

# POLTAVA STATE MEDICAL UNIVERSITY

Internal medicine №1 department

**Dyspepsia**  
**Chronic gastritis**  
**Peptic ulcer**

# Dyspepsia



**Symptoms may include epigastric pain, epigastric burning, postprandial fullness, and early saturation; abdominal bloating and nausea / vomiting, or other manifestations that indicate upper gastrointestinal involvement and lasts for at least 4 weeks**

# **UP TO 40-65% OF THE POPULATION sometimes has dyspeptic disorders due to:**

- ❖ **much meals (surfeit)**
- ❖ **eating different foods during the feast**
- ❖ **fast food**
- ❖ **"Breakdowns" during the diet**
- ❖ **monotonous nutrition**
- ❖ **long bed mode**
- ❖ **medication**



**MOTOR AND PERISTALTICS INVERSION OF ALL THE  
PARTS OF THE GUT**

# **Uninvestigated dyspepsia**

**It is established for all patients during the initial visit to the doctor, before carrying out laboratory and instrumental examination, which allow to determine the final clinical diagnosis.**

**This primary syndrome diagnosis requires:**

- empirical symptomatic or anti-Hp treatment;**
- further examination of the patient (including EGDS) to identify organic or functional causes of dyspepsia.**

# Diagnostic search

**Primary patient  
with dyspeptic  
symptoms**

Required EGDS is indicated:  
Age > 45 years  
Reception of NSAIDs  
Alarming symptoms

Duration of symptoms  
less than 4 weeks:  
calming the patient,  
explanation of symptoms,  
general recommendations

Duration of symptoms more than 4 weeks:  
clinical evaluation of symptoms

GERD

**Uninvestigated dyspepsia**

IBS

Symptoms  
resolution

Different variants of  
patients management :

Empirical treatment  
without examination

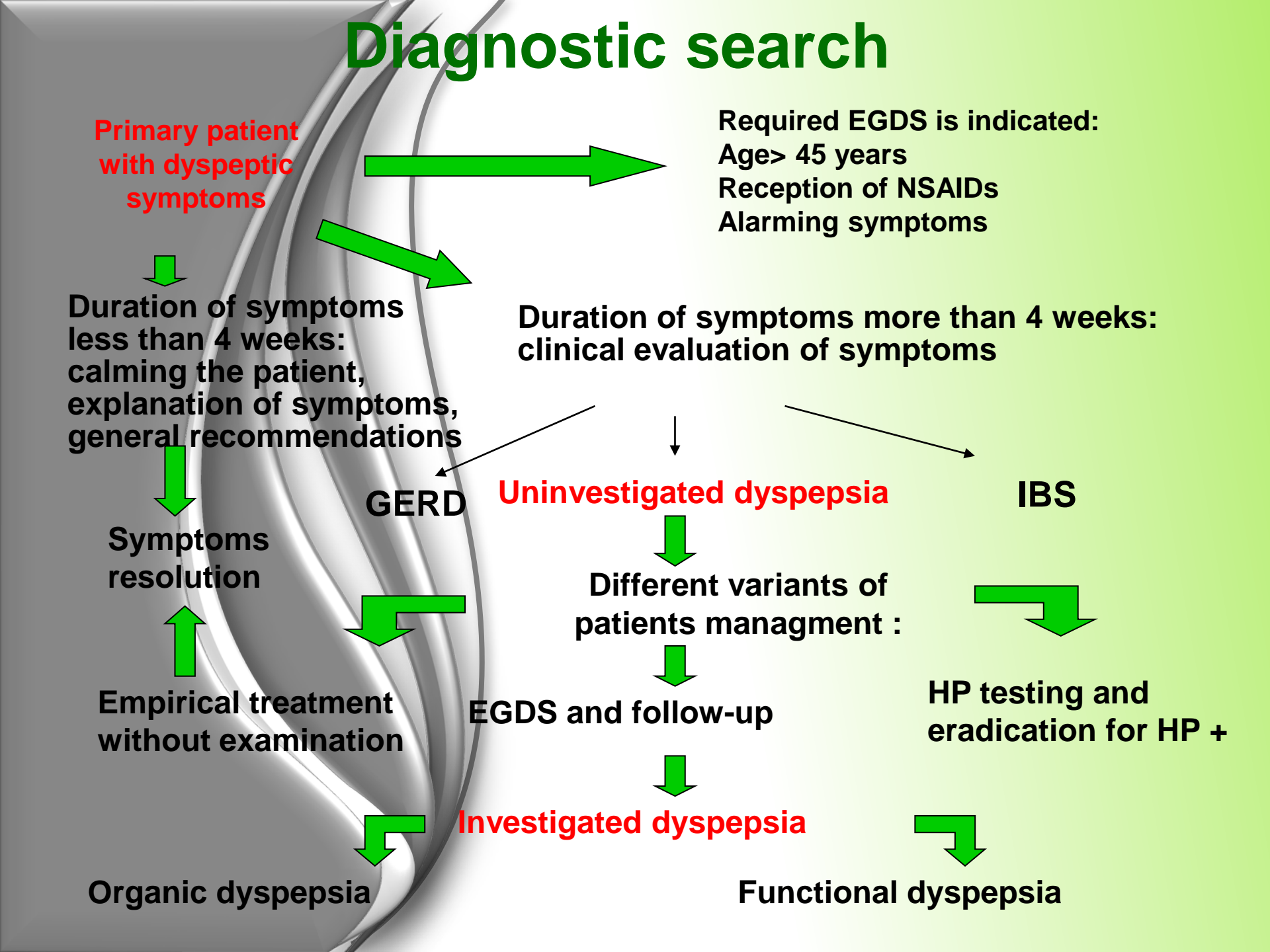
EGDS and follow-up

HP testing and  
eradication for HP +

Organic dyspepsia

**Investigated dyspepsia**

Functional dyspepsia



# **The main symptoms of dyspepsia**

- Pain and / or burning sensation in the epigastrium at midline**
- Feeling of fullness after meals**
- Feeling of early saturation**
- Nausea and / or vomiting**
- Heartburn**
- Belching, aerophagy, regurgitation**
- Abdominal distention in the epigastrium**



# The main signs of dyspepsia

- ❖ **Epigastric pain / discomfort - 90%**
- ❖ **Postprandial belching - 75%**
- ❖ **Bloating - 75%**
- ❖ **Postprandial nausea - 50%**
- ❖ **Abdominal distension - 45%**
- ❖ **Vomiting - 50%**
- ❖ **Weight loss - 30%**
- ❖ **Nausea and vomiting - 20%**

# Potential causes of secondary (organic) dyspepsia

## Structural changes of the gut

### → Frequent:

Peptic ulcers of the stomach and / or duodenum

GERD

Gastritis chronic

### → Less frequent:

Diseases of the biliary tract

Pancreatitis

### → More rare:

Tumors of the stomach, pancreas or gut

Other infiltrative diseases of the stomach

Malabsorption syndrome

Vascular anomalies



# Potential causes of secondary (organic) dyspepsia

## Medicines:

- NSAIDs (including specific COX-2 inhibitors)
- Alcohol
- Oral antibiotics
- Theophylline
- Digitalis
- Iron, potassium containing medicines

# Potential causes of secondary (organic) dyspepsia

Mixed :

- Diabetes mellitus
- Hyper- or hypothyroidism
- Hyperparathyroidism
- Electrolyte imbalance
- CIHD
- Diseases of connective tissue
- Chronic intestinal pseudo-obstruction
- Liver Diseases (Caused by Stretching of the Liver Capsule)

# Dyspepsia uninvestigated and investigated

- All the patients with dyspeptic symptoms are etiologically distributed:
- 1. For organic, systemic or metabolic causes - **secondary** (confirmed by diagnostic methods)
  - PU, gastric cancer, side effect of drugs;
  - HP-associated dyspepsia (Kyoto consensus)
  - disappears after HP eradication
- 2. **Functional dyspepsia** - symptoms are not explained by diagnostic methods

# Functional dyspepsia

- **Functional dyspepsia (FD) is a medical condition that is characterized by one or more of the following symptoms: epigastric pain, epigastric burning, postprandial fullness, and early saturation that are unexplained after a routine clinical evaluation.**

# Functional dyspepsia


## **1. Postprandial Distress Syndrome (PPDS):**

- Dyspeptic complaints related to meals

## **2. EPS:**

- epigastric pain or burning, which occurs not only after meals but also on an empty stomach, while eating and even decreases immediately after meals.

