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Факультет VI по підготовці іноземних студентів

ЗАТВЕРДЖЕНО
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Зав. кафедри _____д.мед.н., професор Л.В. Журавльова

МЕТОДИЧНІ ВКАЗІВКИ
для студентів

з дисципліни «Внутрішня медицина (в тому числі з ендокринологією)
студенти 4 курсу I, II, III медичних факультетів, V та VI факультетів по підготовці іноземних студентів

Диспепсія. Хронічні гастрити

Харків 2016

KHARKOV NATIONAL MEDICAL UNIVERSITY
DEPARTMENT OF INTERNAL MEDICINE N3

METHODOLOGICAL RECOMMENDATIONS FOR STUDENTS

“Non-ulcer dyspepsia. Chronic gastritis.”

Kharkiv 2016

Practical class. «Non-ulcer dyspepsia. Chronic gastritis», 5 hours

Non-ulcer dyspepsia or functional dyspepsia (FD) is the most common disease in people of 25 years old and younger, but it can be common in older persons as well. Women suffer from FD in 1,5-2 times more than men. Prevalence is from 1,5 % to 58,8 % from number of all gastrointestinal disorders. Special symptoms (aerophagia, neurogenic symptoms, vomiting) are met rather seldom and they are more common for women with hysterical type of mentality.

Gastritis describes a group of conditions with one thing in common: inflammation of the lining of the stomach. An estimated 50% of the world population is infected with *H pylori;* consequently, chronic gastritis is extremely frequent. Injury, regular use of certain pain relievers and drinking too much alcohol also can contribute to gastritis. Gastritis may occur suddenly (acute gastritis), or it can occur slowly over time (chronic gastritis) (CG). In some cases, gastritis can lead to ulcers and an increased risk of stomach cancer. For most people, however, gastritis isn't serious and improves quickly with treatment.

The educational purposes:

- to teach students to distinguish the basic symptoms and syndromes of FD and CG;
- to acquaint students with the methods of physical examination in FD and CG;
- to acquaint students with the methods of examination which are applied to the diagnosis of FD and CG; with indications and contra-indications they have; with the techniques of their performance; with the diagnostic value of each of them;
- to teach students to interpret the results of the lead researches;
- to teach students to distinguish and diagnose the complications of FD and CG;
- to teach students to administer the treatment for FD and CG.

What should the student know?

- the frequency of FD and CG occurrence;
- the etiological factors of FD and CG;
- the pathogenesis of FD and CG;
- the common clinical syndromes of FD and CG;
- the general and alarm symptoms of FD and CG;
- the physical symptoms of FD and CG;
- the methods of physical examination of patients with FD and CG;
- the diagnosis of FD and CG;
- diagnostical opportunities of esophagogastroduodenoscopy in FD and CG, indications and contra-indications;
- the morphological examination of stomach mucosa in FD and CG;
- the techniques of carrying out intragastric pH-metry, clinical estimation of the results;
- the methods of H. Pylory diagnosis;
- the radiological methods diagnosis;
- complications in FD and CG;
- treatment of FD and CG (lifestyle, diet, medication).

What should the student be able to do?

- to define the main clinical and physical syndromes of FD and CG;
- to interpret the results of biochemical and immune enzyme assays;
- to interpret the data of esophagogastroduodenoscopy;
- to interpret the data of intragastric pH-metry;
- to interpret the data of radiological methods of diagnostics of FD and CG;
- to administer the therapy for the patients with FD and CG.

The list of practical skills which student should acquire

— inspection of the belly;
— superficial palpation of the belly;
— deep methodical sliding palpation of the abdominal cavity by Obraztsov-Strazhesco;
— the symptoms of irritated peritoneum;
— the survey of skin and mucous membranes;

Topics content

FUNCTIONAL (NON-ULCER) DYSPEPSIA

Functional dyspepsia (FD), a common functional gastrointestinal disorder, is defined by the Rome III criteria as symptoms of epigastric pain or discomfort (prevalence in FD of 89–90%), postprandial fullness (75–88%), and early satiety (50–82%) within the last 3 months with symptom onset at least 6 months earlier. Patients cannot have any evidence of structural disease to explain symptoms and predominant symptoms of gastroesophageal reflux are exclusionary.

