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

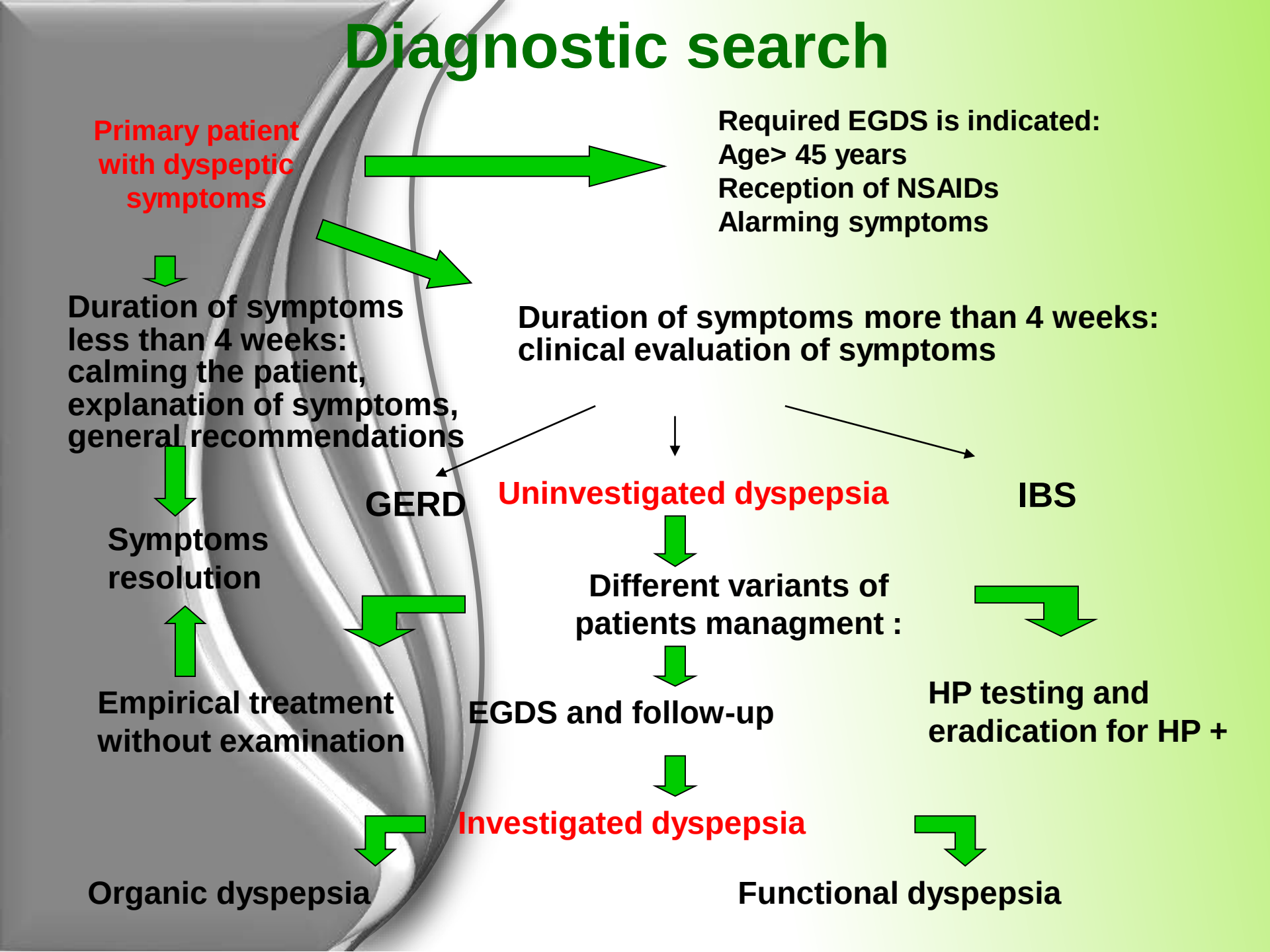
It is established for all patients during the initial visit to the doctor, before carrying out laboratory and instrumental examination, which allow to determine the final clinical diagnosis.

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



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 sighns 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%

American College of Gastroenterology, Can Diego, California, Brain.E, 0ctouber 24, 2009