## **3. Overlap Syndrome - PPDS + EPS**



**Experts from the Roman Foundation  
agreed on the update  
definition of  
functional gastroenterological  
diseases (FGD):  
these are  
disorders of interaction between the  
brain and the digestive system  
(brain-gut disorders).**



# **Classification of the gastroduodenal disorders:**

## **Functional dyspepsia:**

- postprandial distress syndrome (PPDS)
- epigastric pain syndrome (EPS)

## **Disorders accompanied by belching:**

- excessively supragastric
- excessively gastric

## **Vomiting disorders:**

- Chronic nausea and vomiting syndrome
- Cyclic vomiting syndrome
- Cannabinoid vomiting syndrome

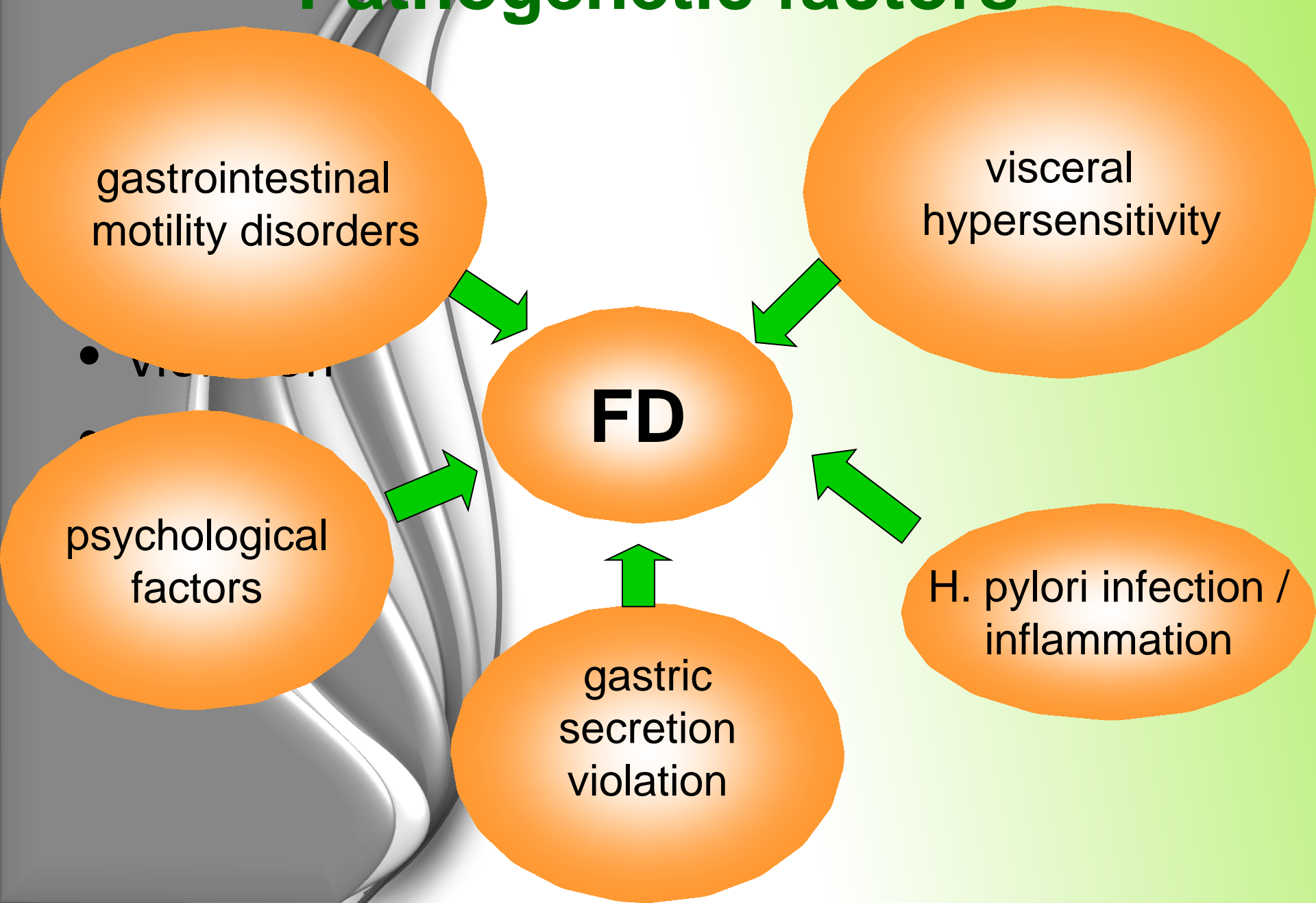
## **Rumination Syndrome**

# FD risk factors

- age and gender (FD at 1.5-2.5 times more common among young women);
- heredity (20-25% of patients);
- social status (more often representatives of "higher" and "lower" social step become ill);
- chronic stress;
- increased individual sensitivity to various external influences;
- bad habits (smoking),  
coffee and alcohol are unrelated;
- uncontrolled medication (NSAIDs)
- *Helicobacter pylori* infection

The frequency of FD - 10-30%.

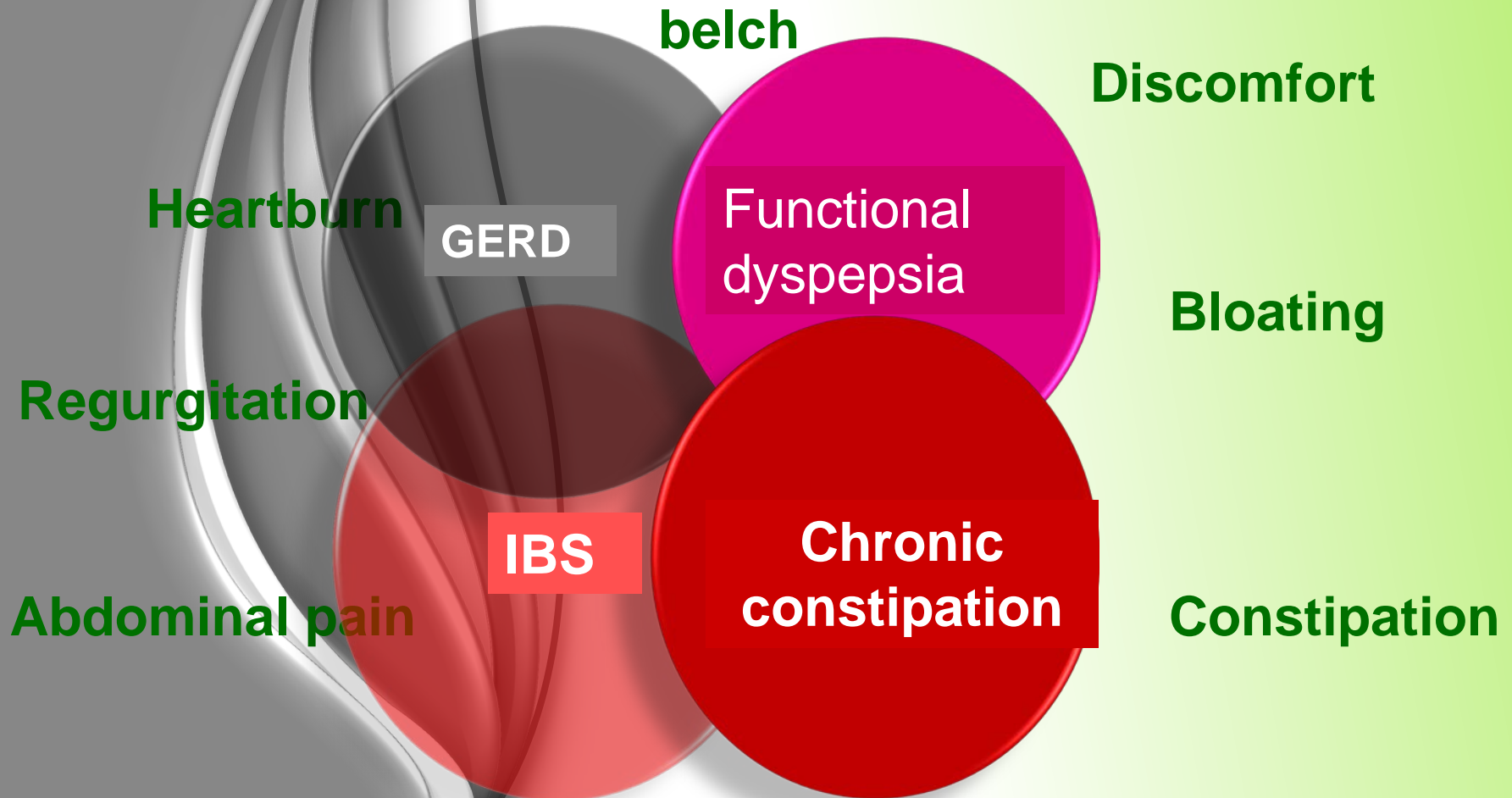
# Pathogenetic factors



# Pathophysiological factors of FD

- increased acidity;
- disorders of gastric motility (25-35% - deceleration; 5% - acceleration);
- increase in visceral afferent sensitivity (about 45%);
- violation of postprandial accommodation of the stomach (33%) - more often with postinfection FD;
- psychological disorders;
- *H. pylori* infection (40-60% of the cases)

# Isolated pathology is rare



# Functional dyspepsia (FD)

## Roma Criteria IV (2016))

the presence of one or more dyspeptic symptoms that has persisted during the last 3 months from the onset of the disease and at least 6 months before diagnosis:

- unpleasant feeling of fullness after meals;
- rapid saturation;
- epigastric pain;
- burning sensation in the epigastrium,

in the absence of any organic, systemic or metabolic changes that explain the symptoms.