Epidemiology

Healthcare providers of all specialties routinely evaluate patients for symptoms of dyspepsia. The prevalence of dyspepsia in the general population has been estimated to be 20–40% and the majority of these patients are believed to have FD. A systematic review found that the prevalence of FD (after normal upper endoscopy) is 12–15%, while the incidence of dyspepsia (most of whom have FD) has been calculated at <1% over 3 months to up to 2.8% per year. The natural history of FD has not been well characterised, although the limited available data suggest that approximately 50% of patients remain symptomatic over a 5-year follow-up period.

Etiology

Potential causes of non-ulcer dyspepsia:

- Duodenogastric reflux.
- Duodenitis.
- carbohydrate malabsorption (lactose, fructose, sorbitol).
- cholelithiasis or choledocholithiasis.
- chronic pancreatitis.
- Systemic disorders (diabetes, thyroid, parathyroid, hypoadrenalism, connective tissue disease).
- Intestinal parasites.
- Psychiatric disorders.
- Visceral hypersensitivity.
- Gastric/small intestinal dysmotility.
- Gallbladder/biliary dysmotility.

Pathophysiology

Several pathophysiological mechanisms have been proposed to underlie symptom generation in functional dyspepsia. The main hypotheses include abnormalities of gastric motor function, visceral hypersensitivity due to central or peripheral sensitization, low-grade inflammatory states

and genetic predisposition. *Helicobacter pylori* (*H. pylori*) is a bacterial infection of the stomach that can lead to inflammation (gastritis) or ulcers. There may be a relationship between infection with *H. pylori* and functional dyspepsia. However, not all people with *H. pylori* have functional dyspepsia.

Gastric Motor Function

Abnormal motor function, especially delayed gastric emptying, has for a long time been considered the main pathophysiological mechanism underlying functional dyspepsia symptom generation. Alterations in gastric anatomy, such as gastric ptosis (downward displacement of the stomach), have been thought to be associated with delayed gastric emptying. The process of digesting food involves a series of events involving the nerves and muscles of the digestive tract. Problems in this system can cause the stomach to empty more slowly than normal, causing nausea and vomiting, feeling full quickly when eating, or bloating. However, not everyone whose stomach empties slowly has functional dyspepsia. More recently, rapid gastric emptying has been implicated in functional dyspepsia symptoms, especially in the PDS group.

Duodenal Hypersensitivity and Low-grade Inflammation

The stomach normally stretches as we eat to hold more food. However, some people are sensitive to this stretching and feel pain.

The duodenum is increasingly being recognized as a site involved in symptom generation in functional dyspepsia through increased sensitivity to acid and lipids. The mechanism underlying duodenal hypersensitivity is unclear, and impaired motor clearance as well as low-grade duodenal inflammation has been implicated. The role of eosinophils in the duodenum in functional dyspepsia was studied. Observations suggest that duodenal local, allergy-driven reactions may contribute to PDS symptoms such as early satiation. More recent observations point towards systemic immune activation that is present in at least a subset of functional dyspepsia patients.

Visceral Hypersensitivity and Altered Brain Processing

Visceral hypersensitivity is considered a key phenomenon underlying unexplained gastrointestinal symptoms, but the underlying mechanisms are incompletely elucidated, and both peripheral (increased permeability, enhanced excitability of afferent nerves) and central (altered brain processing) sensitization have been implicated.

People with functional dyspepsia often have mood problems, like anxiety or depression. Treating the underlying depression or anxiety can improve symptoms of abdominal pain.