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

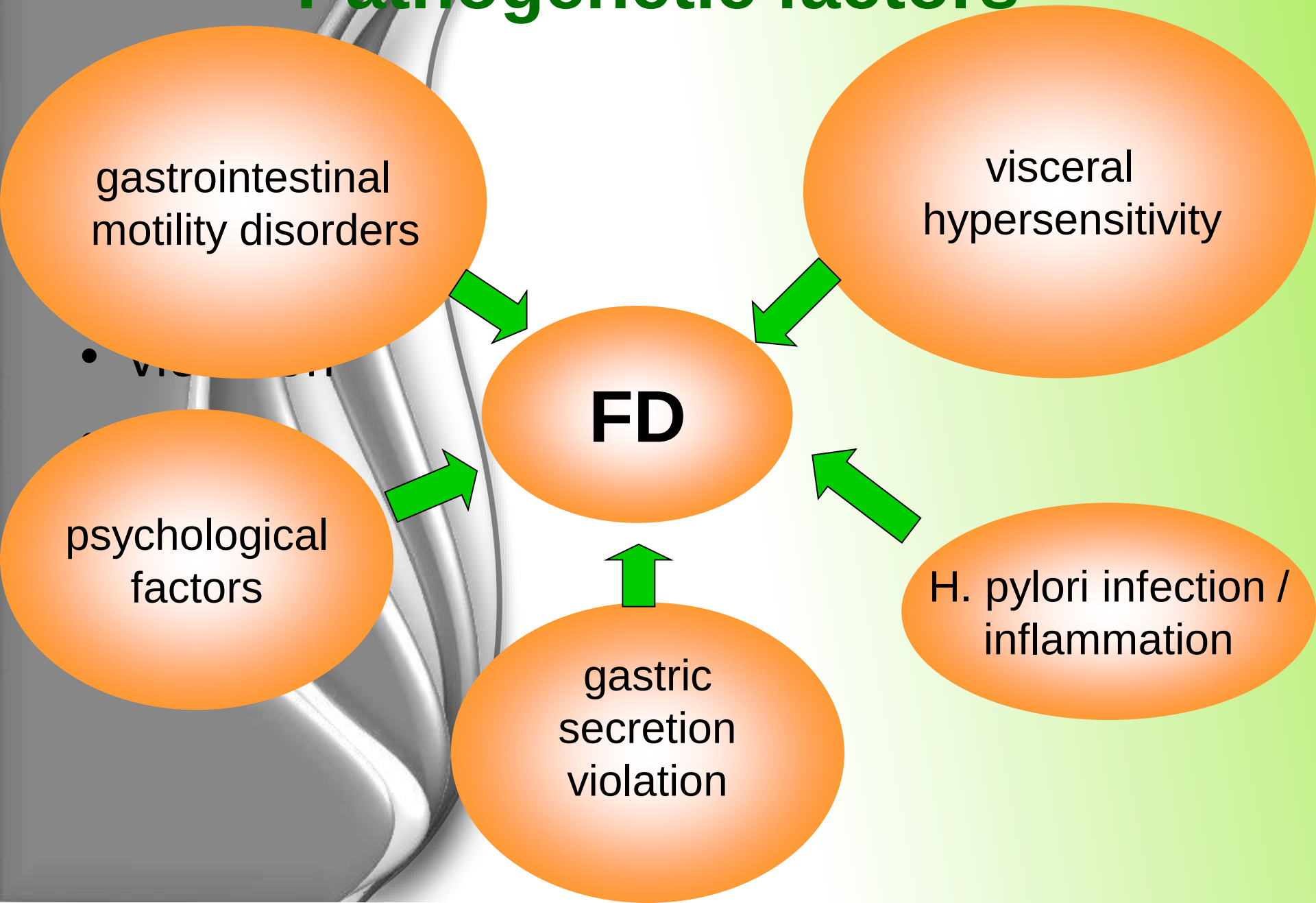
FD risk factors

- 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%.

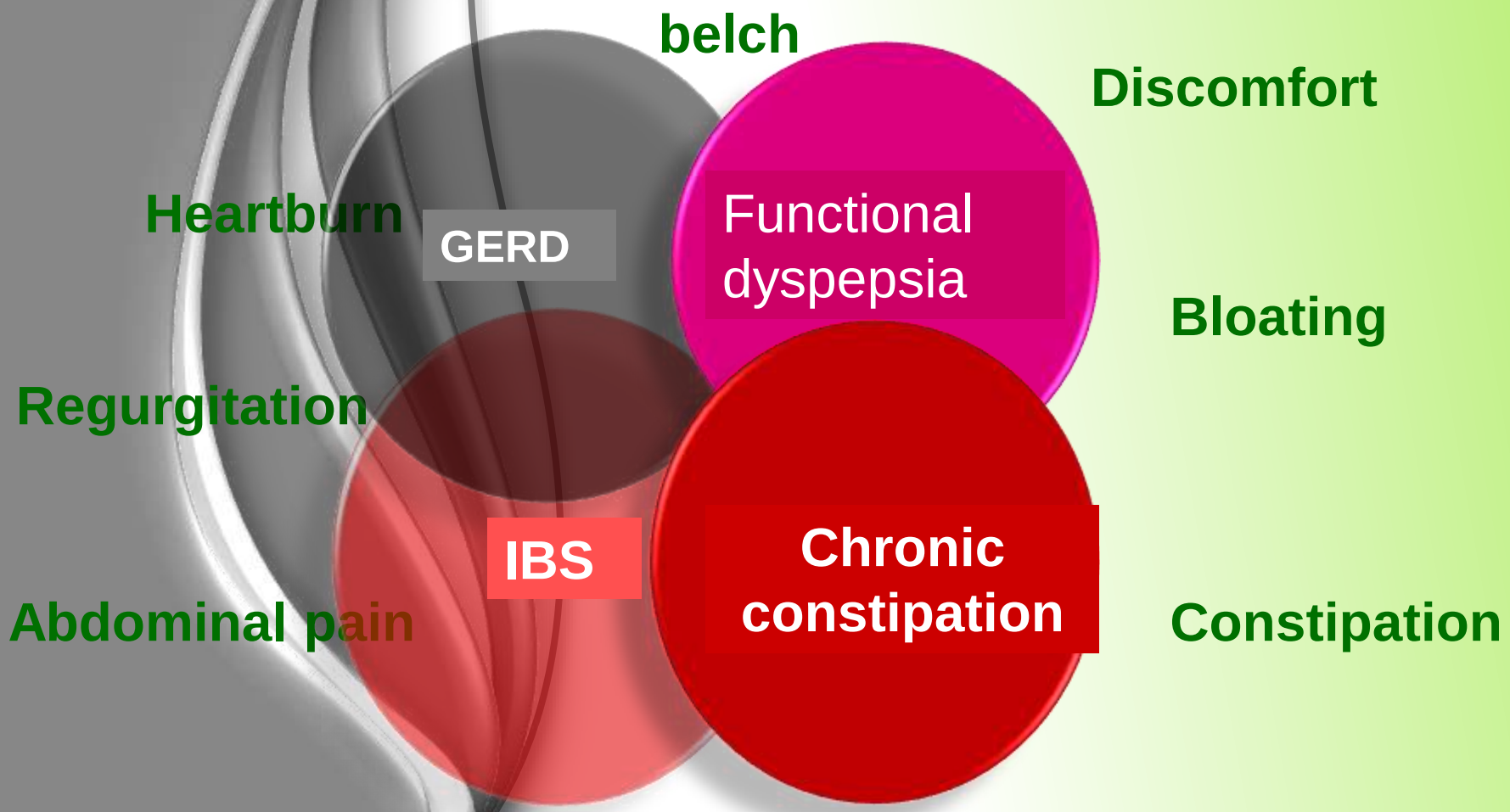
Pathogenetic factors



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



Locke et al., Neurogastroenterol Motil. 2005; 17(1):29-34
Corazziari et al., Clin. Gastroenterol. 2004; 18(4):613-31
Talley et al., Am J. Gastroenterol. 2003; 98; 2454-9