# Epigastric pain

At least during the last 3 months from the beginning of manifestations and not less than 6 months before diagnosis the presence of at least one of the following symptoms for

**at least 1 day a week:**

1. Disturbing epigastric pain  
(its intensity decreases normal activity)

**AND / OR**

2. Disturbing epigastric burning  
(its intensity decreases normal activity)

# Epigastric pain syndrome

- **Auxiliary notes:**

- pain can be caused by eating, decreasing after eating or fasting;
- Epigastric distension, belching and nausea, repeated vomiting suggests another pathology;
- heartburn is not a dyspeptic symptom, but can often be associated;
- existing pain does not mean the criteria of biliary pain;
- symptoms that diminish after bowel movement or discharge from the bowel should not be considered as belonging to dyspepsia

# Postprandial distress syndrome

At least during the last 3 months from the beginning of manifestations and not less than 6 months before diagnosis

the presence of at least one of the following symptoms:

- ▶ feeling of overfull after meals
  - is noted after a single meal
  - or / and
- ▶ feeling of early saturation
  - it is not possible to eat a normal volume of food to the end;

**Occurs at least 3 days a week**

# Postprandial distress syndrome

- **Auxiliary notes:**
  - epigastric pain or burning after meals, epigastric distension, excessive belching and nausea (may be present);
  - the presence of vomiting suggests another pathology;
  - heartburn is not a dyspeptic symptom, but can often be associated;
  - symptoms that diminish after bowel movement or discharge from the bowel should not be considered as belonging to dyspepsia

# FUNCTIONAL DYSPEPSIA

## Factors of FD development :

- ❖ heredity -  $\text{GN}\beta 3$  CC-genotype
- ❖ motor dysfunction of the stomach and intestines
- ❖ *H. pylori* infection
- ❖ psychosocial factors

- alcohol, smoking, NSAIDs, theophylline, digitalis

**Diagnosis: dyspepsia or gastritis?**

# **Survey algorithm (Roma criteria V)**

- **Collection of complaints (based on which the symptoms of dyspepsia are detected)**
- **Collection of anamnesis**
- **Physical examination**



# Diagnosis of FD

Required diagnostic methods :

- General blood tests and biochemical tests
- Feces analysis for hidden blood
- EGDS with biopsy (test and treat strategy justified in regions with high HP infection, in countries with high prevalence of gastric cancer after **40-45 years**, when receiving NSAIDs, presence of alarming symptoms)
- Ultrasound examination of abdominal, thyroid, pelvic organs
- Establishing HP infection:
  - <sup>13</sup>C-urea breathing test
  - fecal antigen test
  - rapid urease test
  - serology (if no eradication was performed)

# Diagnosis of FD

Clarifying diagnostic methods :

- intragastric pH-metry
- intra-esophageal pH monitoring (to exclude concomitant GERD)
- studies of gastroduodenal motility:
- <sup>13</sup>C-octanoic breath test
- video capsule endoscopy
- radiological examination of the stomach, small and large intestine
- Colonoscopy (to exclude organic colon pathology)
- Food intolerance testing

# Alarming symptoms ("red flag" symptoms)

- Progressing dysphagia
- Nausea and vomiting (repetitive)
- Reduction (absence) of appetite
- Weight loss (if unmotivated)
- Pallor of the skin, signs of bleeding
- The first onset of symptoms over the age of 45
- Increased body temperature
- Changes in laboratory parameters (anemia, leukocytosis, ESR acceleration, etc.)

**! FGDS, biopsy if necessary**

# Differential diagnosis

- GERD
- Gastric and duodenal ulcer
- GCD (Gallbladder Calculus Disease)
- Chronic pancreatitis
- CIHD
- Functional diseases (aerophagy, functional vomiting, primary gallbladder dysfunction)
- Secondary changes in systemic scleroderma

# Differential-diagnostic signs of organic and FD

## Sign

## Organic dyspepsia

## Functional dyspepsia

Age

Anyone

Young (and  
middle)

Sex

Any

Mostly female

Addiction to stress

+/-

++++

Duration of anamnesis

Short

Long

Complaints

Monotone

Variable

Localization of pain

Localized

Diffuse, migratory

Concomitant  
functional disorders

+

++++

# Recommendations for the lifestyle modification in FD

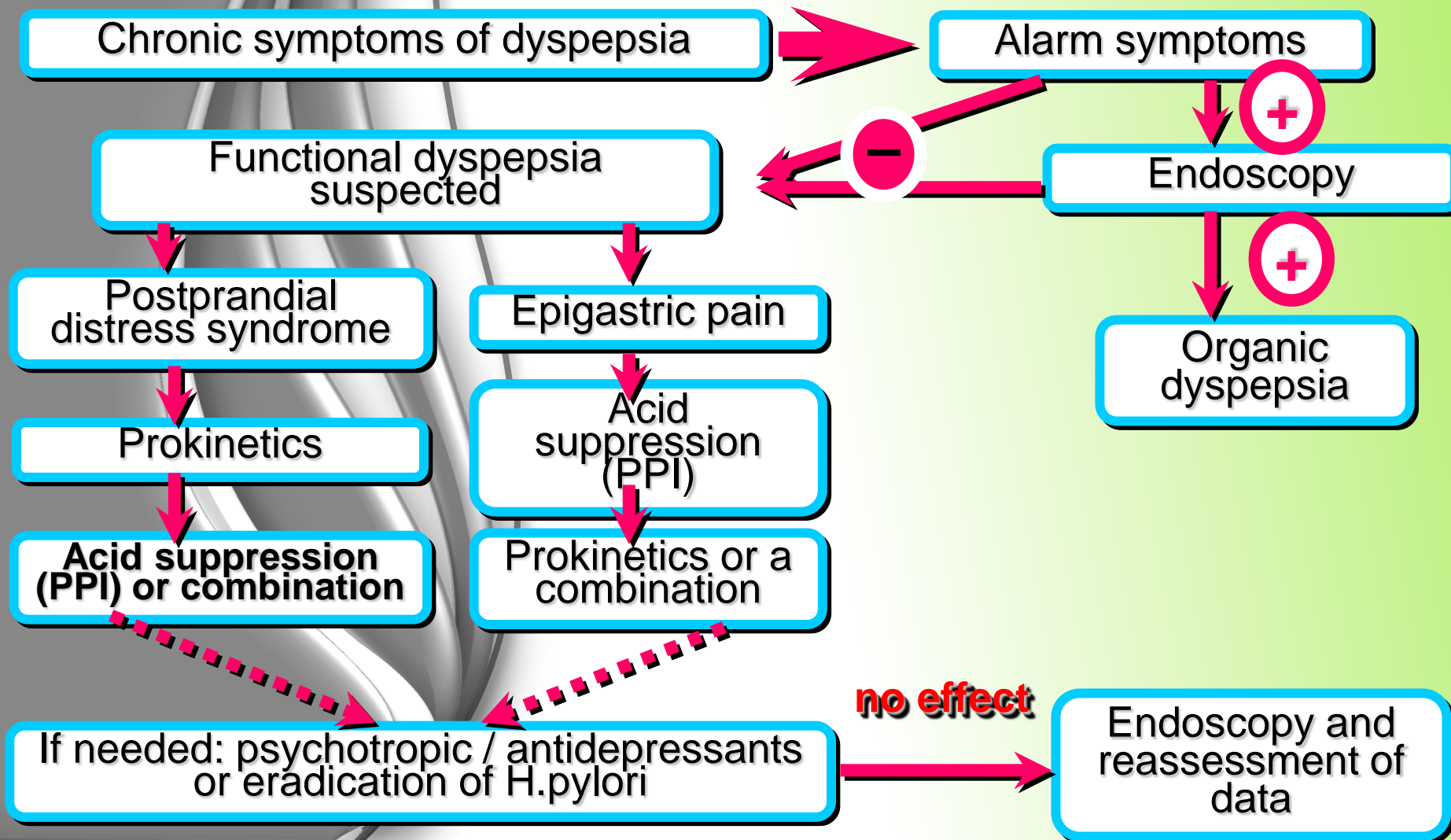
- Restoration of normal mode of work, rest, meals;
- Weight normalization;
- Dynamic sports (jogging, walking, cycling, swimming, etc.), hardening, yoga;
- Frequent stay in the open air;
- Avoid wearing tight clothing, tight belts;
- Refusal of smoking and alcohol drinking.