Genetic Susceptibility

Previous studies have linked functional dyspepsia to a G-protein beta 3 (GNβ3) subunit gene polymorphism (C825T). A number of recent studies investigated this and other polymorphisms in functional dyspepsia.

Clinical presentation

Functional dyspepsia, defined by Rome III criteria, is the presence of symptoms thought to originate in the gastroduodenal region in the absence of any organic, systemic, or metabolic disease likely to explain the symptoms. In their recent guidelines, the Rome committee introduced two new subcategories for FD - postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). Recent studies have shown that these two subcategories accurately reflect clinical patients. Epigastric pain or discomfort is the hallmark symptom in patients with FD. The word discomfort is important to emphasise, as many patients will not complain of pain, but rather state that they have burning, pressure or fullness in the epigastric area, or cannot finish a normal-sized meal (early satiety). Other common symptoms that occur in FD patients include postprandial

nausea, belching and abdominal bloating. Frustratingly, symptoms of FD do not consistently predict underlying pathophysiology and do not reliably guide therapy.

Rome III criteria for functional dyspepsia

For the two categories noted below, criteria must be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis. Patients must have one or more of the following symptoms:

- Postprandial fullness
- Early satiety
- Epigastric burning

In addition, patients cannot have any evidence of structural disease that is likely to explain symptoms (i.e. upper endoscopy is normal).

A. **Postprandial distress syndrome**

Diagnostic criteria must include both the following:

- Bothersome postprandial fullness, occurring after ordinary sized meals, at least several times per week
- Early satiation that prevents finishing a regular meal, at least several times per week
- Other supporting criteria:
- Upper abdominal bloating or postprandial nausea or excessive belching can be present
- Epigastric pain syndrome may coexist

B. **Epigastric Pain Syndrome**

Diagnostic criteria must include all of the following:

- Pain or burning localised to the epigastrium, of at least moderate severity at least once per week
- The pain is intermittent
- Not generalised or localised to other abdominal or chest regions
- Not relieved by defecation or passage of flatus
- Not fulfilling criteria for biliary pain

Supportive criteria:

- The pain may be of a burning quality, but without a retrosternal component
- The pain is commonly induced or relieved by ingestion of a meal, but may occur while fasting
- Postprandial distress syndrome may coexist

<u>Diagnosis</u>

A diagnosis of functional dyspepsia can therefore only be established after exclusion of other causes of dyspepsia. A history, physical examination, and laboratory evaluation are the first steps in the evaluation of a patient with new onset of dyspepsia. A detailed history is necessary to narrow the differential diagnosis and to identify gastroesophageal reflux disease (GERD) and nonsteroidal anti-inflammatory drug (NSAID)-induced dyspepsia, as well as patients with alarm features. The physical examination in patients with dyspepsia is usually normal, except for epigastric tenderness. The presence of epigastric tenderness cannot accurately distinguish organic dyspepsia from functional dyspepsia. Routine blood counts and blood chemistry including liver function tests should be performed to identify patients with alarm features (eg, iron deficiency

anemia) and underlying metabolic diseases that can cause dyspepsia (eg, diabetes, hypercalcemia). The approach to and extent of diagnostic evaluation of a patient with dyspepsia is based on the presence or absence of alarm features, patient age, and the local prevalence of *Helicobacter pylori* (*H. pylori*) infection.

Alarm symptoms

- Anaemia (iron deficiency)
- Loss of weight
- Anorexia
- Recent onset of progressive symptoms
- Melaena / haematemesis
- Swallowing difficulty

According to Rome III guidelines, upper endoscopy is the examination of choice to distinguish functional dyspepsia from organic causes of dyspepsia. However, taking into account the high prevalence of dyspeptic symptoms in the population, performing endoscopy in all patients is not feasible.