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 meen 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 - GNβ3 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:**
  - **13C-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:**
- **13C-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	+	++++

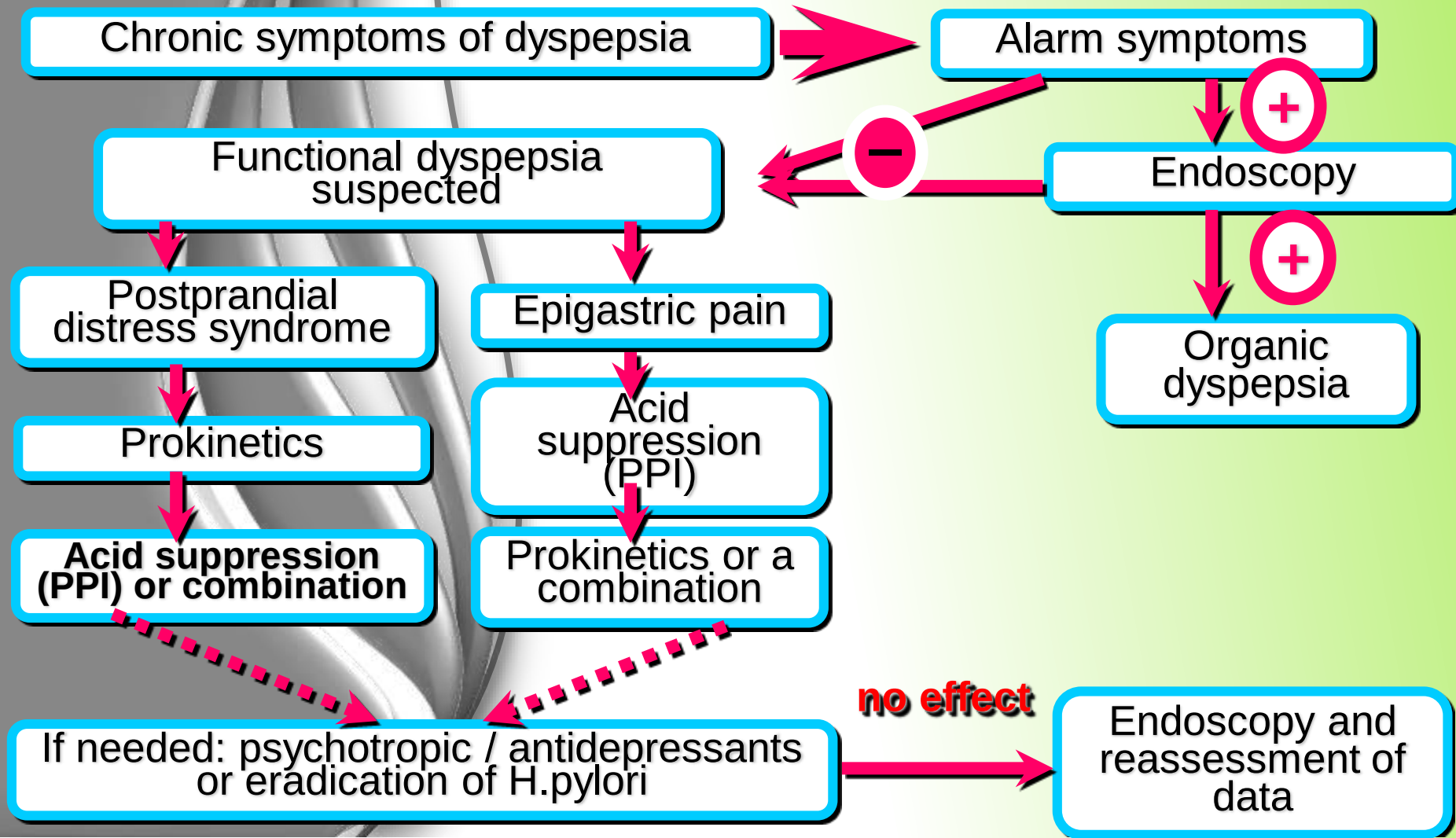
Recommendations for the lifestyle modification in FD

- 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.

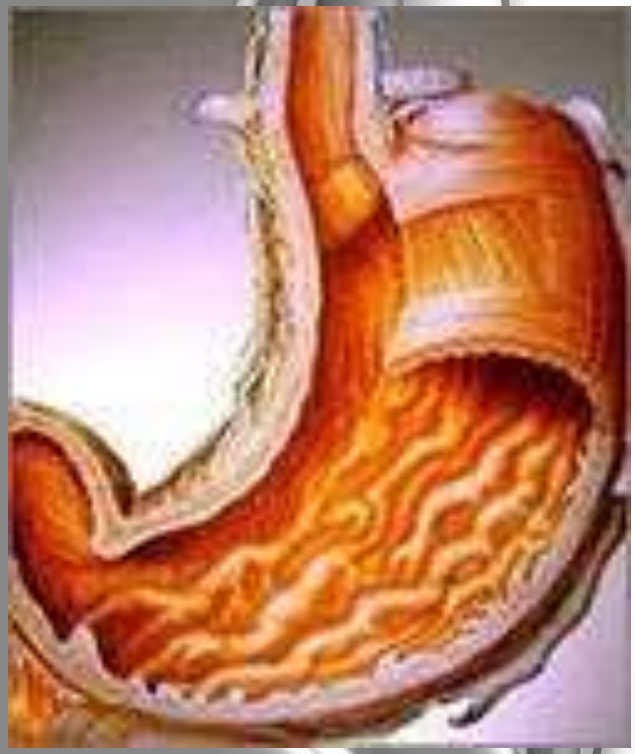
Basic dietary recommendations for FD

- 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.