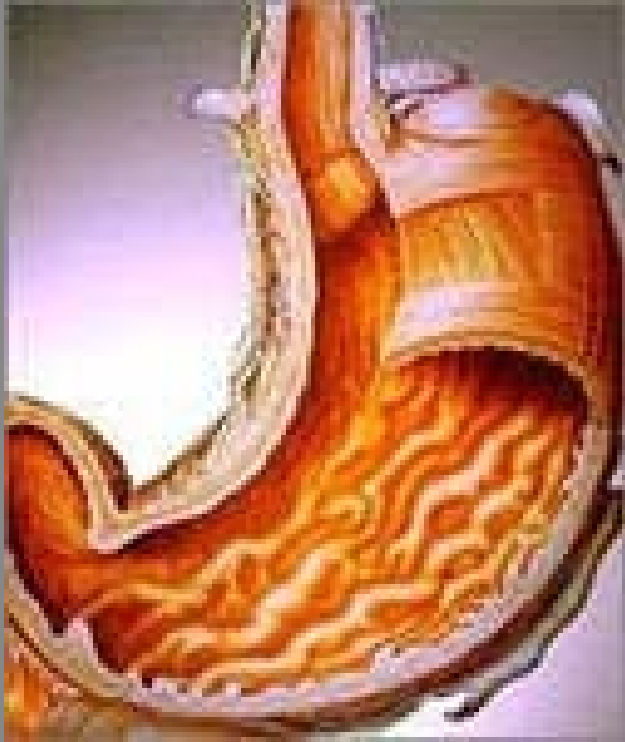
# Basic dietary recommendations for FD

- Consumption at a time of such amount of food that does not cause discomfort (↓ volume of single meals);
- Consumption of food in small portions, but often (5-6 times a day);
- Differentiation of liquid and solid food intake;
- Do not lie down for 2-3 hours after meals;
- Do not eat before bed;
- Prohibition of exercise after eating;
- Complete rejection of products that cause symptoms;
- Limited amount of fat, protein in the diet;
- Restrictions of coffee, alcohol, chocolate, citrus fruits, tomatoes, grapes, plums, apples and other foods that slow gastric emptying.

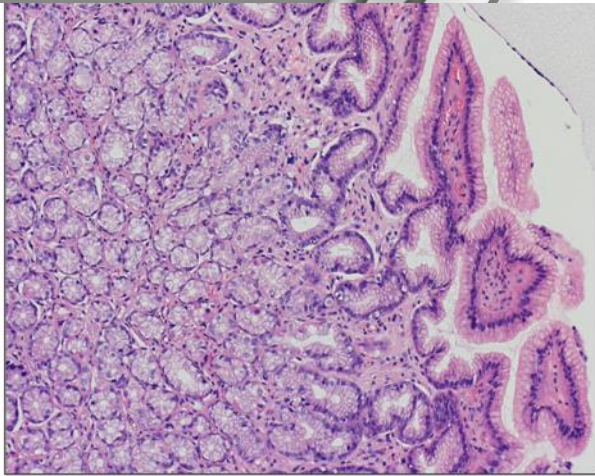
# Algorithm for diagnosis and treatment of FD



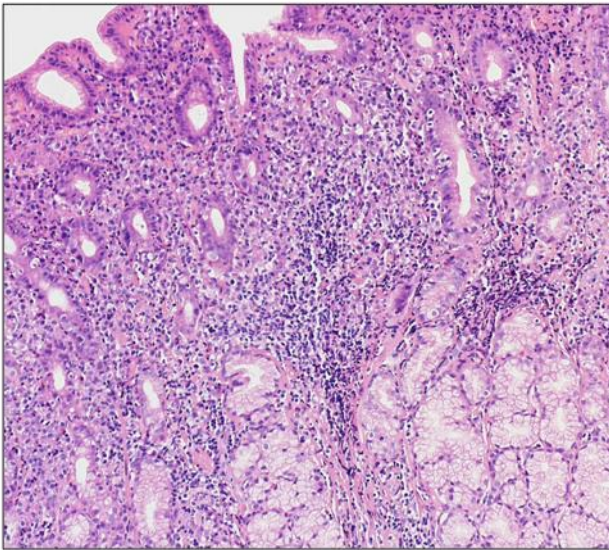
# Gastritis Chronic



chronic inflammatory-dystrophic process in the gastric mucosa, accompanied by impaired cellular regeneration and progressive atrophy of the glandular epithelium.



**normal gastric mucosa**



**gastric mucosa atrophy**



**Diagnosis of GC is morphological, it is entitled to exist only in cases when the corresponding assessment of biopsy specimens by the pathomorphologist and the presence of GC is confirmed histologically.**

**For the morphological investigation of samples the study of 5 gastrobiopsates (1 - from the angle of the stomach, 2 - from the body and 2 - from the antrum) is recommended with a description of the main pathomorphological changes.**

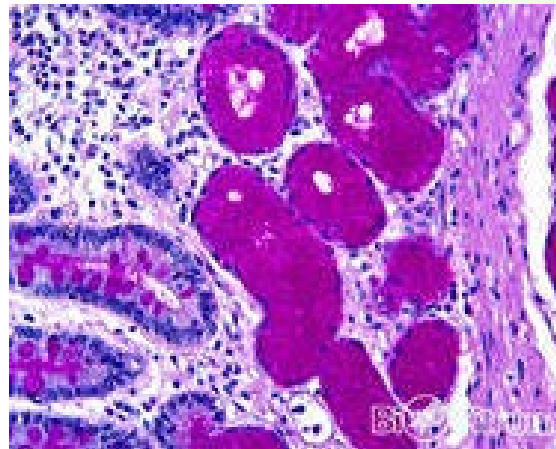
# Epidemiology

- Type A (autoimmune) —3-6%
- Type B or gastritis associated with *H. pylori* - 80-90%
- Type C - 7-15% of cases



# Gastric cells

- parietal (HCl, internal Castl factor, gastroferrin)
- main cells (pepsinogen)
- goblet cells (mucus)
- G-cells (gastrin)
- D-cells (histamine)
- EXK (гистамин)





# Etiology

## → Causes:

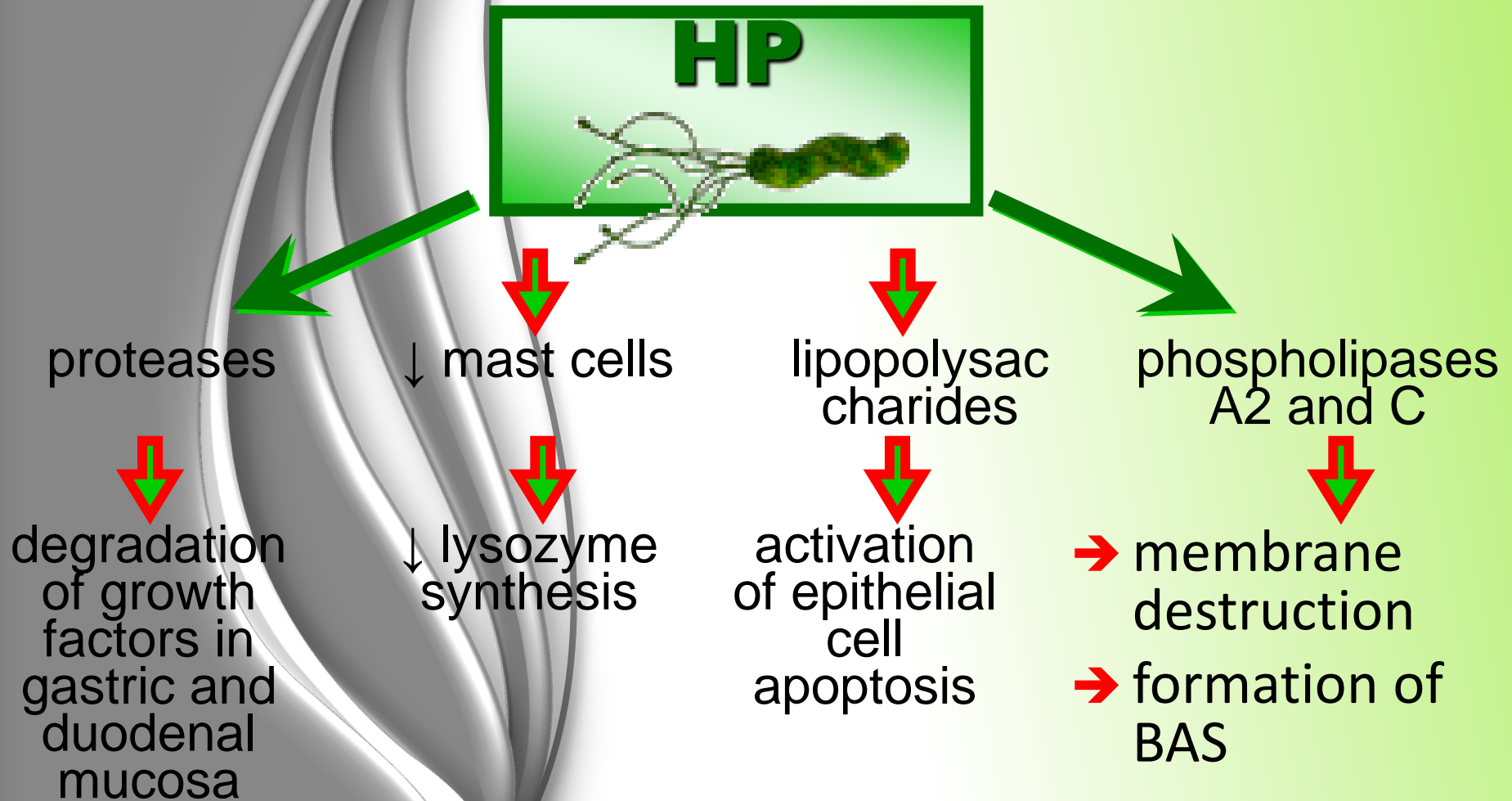
- H. pylori (for type B) - about 90% of all GC.
- genetic predisposition (for type A) is about 5-10% of all GC.
- duodeno-gastric bile reflux - about 5% of all GC.