Upper endoscopy should be performed for the evaluation of new onset dyspepsia in patients with alarm features or those age ≥50 years (guidelines also suggest that the age cutoff may vary between countries, depending upon the prevalence of gastric cancer). Upper endoscopy provides a gold standard for establishing a specific cause in patients with upper abdominal pain. Biopsies of the stomach should be obtained to rule out *H. pylori*. Patients with *H. pylori* should receive eradication therapy in addition to treatment based on the underlying diagnosis. If the upper endoscopy is normal, patients with alarm features or persistent symptoms of dyspepsia should undergo further evaluation to exclude other etiologies. However, most patients with a normal upper endoscopy and routine laboratory tests have functional dyspepsia. Endoscopic evaluation of patients with dyspepsia without alarm features provides a very small additional benefit over a strategy to test and treat for *H. pylori* and is unlikely to be cost-effective. It is therefore reserved for patients with persistent symptoms despite antisecretory therapy and *H. pylori* testing/treatment.

Recommendations

- Patients with dyspepsia who are older than 50 years of age and/or those with alarm features should undergo endoscopic evaluation.
- Patients with dyspepsia who are younger than 50 years of age and without alarm features may undergo an initial test-and-treat approach for H. pylori.
- Patients who are younger than 50 years of age and are H. pylori negative can be offered an initial endoscopy or a short trial of PPI acid suppression.
- Patients with dyspepsia who do not respond to empiric PPI therapy or have recurrent symptoms after an adequate trial should undergo endoscopy.

Test and treat for Helicobacter pylori. The rationale for *H. pylori* testing in patients with dyspepsia is based upon the recognition of *H. pylori* as an etiologic factor in peptic ulcer disease. Testing for *H. pylori* should be performed with a urea breath test or stool antigen assay. Serologic testing should not be used due to their low positive predictive value.

Antisecretory therapy. Empiric antisecretory therapy without *H. pylori* testing/treatment should be recommended in areas of very low prevalence for *H. pylori* (<5 percent) and may also be considered in areas with prevalence of 5 to 10 percent. Proton pump inhibitor therapy is more effective in relieving symptoms of dyspepsia as compared with H2 antagonists.

<u>Differential diagnosis</u>

- Gastro-oesophageal reflux disease.
- Peptic ulcer disease.
- Medication related: non-steroidal anti-inflammatory drugs, antibiotics, iron, potassium supplements, digoxin.
- Carbohydrate malabsorption (lactose, fructose, sorbitol).
- Cholelithiasis or choledocholithiasis.
- Chronic pancreatitis.
- Systemic disorders (diabetes, thyroid, parathyroid, hypoadrenalism, connective tissue disease).
- Intestinal parasites.
- Abdominal malignancy (especially pancreatic and gastric cancer).
- Chronic mesenteric ischaemia.

Treatment

Treatment options for functional dyspepsia are limited. No drugs with established efficacy are widely available, and drug development is hampered by the large placebo effect as well as the lack of well validated endpoints for the Rome III-based definitions of functional dyspepsia.
Pharmacological approaches to correct abnormal gastric motility or sensitivity are considered a valid therapeutic approach in upper gastrointestinal motor disorders. Gastrointestinal prokinetics, drugs that stimulate gastric smooth muscle contractions, have long been considered the drugs of choice for the treatment of functional dyspepsia and gastroparesis. Traditional prokinetic agents are dopamine2 receptor (D2) antagonists or 5-HT4 receptor agonists. The Rome III consensus suggested that EPS might respond to acid-suppressive or antacid therapy, whereas PDS might respond to prokinetic or motility-modifying therapy.
Patients who are test positive for an infection with *H. pylori* should undergo treatment with eradication therapy. Most dyspeptic patients who are *H. pylori* positive and who are treated with appropriate antibiotic therapy persist with dyspeptic symptoms; the number needed to treat to successfully relieve dyspeptic symptoms is estimated at 1 in 14. Patients who have continued symptoms after successful eradication of *H. pylori* should be treated with antisecretory therapy with a proton pump inhibitor for four to eight weeks. However, some patients may continue to have symptoms of dyspepsia and may require additional evaluation.