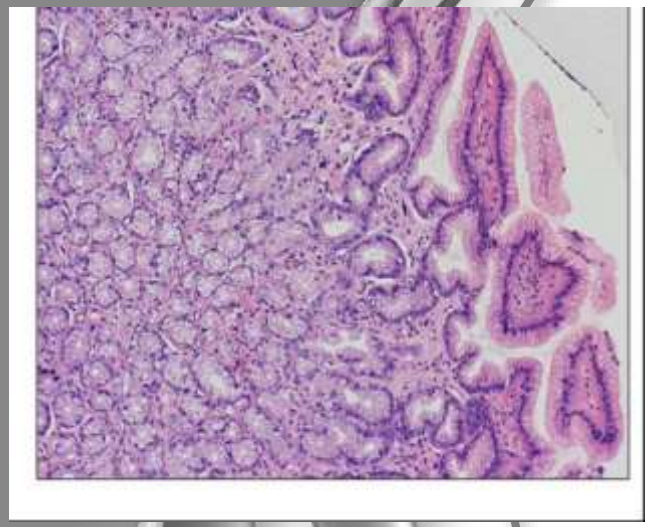
Algorithm for diagnosis and treatment of FD



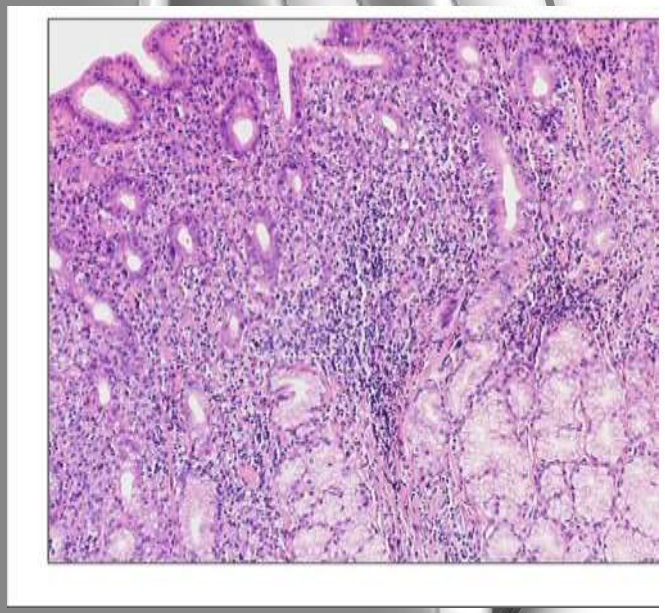
Gastritis Chronic



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.

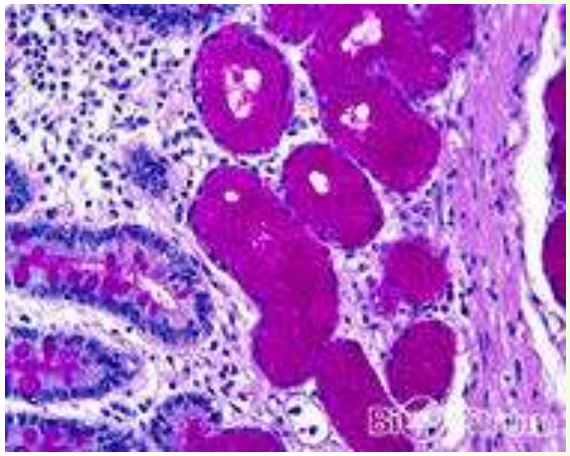
For the morphological investigation of samples the study of 5 gastrobioptates (1 - from the angle of the stomach, 2 - from the body and 2 - from the antrum) is recommended with a description of the main pathomorphological changes.

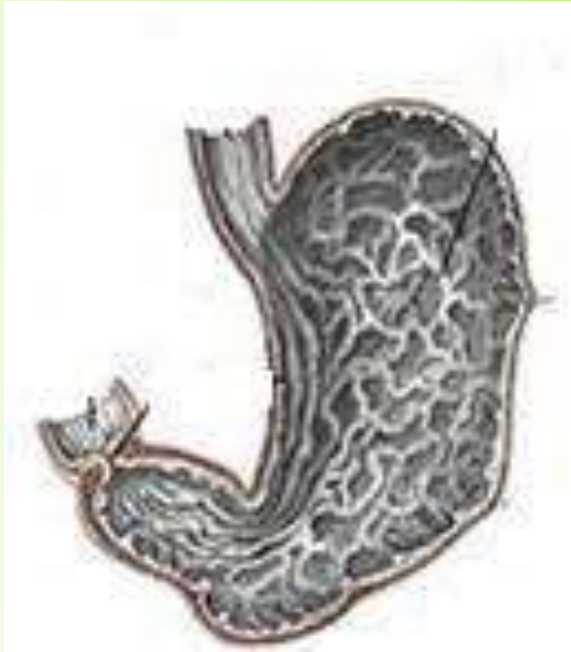
Epidemiology

- 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)
- ЕХК (гістамін)