## → Aggravating factors:

- receiving NSAIDs (NSAIDs-gastropathy).
- food intake disorders.
- bad chewing condition.
- smoking and alcohol.
- chemical substances.
- other diseases (diabetes, hyperthyroidism, hypoparathyroidism, Crohn's disease, CRF).

# HP is associated with glycerolipids in epitheliocytes

*A.P.Moran. 1999*



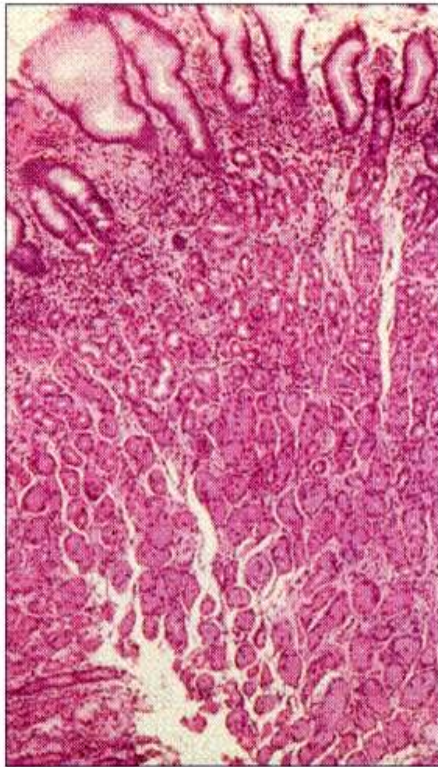
*И.В.Зверьков и соавт., 1996*  
*N.Lambrecht et al., 1999*

*T.J.Jang, J.R.Kim, 2000*  
*X.Jiang, M.P.Doyle, 2000*

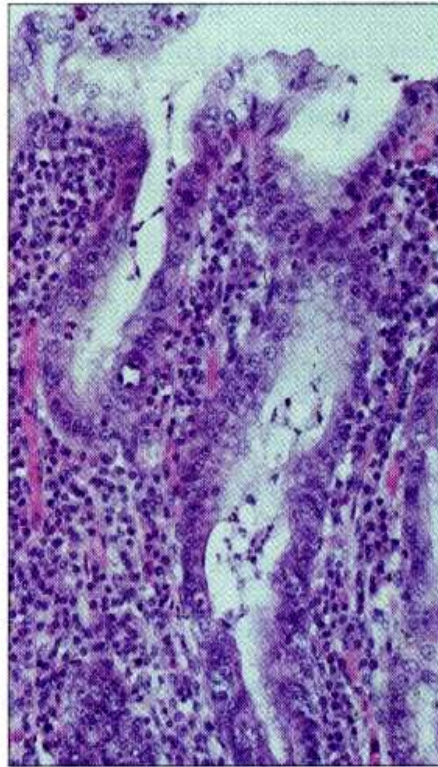


# Histological changes in the stomach with *H. pylori* infection

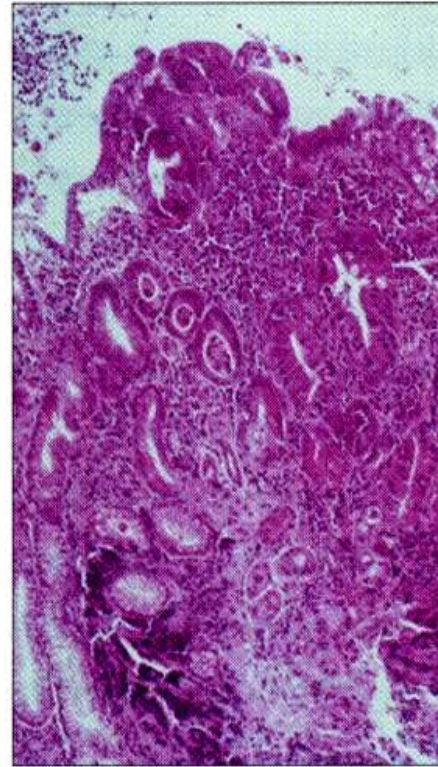
## Gastritis



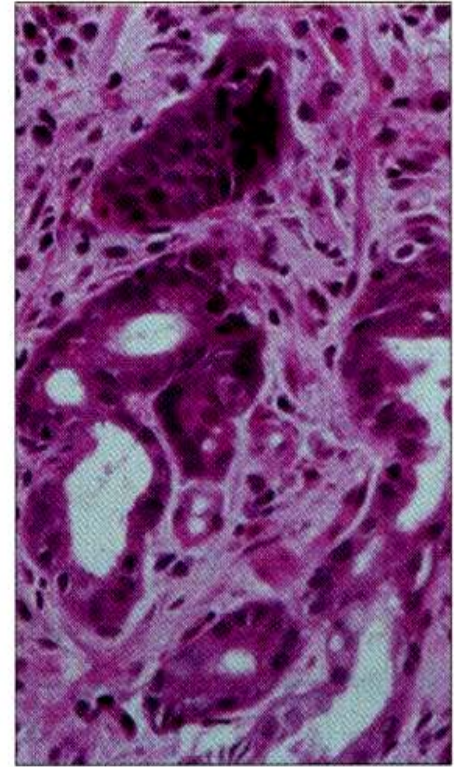
Superficial



Active



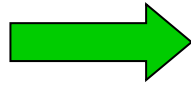
Active chronic



Atrophic

# Gastric secretion physiology and atrophic gastritis

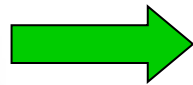
**Pepsinogen I (Pg I) is produced by the major cells of the stomach body**



**In gastric atrophy serum level of pepsinogen-1 decreases in proportion to the degree of atrophy**

**Pepsinogen-II (Pg II) is produced in all parts of the stomach and duodenum**

**Gastrin 17 (G 17) is produced by G-cells in the antral part of the stomach in response to stimulation by several factors, including food proteins**



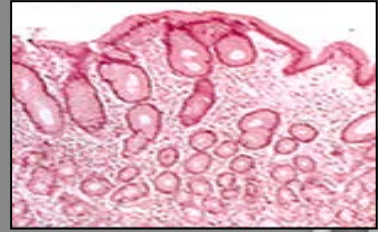
**In atrophic gastritis in the antral part the level of G-17 decreases in proportion to the degree of atrophy**



# Factors of gastric carcinogenesis

- **H. pylori - in 20% of cases causes chronic atrophic gastritis and in 3% of gastric adenocarcinoma cases**
- **IL-6 and STAT3 interleukins, TNF- $\gamma$  and IL-1 $\alpha$  cytokines promote gastric epithelium proliferation**
- **Interleukin IL-11 has carcinoprotected properties**

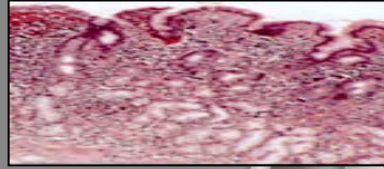
# Multilevel gastric carcinogenesis ("Correa Cascade")



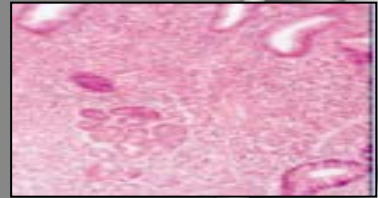
**Normal gastric mucosa**



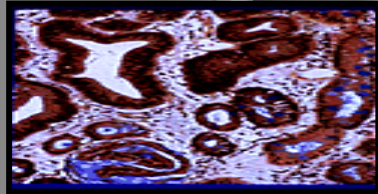
*H. pylori*



**Chronic gastritis**



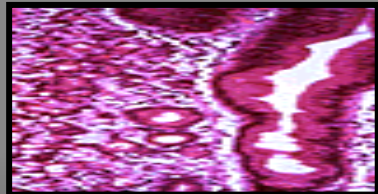
**Atrophic gastritis**



**Intestinal metaplasia**



**Dysplasia**



**Gastric adenocarcinoma**

Correa P.  
Cancer Res. 1992;  
52:6735-6740.