CHRONIC GASTRITIS

Gastritis describes a group of conditions with one thing in common: inflammation of the lining of the stomach. The inflammation of gastritis is most often the result of infection with the same bacterium that causes most stomach ulcers. Injury, regular use of certain pain relievers and drinking too much alcohol also can contribute to gastritis. Gastritis may occur suddenly (acute gastritis), or it can occur slowly over time (chronic gastritis). In some cases, gastritis can lead to ulcers and an increased risk of stomach cancer. For most people, however, gastritis isn't serious and improves quickly with treatment.

The chronic gastritides are classified on the basis of their underlying cause (eg, *H pylori*, bile reflux, nonsteroidal anti-inflammatory drugs [NSAIDs], autoimmunity or allergic response) and histopathologic pattern, which may suggest the cause and the likely clinical course (eg, *H pylori*–associated multifocal atrophic gastritis). Other classifications are based on the endoscopic appearance of the gastric mucosa (eg, varioliform gastritis). It is important to distinguish between gastritis and gastropathy (in which there is cell damage and regeneration, but minimal inflammation).

Epidemiology

An estimated 50% of the world population is infected with *H pylori;* consequently, chronic gastritis is extremely frequent. *H pylori* infection is highly prevalent in Asia and in developing countries, and multifocal atrophic gastritis and gastric adenocarcinomas are more prevalent in these areas. Autoimmune gastritis is a relatively rare disease, most frequently observed in individuals of northern European descent and black people. Age is the most important variable relating to the prevalence of *H pylori* infection, with persons born before 1950 having a notably higher rate of infection than those born after 1950. Chronic *H pylori*- associated gastritis affects both sexes with approximately the same frequency, though some studies have noted a slight male predominance. The female-to-male ratio for autoimmune gastritis has been reported to be 3:1. Lymphocytic gastritis affects men and women at similar rates.

Etiology

Chronic gastritis may be caused by either infectious or noninfectious conditions.
Infectious forms of gastritis include the following:

- Chronic gastritis caused by *H pylori* infection – This is the most common cause of chronic gastritis.
- Gastritis caused by *Helicobacter heilmannii* infection
- Granulomatous gastritis associated with gastric infections in mycobacteriosis, syphilis, histoplasmosis, mucormycosis, South American blastomycosis, anisakiasis, or anisakidosis
- Chronic gastritis associated with parasitic infections - *Strongyloides* species, schistosomiasis, or *Diphyllobothrium latum*
- Gastritis caused by viral (eg, CMV or herpesvirus) infection

Noninfectious forms of gastritis include the following:

- Autoimmune gastritis
- Chemical gastropathy- usually related to chronic bile reflux, NSAID and aspirin intake [44]
- Uremic gastropathy
- Chronic noninfectious granulomatous gastritis – this may be associated with Crohn disease, sarcoidosis, Wegener granulomatosis, foreign bodies, cocaine use, isolated granulomatous gastritis, chronic granulomatous disease of childhood, eosinophilic granuloma, allergic granulomatosis and vasculitis, plasma cell granulomas, rheumatoid nodules, tumoral amyloidosis and granulomas associated with gastric carcinoma, gastric lymphoma, or Langerhans cell histiocytosis
- Lymphocytic gastritis, including gastritis associated with celiac disease (also called collagenous gastritis)
- Eosinophilic gastritis
- Radiation injury to the stomach
- Graft-versus-host disease (GVHD)
- Ischemic gastritis
- Gastritis secondary to drug therapy (NSAIDs and aspirin)

Some patients have chronic gastritis of undetermined etiology or gastritis of undetermined type (eg, autistic gastritis).