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

proteases → degradation of growth factors in gastric and duodenal mucosa

↓ mast cells → ↓ lysozyme synthesis

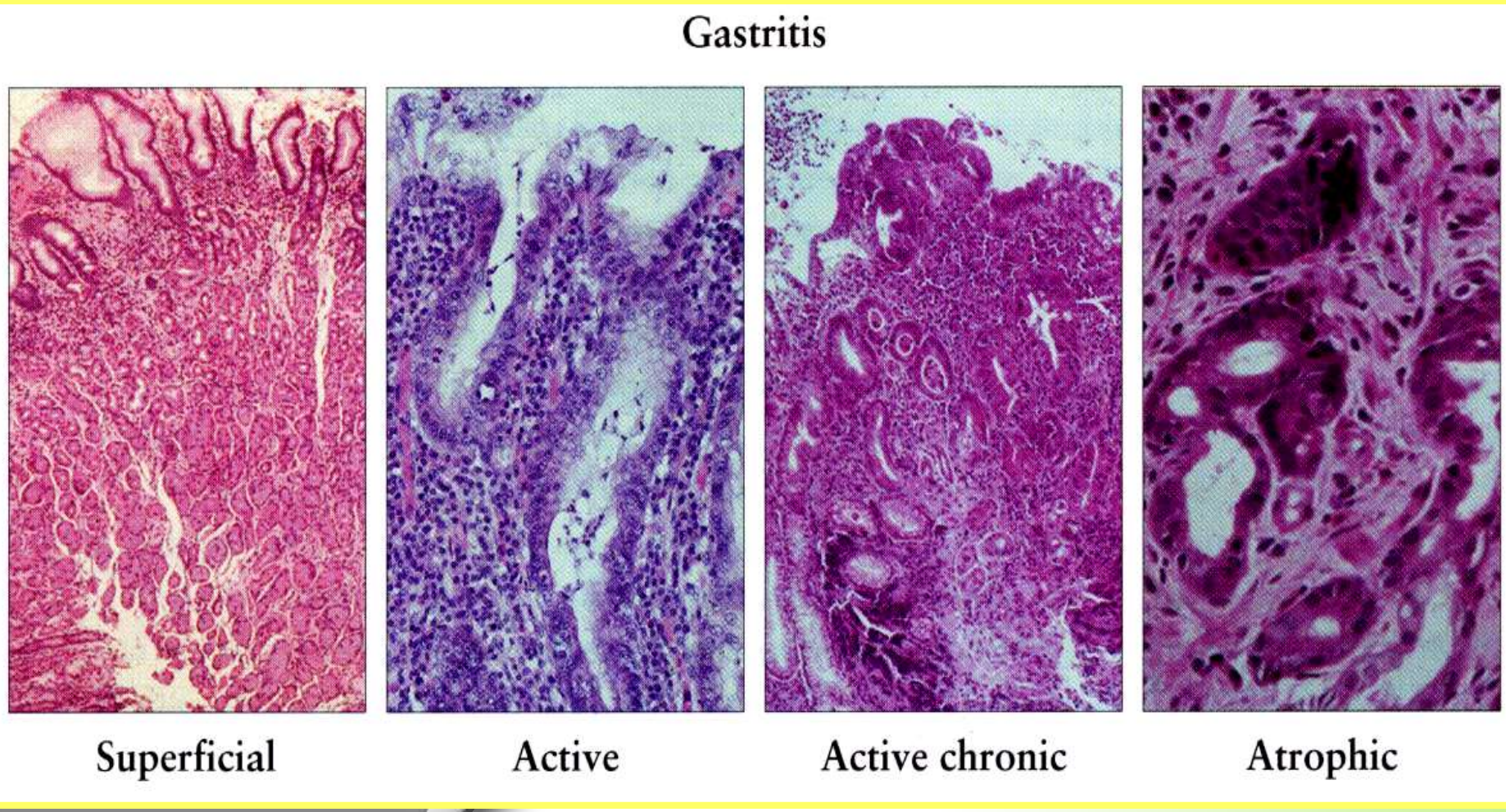
lipopolysac charides → activation of epithelial cell apoptosis

phospholipases A2 and C → membrane destruction; → formation of BAS

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



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

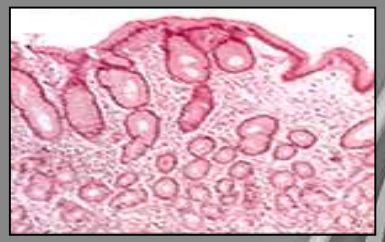
Gastrin 17 (G 17) is produced by G-cells in the antral part of the stomach in response to stimulation by several factors, including food proteins

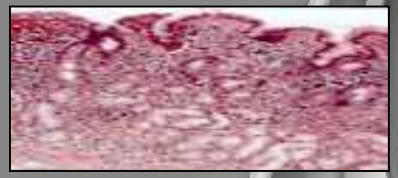
In atrophic gastritis in the antral part the level of G-17 decreases in proportion to the degree of atrophy

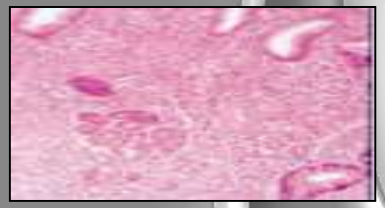
Factors of gastric carcinogenesis

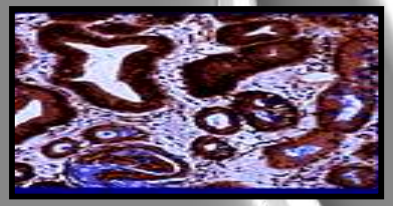
- H. pylori - in 20% of cases causes chronic atrophic gastritis and in 3% of gastric adenocarcinoma cases
- IL-6 and STAT3 interleukins, TNF-γ and IL-1α cytokines promote gastric epithelium proliferation
- Interleukin IL-11 has carcinoprotected properties