# **Morphological classification of atrophic gastritis**

**(Міжнародна група по вивченню атрофії, 2002)**

- There is no atrophy**
- Unspecified atrophy**
- Atrophy:**
  - metaplastic:**
    - insignificant**
    - moderate**
    - severe**
  - non-metaplastic:**
    - insignificant**
    - moderate**
    - severe**

# Atrophic gastritis

At atrophy of a mucosa :

- disappear specialized glands and develop intestinal metaplasia (replacement of gastric epithelium by intestinal);
- apoptosis processes are disturbed

Degrees of atrophy:

- loss of <30% of glands - mild (slight)
- loss of 30-60% of glands - moderate
- loss of > 60% of glands - severe

# Sydney classification of GC

## *Type of gastritis*

- acute
- chronic

### **"Special" forms:**

- reactive;
- lymphocytic;
- eosinophilic;
- hypertrophic;
- granulomatous;
- others.

## ***Localization of the lesion***

- Antral partm
- The body of the stomach
- Pangastritis (gastritis of the antrum and body of the stomach)

## *Morphological changes*

- the degree of inflammation
- activity of inflammation
- atrophy of the gastric glands
- metaplasia
- Hp contamination of the mucosa

## ***Etiological factors***

- Infectious (H. pylori)
- Non-infectious:
  - autoimmune
  - alcoholic
  - post-gastroresection
  - caused by the administration of NSAIDs
  - due to chemical agents

# Houston Classification of GC

## Type of gastritis

**Non-atrophic**

**Atrophic  
autoimmune**

## Synonyms

Superficial,  
chronic antral,  
type B

Diffuse fundus,  
type A  
associated with  
pernicious anemia

## Etiological factors

***H. pylori***

Autoimmune reactions,  
N. pylori,  
environmental factors

## **Special forms of GC:**

**Chemical**

**Reactive  
gastritis, reflux  
type C**

**Chemicals, bile, NSAIDs**

**Radiative  
Lymphocytic**

**Lymphocytic**

**Radiation lesions  
Idiopathic, immune  
mechanisms, H. pylori**

**Non-infectious  
granulomatous**

**Granulomatous**

**Crohn's disease,  
sarcoidosis, Wegener's  
granulomatosis, foreign  
bodies**

**Eosinophilic**

**Allergic**

**Food allergy, other allergens**

**Other infectious**

**Other bacteria (except H.  
pylori), viruses, fungi,  
parasites**

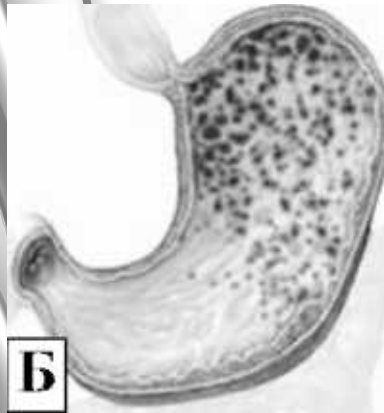
# Localization of CG

## → Pangastritis (gastritis of the body of the stomach):

- ↓ gastric secretion
- ↑ risk of carcinogenesis

## → Antral gastritis :

- ↑ gastric secretion
- ↑ risk of duodenal ulcerogenesis



A - antral gastritis (gastritis type B);

B - gastritis of the body of the stomach (gastritis type A);

C - multifocal gastritis (pangastritis)



# Clinic

- **Gastric dyspepsia (heaviness and pressure in the epigastrium area after meals, belching, vomiting, nausea, bad taste in the morning, sometimes heartburn);**
- **Epigastric pain after meals (especially after ingesting hot, coarse, fried, smoked food);**
- **Intestinal dyspepsia (constipation or diarrhea, flatulence, grunts and transfusions in the abdomen);**
- **Astheno-neurotic syndrome;**
- **Signs of hypovitaminosis, pallor of the skin (only with autoimmune gastritis).**

# Differential-diagnostic criteria of CG A and B

## Criteria

	Gastritis B. ( <i>Helicobacter</i> )	Gastritis A. (autoimmune)
Localization	antrum	fundus, body
Inflammation	expressed, active	not expressed
Erosion	very often	rarely
H. pylori	+	-
Antibodies to parietal cells	-	+
Antibodies to the internal factor	-	+
Hypergastrinemia	-	+++
B12-deficiency anemia	-	+
Hypoacidity	any type of secretion	expressed
Pairing with ulcer	very often	rarely

# Differential diagnosis

→ **Chemical gastritis** - after surgery at the stomach (resection, pyloroplasty, gastroduodenoanastomosis) due to persistent bile reflux, prolonged alcohol and nicotine abuse.

Smooth muscle proliferation, atrophy and intestinal metaplasia of gastric mucosa with an increase effect of a harmful factor.

→ **Radiation gastritis** - at external or internal irradiation with the development of coagulation necrosis (focal to advanced) with the appearance of secondary inflammatory infiltrates (regress after about 4 months). It can also lead to gastric fibrosis.

# Differential diagnosis

→ **Granulomatous CG**— most often with Crohn's disease, rarely with sarcoidosis, Wegener's granulomatosis, foreign bodies of the stomach. Often, in endoscopic picture, it is similar to gastric adenocarcinoma.

Available epithelioid cell granulomas in combination with inflammatory gastric mucosa infiltration.

→ **Eosinophilic CG** most often caused by food allergies or connective tissue diseases. Characteristic prevalence of the process with concomitant bowel damage, the presence of eosinophilic infiltrates in the own plate of gastric mucosa, eosinophilia of the peripheral blood.

# Differential diagnosis

→ **Other infectious CG** can be caused by *Gastrospirillum hominis*, other types of helicobacteria, cytomegalovirus, *Candida* fungi, *Mycobacterium tuberculosis*, various parasites (*Strongiloidosis*, *cryptosporidiosis*, *anazaconiosis*), occur with tertiary syphilis.

# Methods of diagnosis

- EGDS with biopsy for morphological confirmation of CG, presence of atrophy, dysplasia and H. pylori infection (histology - the "gold standard" of invasive diagnostics)
- Other methods for the determination of H. pylori (serology, rapid urease test,  $^{13}\text{C}$ -urea breathing test, determination of HP faecal antigen)
- Intragastric pH-metry
- Serological tests - study of serum levels of pepsinogen I and gastrin-17, antibodies to parietal cells ("serological biopsy")



# Identification of H. pylori

**Invasive  
(biopsy study)**

**Ureasy  
Cytological  
Histological  
Molecular (PCR)**

**Less invasive  
(peripheral blood  
examination)**

**Determination of antibodies  
(enzyme-linked immunosorbent) \*  
Molecular**

**Non-invasive (study  
of other biological  
environments:  
exhaled air; feces,  
saliva, urine)**

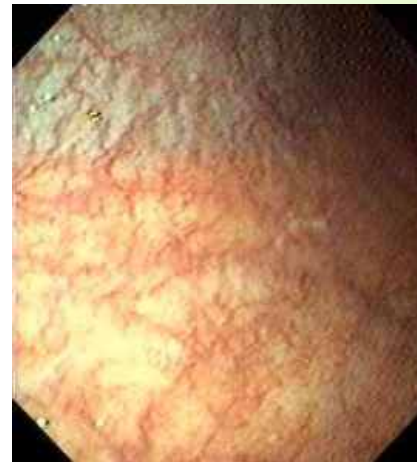
**Ureas breathing  
Stool test \*\*  
Determination of  
antibodies  
Molecular**