Pathophysiology

H pylori–associated chronic gastritis. *Helicobacter pylori* is the leading cause of chronic gastritis,

peptic ulcer disease, gastric adenocarcinoma and primary gastric lymphoma. First described by Marshall and Warren in 1983, *H pylori* is a spiral gram-negative rod that has the ability to colonize and infect the stomach. The bacteria survive within the mucous layer that covers the gastric surface epithelium and the upper portions of the gastric foveolae. The infection is usually acquired during childhood. Once present in the stomach, the bacteria passes through the mucous layer and becomes established at the luminal surface of the stomach causing an intense inflammatory response in the underlying tissue. The presence of *H pylori* is associated with tissue damage and the histologic finding of both an active and a chronic gastritis. The host response to *H pylori* and bacterial products is composed of T and B lymphocytes, denoting chronic gastritis, followed by infiltration of the lamina propria and gastric epithelium by polymorphonuclear leukocytes (PMNs) that eventually phagocytize the bacteria. The presence of PMNs in the gastric mucosa is diagnostic of active gastritis. High levels of cytokines, particularly tumor necrosis factor-α (TNF-α) and multiple interleukins (eg, IL-1β, IL-6, IL-8, IL-10, IL-12, IL-17 and IL-18), are detected in the gastric mucosa of patients with *H pylori* gastritis.

H pylori- associated chronic gastritis progresses according to the following 2 main topographic patterns, which have different clinical consequences:

- Antral predominant gastritis – This is characterized by inflammation and is mostly limited to the antrum; individuals with peptic ulcers usually demonstrate this pattern
- Multifocal atrophic gastritis – This is characterized by the involvement of the corpus and gastric antrum with progressive development of gastric atrophy (loss of the gastric glands) and partial replacement of gastric glands by an intestinal-type epithelium (intestinal metaplasia); individuals who develop gastric carcinoma and gastric ulcers usually demonstrate this pattern.

Infectious granulomatous gastritis is a rare entity. Tuberculosis may affect the stomach and cause caseating granulomas. Fungi can also cause caseating granulomas and necrosis. Granulomatous gastritis has also been associated with *H pylori* infection.

Autoimmune atrophic gastritis. Autoimmune atrophic gastritis is associated with serum anti-parietal and anti–intrinsic factor (IF) antibodies. The gastric corpus undergoes progressive atrophy, IF deficiency occurs, and patients may develop pernicious anemia.

The development of chronic atrophic gastritis (sometimes called type A gastritis) limited to corpus-fundus mucosa and marked diffuse atrophy of parietal and chief cells characterizes autoimmune atrophic gastritis. In addition to hypochlorhydria, autoimmune gastritis is associated with serum anti-parietal and anti-IF antibodies that cause IF deficiency, which, in turn, causes decreased availability of cobalamin, eventually leading to pernicious anemia in some patients. Hypochlorhydria induces G-Cell (Gastrin producing) hyperplasia, leading to hypergastrinemia. Gastrin exerts a trophic effect on enterochromaffin-like (ECL) cells and is hypothesized to be one of the mechanisms leading to the development of gastric carcinoid tumors (ECL tumors).

Chronic reactive chemical gastropathy. Chronic reactive chemical gastritis is associated with long-term intake of aspirin or NSAIDs. It also develops when bile-containing intestinal contents reflux into the stomach. Pancreatic juice enhances epithelial injury in addition to bile acids. In contrast to other chronic gastropathies, minimal inflammation of the gastric mucosa typically occurs in chemical gastropathy.

Gastritis in patients who are immunosuppressed. Cytomegalovirus (CMV) infection of the stomach is observed in patients with underlying immunosuppression. Histologically, a patchy, mild inflammatory infiltrate is observed in the lamina propria. Other infectious causes of chronic gastritis in immunosuppressed patients, include the Herpes simplex virus (HSV), which causes basophilic intranuclear inclusions in epithelial cells. Mycobacterial infections involving *Mycobacterium avium-intracellulare* are characterized by diffuse infiltration of the lamina propria

by histiocytes, which rarely form granulomas.