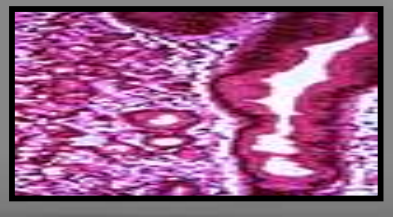
Multilevel gastric carcinogenesis ("Correa Cascade")











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

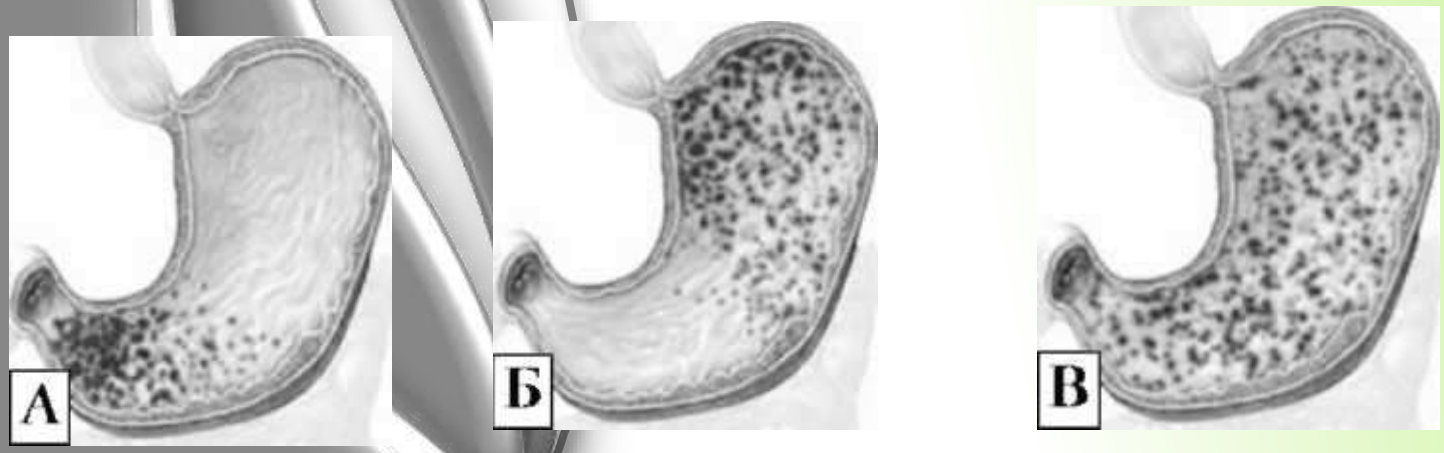
Type of gastritis	Synonyms	Etiological factors
Non-atrophic	Superficial, chronic antral, type B	***H. pylori***
Atrophic autoimmune	Diffuse fundus, type A associated with pernicious anemia	Autoimmune reactions, N. pylori, environmental factors

Special forms of GC:

Chemical	Reactive gastritis, reflux type C	Chemicals, bile, NSAIDs
Radiative		Radiation lesions
Lymphocytic	Lymphocytic	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. (Helicobacter)	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, gastroduodenoanasto-mosis) 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 Gastrospirillium 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, 13C-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

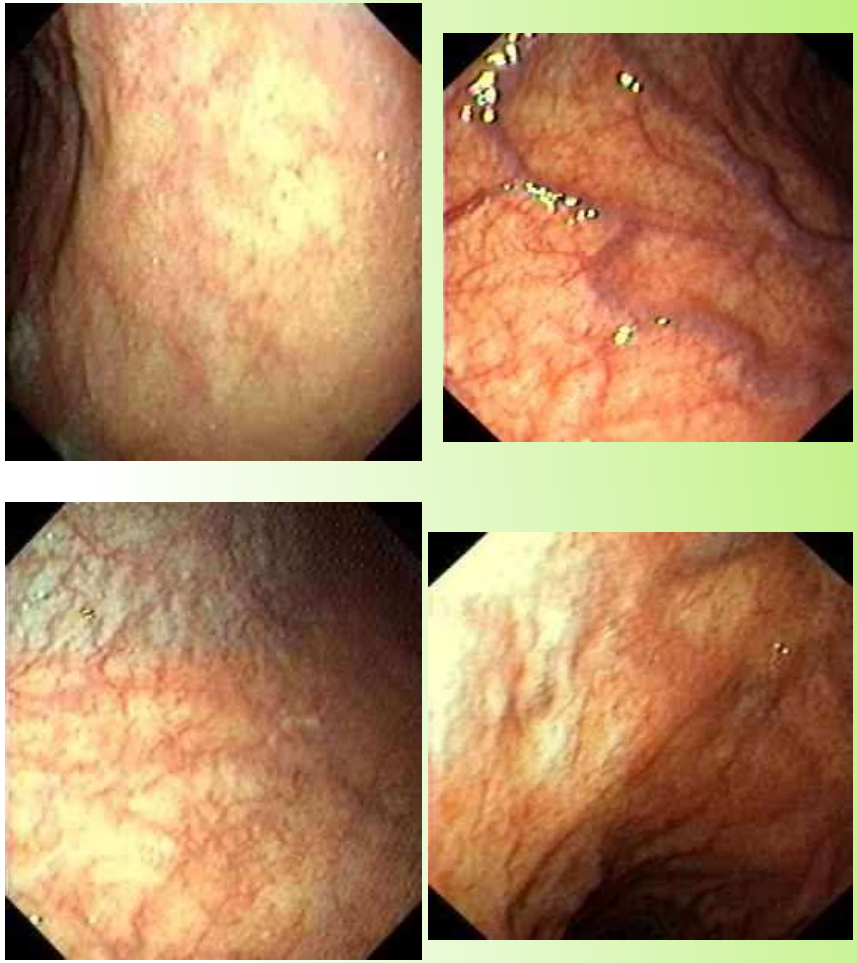
Invasive (biopsy study)	**Ureasy** **Cytological** **Histological** **Molecular (PCR)**
Less invasive (peripheral blood examination)	**Determination of antibodies (enzyme-linked immunosorbent) *** **Molecular**
Non-invasive (study of other biological environments: exhaled air; feces, saliva, urine)	**Ureas breathing** **Stool test **** **Determination of antibodies** **Molecular**

