over 1 hour after pentagastrin stimulation**
- ✓ **Normal = 5 – 20 mEq/hr**

BAO:MAO ratio - normally 0.20:1

Detection of *H. pylori*

Diagnostic methods	Sensitivity
Noninvasive type	
- Urea breath test	>95%
- Stool antigen test	>90%
- Serology: IgG	80-90%
Invasive type	
- Histology	>95%
- Microbiological culture biopsy	>95%
- Rapid urease test	>95%

Treatment goals

- Eradicate contamination of Hp-infection

- To reduce Peptic Ulcer symptoms and provide reparation of ulcer defect

- Not only get the healing of defect but restitute functional capacity of mucous membrane

- Prevent development of exacerbations and complications

Basic principles of the managing the patient with the Peptic Ulcer

- Reject of smoking, alcohol taking.

- Stop to get non-steroid and steroid medications, if it can’t be stopped to decrease dosages.

- Rational feeding. It means frequent intake 5-6 times per day with excluding of spicy products.

Medication treatment

- Helicobacter pylori eradication.

- Suppressing of acidity and peptic factors production.

- Correct motor evacuative function.

- Stimulation of reparative processes.

Management of Hp-infection

The Maastricht Consensus V

Algorithm of the Anti-Helicobacter pylori therapy – 1st line

Low (<15%)	High (>15%) clarithromycin resistance		
	Low metronidazole resistance	Low dual clarithromycin and metronidazole resistance (<15%)	High dual clatithromycin and metronidazole resistance (>15%)
Standard Triple therapy (PPI-CLA-AMO) or bismuth containing quadruple therapy	Triple therapy (PPI-amoxicillin-metronidazole)	Bismuth quadruple or concomitant non bismuth containing quadruple therapy	Bismuth containing quadruple therapies

Management of Hp-infection

The Maastricht Consensus V

Algorithm of the Anti-Helicobacter pylori therapy – 2nd line

Ineffectiveness of standart triple therapy (PPI-CLA-AMO)	Ineffectiveness of bismuth containing quadruple therapy	Ineffectiveness of non bismuth containing quadruple therapy
Bismuth containing quadruple therapy or triple/ quadruple therapy with levofloxacin	Triple/ quadruple therapy with levofloxacin	Bismuth containing quadruple therapy or triple/ quadruple therapy with levofloxacin

Management of Hp-infection

The Maastricht Consensus VI (2022)

- In the modern algorithm of eradication therapy in accordance with the Maastricht VI / Florence Consensus, preference has been given to quadruple therapy with the use of bismuth drugs.

- The value of triple therapy with clarithromycin has decreased.

- There is a rapid increase in the resistance of H.pylori to fluoroquinolones.

- Bismuth-containing quadruple therapy with amoxicillin and tetracycline and triple therapy with rifabutin are among the final eradication protocols.

Evaluation/Follow-up/

- H. Pylori Positive: retesting for control efficacy
  - Urea breath test—no sooner than 4-6 weeks after therapy to avoid false negative results
  - Stool antigen test—an 8 week interval must be allowed after therapy.
- H. Pylori Negative:
  - evaluate symptoms after one month.

Indications for surgical treatment of Peptic Ulcers

- Complications of ulcers (penetration, bleeding, perforation, stenosis, malignisation)

- Ineffectiveness of modern conservative treatment

- Long-term incurable stomach ulcers

- Symptomatic ulcers with hyperparathyroidism, gastrinoma

Hypertrophic Gastropathies: Zollinger-Ellison Syndrome

- **The cause of the formation of peptic ulcers is a gastrin-secreting tumors (gastrinomas) most commonly found in pancreas or duodenum**
  - ✓ **60% - 90% of gastrinomas malignant**
  - ✓ **25% of patients - men**

- **Clinical: duodenal ulcers or chronic diarrhea**

- **Morphology:**
  - ✓ **fivefold increase in number of parietal cells - doubling of oxyntic mucosal thickness**
  - ✓ **Hyperplasia of mucous neck cells**
  - ✓ **Mucin hyperproduction**
  - ✓ **Proliferation of endocrine cells within mucosa**

Zollinger-Ellison Syndrome

- **0.1 to 1 percent of patients with peptic ulcer disease**
- **Underestimation!**
  - **symptoms similar to typical peptic ulcer**
  - **symptoms may not be controlled by standard doses of an antisecretory drug**
  - **patients may not be tested for hypergastrinemia**
- **Multiple ulcers and large ulcers**
- **Persistent recurrence and frequent complications**
- **Ulcers combined with poorly controlled diarrhea**
- **Ulcer in atypical site-postbulbar part of the duodenum, jejunum**
- **Resistant ulcer**
- **Enlarged folds**
- **Ulcers after surgery**
- **Concomitant severe reflux-esophagitis**