# **HP tests recommended by Maastricht IV**

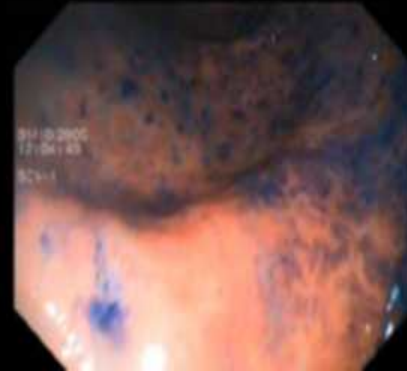
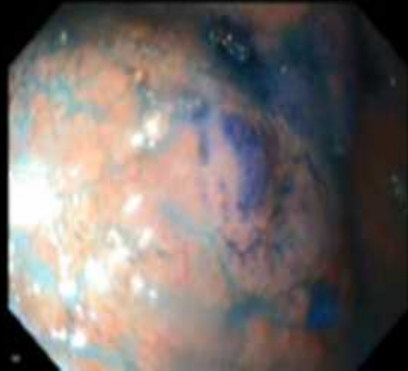
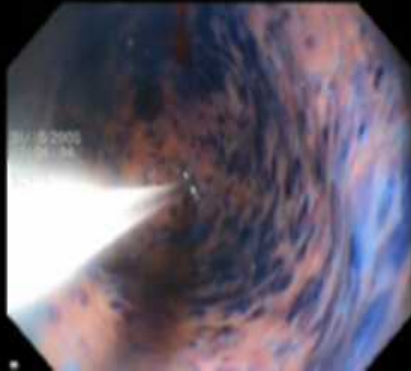
- **Urease Breath Test (UBT)**
- **Stool antigen test (using monoclonal antibodies)**
- **Biopsy urease test (rapid urease test)**
- **Enzyme-linked immunosorbent assay (serological, serum IgJ determination)**

# Videodoscopic signs of gastric atrophy

- Pallor of the gastric mucosa
- Smoothness of the stomach folds
- More significant vascular pattern



# Gastroendoscopy with biopsy



## CHROMOGASTROSCOPY

(intravital mucous staining with methylene blue) allows to identify areas of intestinal metaplasia for performing biopsy sighting

# Endoscopic categories of GC

- erythematous / exudative gastritis (superficial gastritis);
- flat erosion;
- elevated erosion;
- hemorrhagic gastritis;
- hyperplastic gastritis;
- gastritis accompanied by DGR (reflux gastritis).



# The diagnosis of GC

- ▶ **localization of the pathological process;**
- ▶ **histological changes in GM;**
- ▶ **macroscopic changes in GM that are detected by endoscopy;**
- ▶ **etiological factor;**
- ▶ **stage of disease course (exacerbation, remission);**
- ▶ **functional evaluation of the stomach secretory function (normal, increased or decreased hydrochloric acid secretion)**



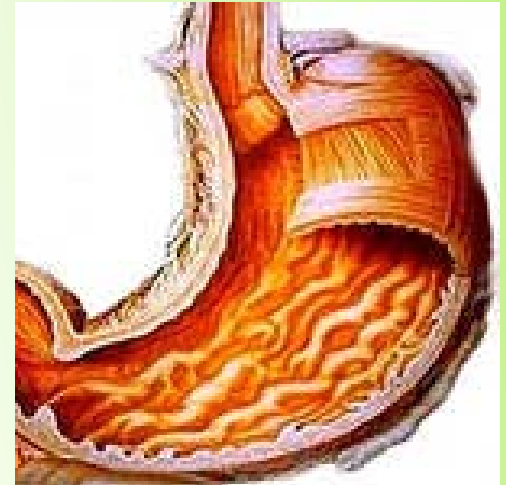
# Principles of treatment

- ▶ **Diet is sparing**
- ▶ **HP eradication;**
- ▶ **PPI and H2-GB;**
- ▶ **Immunophan 0.005% 1 ml IM or T-activin 0.01% 1 ml SC or alternate No. 10 (with GC A);**
- ▶ **Vit. B12, antioxidants**

# Chronic gastritis C

**(synonymous - chemical, reactive, alkaline, reflux - gastritis), caused by duodenogastric bile reflux observed after surgery at the stomach, or associated with NSAIDs.**

**The average age of patients with GC type C is 66 years old**



# **Etiology**

- ▶ **operations for Billroth I or Billroth II (especially if these interventions were accompanied by pyloroplasty and the imposition of gastrointestinal anastomosis);**
- ▶ **different types of vagotomy;**
- ▶ **cholecystectomy;**
- ▶ **pyloric sphincter dysfunction;**
- ▶ **Treatment by NSAIDs.**

# Risk factors for NSAIDs-gastropathy

## → Moderate

- ▶ old age without additional risk factors;
- ▶ ulcers (peptic ulcer);
- ▶ anamnesis (rare recurrence of ulcers);
- ▶ concomitant administration of corticosteroids;
- ▶ smoking and alcohol drinking;
- ▶ HP infection

## → High

- ▶ ulcerative history;
- ▶ administration of aspirin, anticoagulants and other blood clotting drugs

## → Very high

- ▶ ulcers complicated by bleeding or perforation;
- ▶ recurrent ulcers (especially NSAID-induced);
- ▶ combination of two or more risk factors

# Pathogenesis

↑ the formation of  
free radicals and  
TNF- $\alpha$

**NSAIDs**



inhibitory effect on  
COX-1



↑ apoptosis of  
epithelial cells



bile acids

lysolecithin



solubilization of superficial  
epithelium membranes  
lipids

disrupted Pg  
synthesis in gastric  
mucosa and ↓ its  
cytoprotective  
properties

# Morphological features of type C GC



- ▶ foveolar hyperplasia;
- ▶ "Spherical" elongation and tortuosity of the gastric mucosa folds;
- ▶ proliferation of muscle fibers of own plate;
- ▶ blood stasis in enlarged capillaries;
- ▶ reduction of mucus content on the surface of epithelial cells;
- ▶ slight lymphocytic and plasma cell infiltration, usually without granulocytes.



# Principles of treatment

- ▶ **Non-absorbable antacids;**
- ▶ **Sucralfate;**
- ▶ **UDCA 250 mg twice a day for 2 months;**
- ▶ **Prokinetics (domperidone, itoprid);**
- ▶ **In NSAIDs. gastritis - PPI and H2-GB (possible double doses)**



# Peptic ulcer

# Peptic ulcer: etiology, pathogenesis

... *view of the early twentieth century*

## Excess HCl production

Genetic predisposition

Increase in weight of  
parietal cells

increasing gastrin  
production in response  
to food intake

Disorders of  
neuroendocrine  
regulation

Increasing vagal  
influence

G-cell hyperplasia and  
hyperfunction, gastrin  
and histamine-  
producing ECL cells



**No acid - no ulcer**

*K. Schwarz, 1910*

# Peptic ulcer: etiology, pathogenesis

*... view at the end of the twentieth century*



**No *H. pylori* - no ulcer**  
*Warren & Marshall, 1983*

***H. pylori***





# Peptic ulcer: etiology, pathogenesis

The crucial link is the imbalance between the factors of aggression and the factors of protection of the gastric and the duodenum mucosa.

## Factors of aggression

- Hydrochloric acid
- Pepsin
- Disorders of the motor-evacuation function of the stomach
- Duodenal-Gastric Reflux



## Protection factors

- The formation of mucus
- Secretion of bicarbonates
- Proper blood flow
- Epithelial regeneration
- Prostaglandins
- Immune protection



*Helicobacter pylori*

Strengthening

ULCER

Weakening



*'At last: The truth about the Maastricht Treaty'*  
The Sunday Telegraph



CONSOLIDATED TREATY ON EUROPEAN UNION

The full text of all the changes and additions proposed by the Maastricht Treaty incorporated into the Treaty of Rome and the Single European Act together with an analysis of the proposed extra powers of the European Community Institutions



British Movement for European Reform

# MASTRICHT V



# Modern views

- Modern medicine addresses the tactical and strategic issues of diagnosis and treatment from the standpoint of evidence-based medicine.
- These regulations are formulated in the form of international agreement documents.
- A typical example of this development in gastroenterology is the Maastricht Consensus Series on the management of patients with HP infection.

# Maastricht V

- **HP resistance to antibiotics is increasing** in most regions of the world. Sensitivity results should be based on both population and individual data.
- In regions with high ( $> 15\%$ ) resistance to **Clarithromycin** recommended **quadrotherapy with bismuth and without bismuth**, and concomitant therapy (**PPI, Amoxicillin, Clarithromycin and nitroimidazole**)

# Maastricht V

- In regions with **high resistance** to **Clarithromycin** and **Metronidazol** at the same time **bismuth-quadrotherapy** is recommended as Line I therapy. The duration of therapy should be extended to **14 days**.
- In regions with **low resistance** to Clarithromycin standard three-component therapy is recommended as a first-line empirical therapy.
- **Bismuth quadrotherapy** is an alternative.