HP tests recommended by Maastricht IV

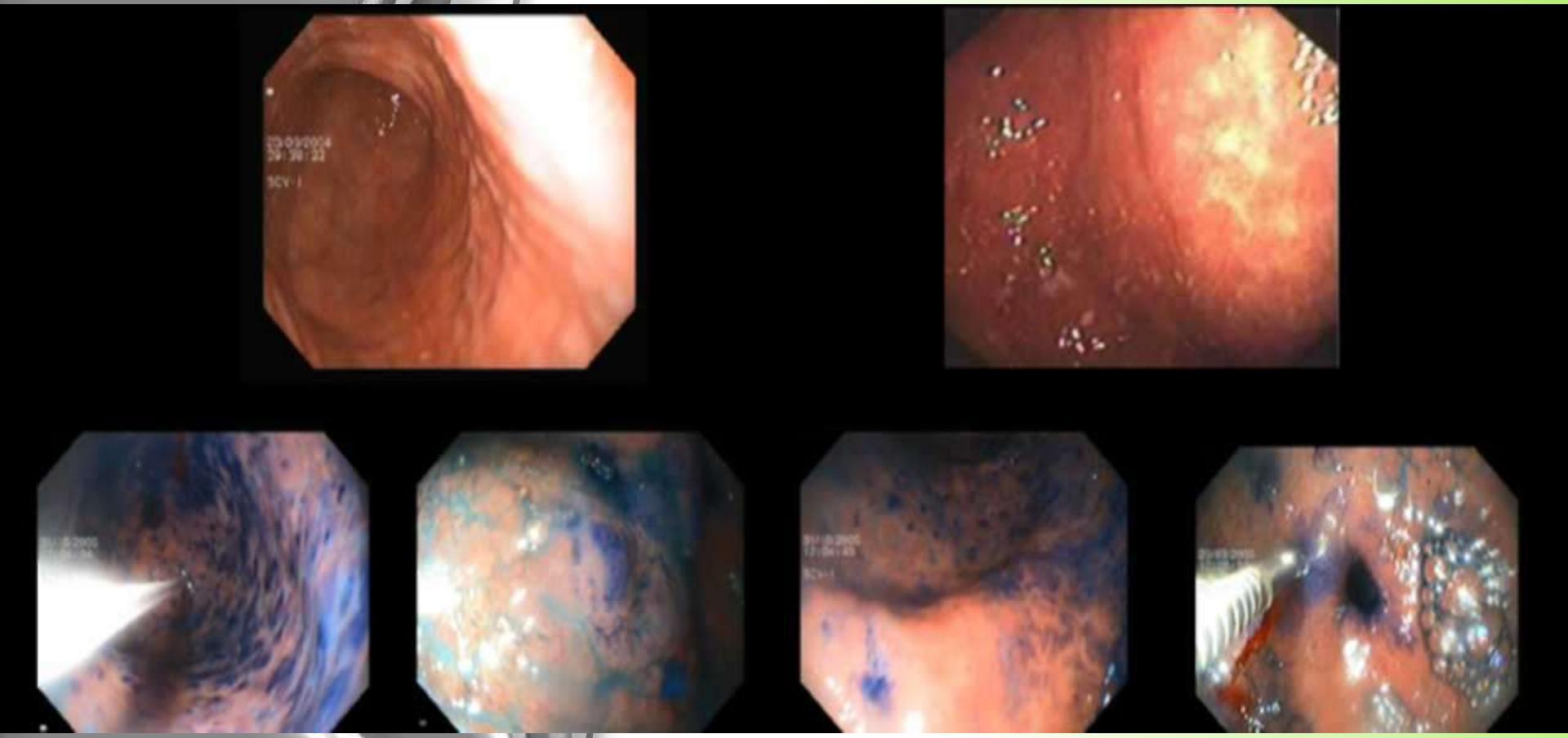
- Urease Breath Test (UBT)
- Stool antigen test (using monoclonal antibodies)
- Biopsy urease test (rapid urease test)
- Enzyme-linked immunosorbent assay (serological, serum IgJ determination)

Videodoscopic signs of gastric atrophy

- Pallor of the gastric mucosa
- Smoothness of the stomach folds
- More sugnificant 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