Chronic noninfectious granulomatous gastritis. Noninfectious diseases are the usual cause of gastric granulomas; these include Crohn disease, sarcoidosis, and isolated granulomatous gastritis. An underlying cause of chronic granulomatous gastritis cannot be identified in up to 25% of cases. These patients are considered to have idiopathic granulomatous gastritis (IGG).

Lymphocytic gastritis. Lymphocytic gastritis is a type of chronic gastritis characterized by dense infiltration of the surface and foveolar epithelium by T lymphocytes and associated chronic infiltrates in the lamina propria.

Eosinophilic gastritis. Large numbers of eosinophils may be observed with parasitic infections. Eosinophilic gastritis can be part of the spectrum of eosinophilic gastroenteritis. Although the gastric antrum is commonly affected and can cause gastric outlet obstruction, this condition can affect any segment of the GI tract and can be segmental. Patients frequently have peripheral blood eosinophilia. In some cases, especially in children, eosinophilic gastroenteritis can result from food allergy, usually to milk or soy protein. Eosinophilic gastroenteritis can also be found in some patients with connective tissue disorders, including scleroderma, polymyositis, and dermatomyositis.

Radiation gastritis. Radiation gastritis usually occurs 2-9 mo after initial radiotherapy. The dose at which 5 percent of patients develop complications at five years, when the entire stomach is irradiated, is estimated to be 50 Gy. Small doses of radiation (up to 15 Gy) cause reversible mucosal damage, whereas higher doses cause irreversible damage with atrophy and ischemic-related ulceration.

Ischemic gastritis. Ischemic gastritis is believed to result from atherosclerotic thrombi arising from the celiac and superior mesenteric arteries.

Clinical presentation

In the vast majority of cases, chronic gastritis causes no symptoms. When the damage to the mucosa is severe and long standing, the stomach loses its ability to produce acid. This may cause digestive upsets. However, upper central abdominal pain is the most common symptom; the pain may be dull, vague, burning, aching, gnawing, sore, or sharp. Pain is usually located in the upper central portion of the abdomen, but it may occur anywhere from the upper left portion of the abdomen around to the back.
Other signs and symptoms may include the following:

- nausea
- vomiting (if present, may be clear, green or yellow, blood-streaked, or completely bloody, depending on the severity of the stomach inflammation)
- belching (if present, usually does not relieve the pain much)
- bloating
- early satiety
- loss of appetite
- unexplained weight loss

H pylori-associated chronic gastritis, which is usually asymptomatic but may manifest as epigastric pain, nausea, vomiting, anorexia, early satiety or weight loss. Symptoms may occur with the development of complications of chronic *H pylori* gastritis, which include peptic ulcers, gastric adenocarcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma.

The clinical manifestations of autoimmune gastritis are primarily related to the deficiency in cobalamin, which is not adequately absorbed because of intrinsic factor (IF) deficiency resulting from severe gastric parietal cell atrophy. The disease has an insidious onset and progresses slowly. Cobalamin deficiency affects the hematologic, gastrointestinal (GI), and neurologic systems. The most significant hematologic manifestation is megaloblastic anemia, symptoms include weakness, light-headedness, vertigo, tinnitus, palpitations, angina and symptoms of congestive heart failure. Gastrointestinal manifestations: glossitis; anorexia with moderate weight loss that is occasionally associated with diarrhea may result from malabsorption associated with megaloblastic changes of the small intestinal epithelial cells. Neurologic manifestations: numbness and paresthesias in the extremities, weakness, and ataxia. Sphincter disturbances may occur. Mental function disturbances range from mild irritability to severe dementia or psychosis.
Patients with Crohn disease and gastric involvement may report abdominal pain, nausea, and vomiting.
Some patients with eosinophilic gastroenteritis have underlying connective tissue disorders. Those with predominant mucosal involvement may report nausea, vomiting, and abdominal pain related to the ingestion of specific foods. Many patients have a history of allergy, peripheral eosinophilia, asthma, eczema, or food sensitivity. Some respond to removal of these items from the diet, and steroid treatment is often helpful.