# Maastricht V

- **Esomeprazole** and **rabeprazole** may be of benefit in Europe and North America, where the prevalence of extensive PPI metabolizers is high
- In case of inefficiency of **bismuth**-quadrotherapy, three-component or quadrotherapy with **fluoroquinolone** may be recommended.
- In cases of high quinolone resistance, the **combination** of **bismuth** with other **antibiotics** and **rifabutin** may be optimal.

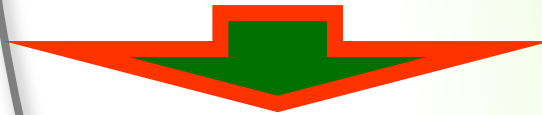
# How to treat?

## First-line therapy:

- ▶ PPI - 2 times a day
  - ▶ amoxicillin - 1000 mg 2 times a day
  - ▶ clarithromycin - 500 mg 2 times a day  
(if primary HP resistance to clarithromycin <15-20% in the region)
- or
- ▶ PPI - 2 times a day
  - ▶ amoxicillin - 1000 mg 2 times a day
  - ▶ metronidazole - 500 mg 2 times a day  
(if HP resistance to metronidazole <40%)

Duration - 10-14 days,  
Eradication by 5% (A, 1a)

**High (double) doses of PPI 2 times a day  
→ ↑ 8-12% eradication (A, 1b)  
If resistance to CLA > 15-20%  
the sensitivity of HP to antibiotics is not  
determined**



**Triple therapy is not prescribed, and as a first line -  
quadrotherapy**

### **First-line quadrotherapy - 14 days:**

- ▶ **PPI - 2 times a day**
- ▶ **bismuth subcitrate - 120 mg 4 times a day or - 240 mg 2 times a day**
- ▶ **metronidazole - 500 mg 2 times a day**
- ▶ **tetracycline - 500 mg 4 times a day**



# If quadrotherapy is not available:

- ▶ **sequential therapy (14 days)**
- ▶ **or**
- ▶ **quadrotherapy without bismuth (14 days):**
- ▶ **PPI - 2 times a day**
- ▶ **clarithromycin 500 mg 2 times**
- ▶ **amoxicillin 1 g 2 times**
- ▶ **metronidazole 500 mg 2 times**

**(A, 1a)**

# Second Line Therapy (14 days):

- ▶ PPI - 2 times a day
- ▶ bismuth subcitrate - 120 mg 4 times a day or - 240 mg 2 times a day
- ▶ metronidazole - 500 mg 2 times a day
- ▶ tetracycline - 500 mg 4 times a day (A, 1a)

or

PPI (standard dose 2 times)

+

amoxicillin 1.0 2 times

+

levofloxacin 0.5

(A, 1a)

**! Levofloxacin ↑ resistance (B, 2b)  
should be considered**

**The following protocols for eradication are recommended in the national protocol for assisting with Hp-associated diseases**

**Three-component therapy:**

**PPIs in standard dose twice a day**

**+ amoxicillin 1000mg twice a day**

**+ clarithromycin 500mg twice a day**

**for 10-14 days (for allergies to penicillin - instead of amoxicillin-metronidazole 500 mg 2 twice a day)**

**Sequential therapy:**

**STI at standard dose 2 t / d + amoxicillin 1000mg 2 t / d for 5 days, followed by switching to PPI + clarithromycin 500mg 2 t/ g + metronidazole 500 mg 2 t / d for 5 days**

# Second line therapy (quadrotherapy)

**Assigned for ineffectiveness of three-component or sequential, intolerance or resistance to clarithromycin**

- ▶ **PPI - twice a day**
- ▶ **bismuth subcitrate - 120 mg 4 times a day**
- ▶ **metronidazole - 500 mg 3 times a day**
- ▶ **tetracycline - 500 mg 4 times a day**
- ▶ **within 10-14 days**

# **Rescue Therapy**

**It is prescribed in the absence of HP eradication after the second course of treatment**

**PPIs in standard dose twice a day**













































































































































**+ amoxicillin 1000mg twice a day**

**+ levofloxacin 500 mg 1 g / d,**

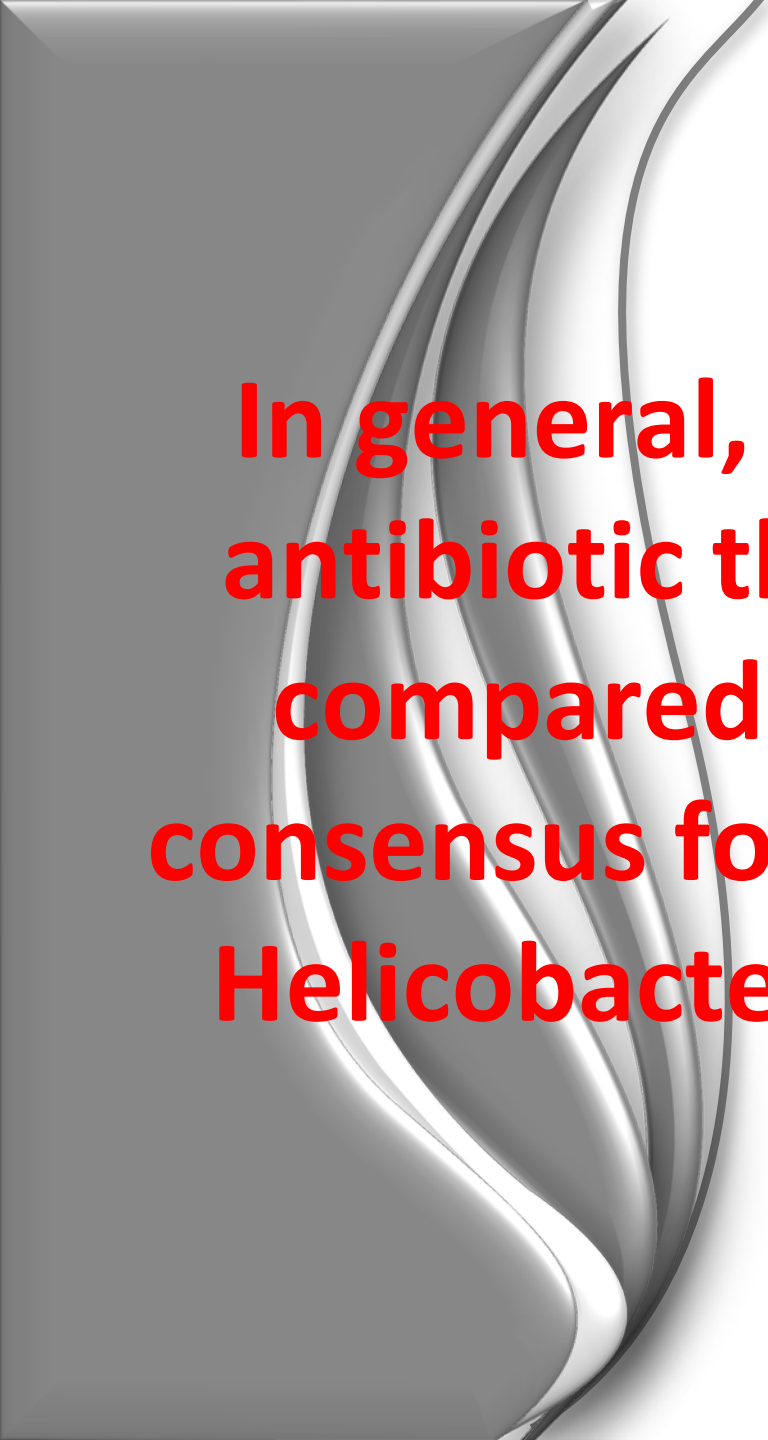
**or**

**rifabutin 300 mg 1 g / d for 10-14 days**

# Concomitant therapy

		1	2	3	4	5	6	7	8	9	10	11	12	13	14
breakfast	Omeprazole 40 mg														
	Amoxicillin 1g														
	Clarithromycin 500 mg														
	Metronidazole 250 mg Tinidazole 250 mg	 	 	 	 	 	 	 	 	 	 	 	 	 	 
dinner	Omeprazole 40 mg														
	Amoxicillin 1g														
	Clarithromycin 500 mg														
	Metronidazole 250 mg Tinidazole 250 mg	 	 	 	 	 	 	 	 	 	 	 	 	 	 





**In general, more aggressive  
antibiotic therapy is offered  
compared to the previous  
consensus for the treatment of  
*Helicobacter pylori* infection**