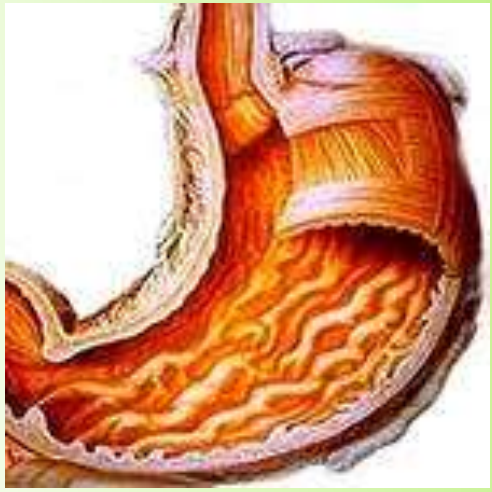
Principles of treatment

- 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

bile acids lysolecithin

↑ the formation of free radicals and TNF-α

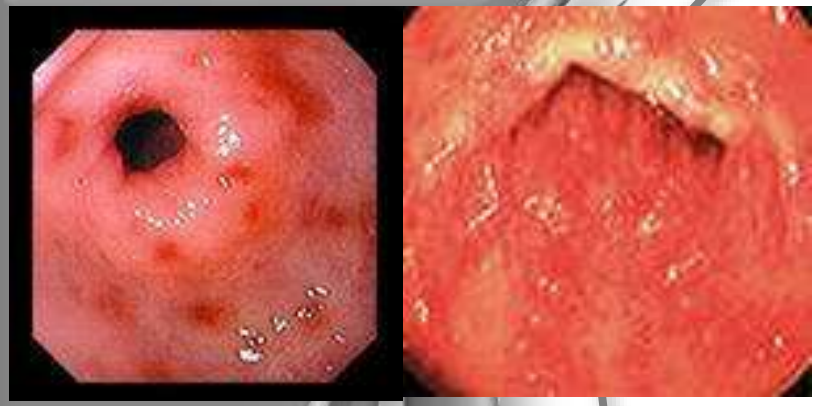
solubilization of superficial epithelium membranes lipids

NSAIDs

↑ apoptosis of epithelial cells

inhibitory effect on COX-1

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

No acid - no ulcer

K. Schwarz, 1910

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

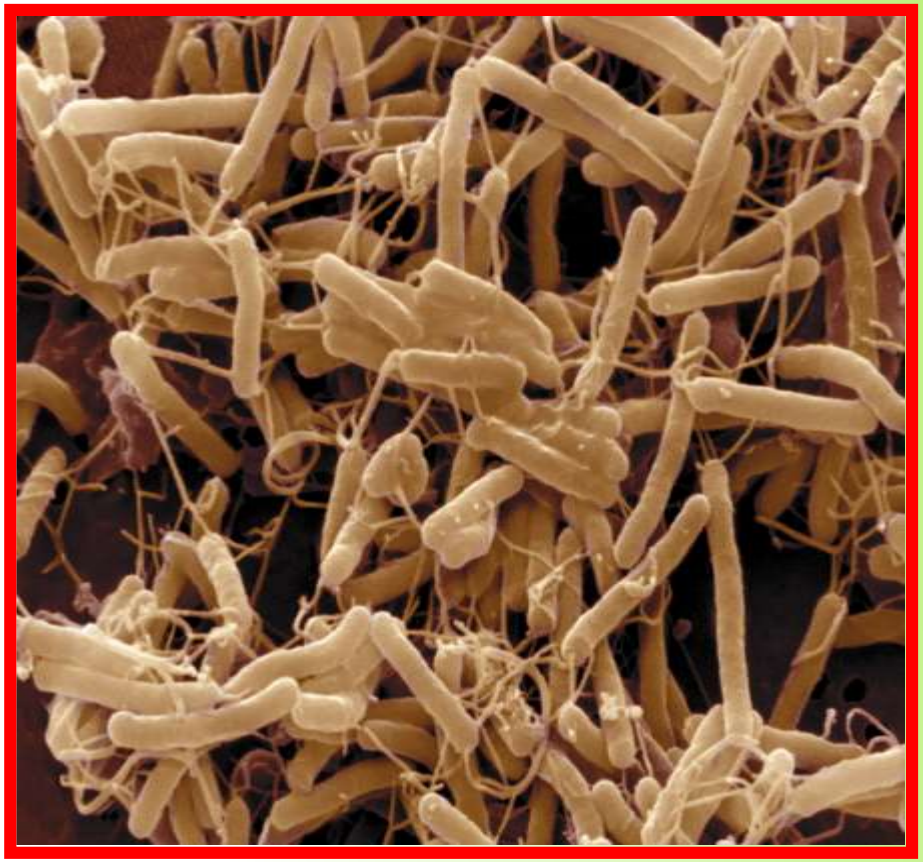
Peptic ulcer: etiology, pathogenesis

... 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

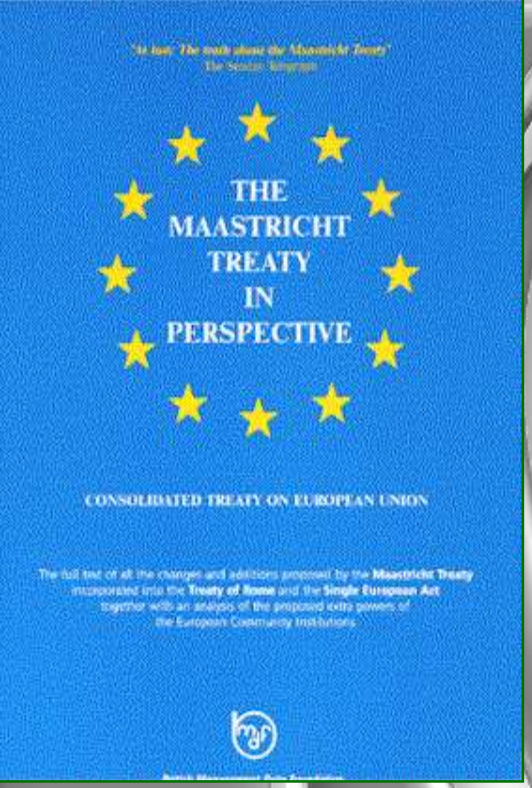
- Hydrochloric acid
- Pepsin
- Disorders of the motor-evacuation function of the stomach
- Duodenal-Gastric Reflux

Protection factors

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

Helicobacter pylori

Strengthening → **ULCER** ← **Weakening**


THE
MAASTRICHT
TREATY
IN
PERSPECTIVE
CONSOLIDATED TREATY ON EUROPEAN UNION

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