Diagnosis

The diagnosis of chronic gastritis can only be established on histologic grounds. Therefore, histologic assessment of endoscopic biopsies is essential. Identification of the underlying cause of chronic gastritis and assessment of specific complications can require several laboratory tests.

Endoscopy

Upper GI endoscopy is essential for establishing the diagnosis of gastritis. Multiple biopsy specimens should be obtained. Tissue sampling from the gastric antrum, incisura, and corpus is essential to establish the topography of gastritis and to identify atrophy and intestinal metaplasia, which usually is patchy.

Laboratory Studies

Atrophic gastritis may be assessed by measuring the ratio of pepsinogen I (PGI, PGA) to pepsinogen II (PGII, PGC) in the serum. PGI and PGII are synthesized and secreted by gastric chief cells. After being secreted into the gastric lumen, they are converted into proteolytic active pepsins. The level of PGI in the serum decreases as gastric chief cells are lost during gastric atrophy, resulting in a decreased PGI/PGII ratio. Gastric carcinoma occurs, especially the intestinal type, usually in association with severe atrophic gastritis.

The following test results suggest the diagnosis of *autoimmune gastritis*:

- Antiparietal and anti–intrinsic factor (IF) antibodies in the serum
- Achlorhydria, both basal and stimulated, and hypergastrinemia
- Low serum cobalamin (vitamin B-12) levels (<100 pg/mL)
- Possible abnormal result on Schilling test (this can be corrected by IF)

Diagnostic Testing for Helicobacter pylori.

Endoscopic Testing:

1. Histology
2. Rapid urease testing
3. Culture
4. Polymerase chain reaction

Nonendoscopic Testing:

1. Antibody testing (quantitative and qualitative)
2. Urea breath tests (13C and 14C)
3. Fecal antigen test

Treatment

Treatment of chronic gastritis can be aimed at a specific etiologic agent, if such an agent is known. When gastritis represents gastric involvement of a systemic disease, treatment is directed toward the primary disease.

Pharmacotherapy for H pylori. The most widely used regimens for eradicating *H pylori* are triple therapies, which are recommended as first-line treatments; quadruple therapies are recommended as second-line treatment when triple therapies fail. With either type of regimen, the best results are achieved by administering therapy for 10-14 days, though some studies have limited the duration of treatment to 7 days. The accepted definition of cure is that no evidence of *H pylori* exists for 4 or more weeks after ending the antimicrobial therapy.

Do not administer antibiotic therapy if the patient does not have a confirmed infection, and be sure to assess the results of the therapy carefully. Manage cases of subsequent *H pylori* eradication failure on a case-by-case basis, and base antibiotic selection on pretreatment antibiotic sensitivity test results.

Triple therapies (with indicated adult dosing)

Twice-daily PPI or ranitidine bismuth citrate triple therapies include the following:

- Lansoprazole 30 mg, omeprazole 20 mg, or ranitidine bismuth citrate 400 mg orally twice daily
- Clarithromycin 500 mg orally twice daily
- Amoxicillin 1000 mg or metronidazole 500 mg orally twice daily

Quadruple therapies (with indicated adult dosing)

Quadruple therapy for *H pylori* infection typically includes the following:

- PPI (lansoprazole 30 mg or omeprazole 20 mg) orally twice daily
- Tetracycline HCl 500 mg orally 4 times daily
- Bismuth subsalicylate 120 mg orally 4 times daily
- Metronidazole 500 mg orally 3 times daily

If a patient was treated for *H pylori* infection, confirm that the organism has been eradicated. Evaluate eradication at least 4 weeks after the beginning of treatment. Eradication may be assessed by means of noninvasive methods such as the urea breath test or the stool antigen test.

Medications that block acid production and promote healing. Proton pump inhibitors reduce acid by blocking the action of the parts of cells that produce acid. These drugs include the prescription and over-the-counter medications omeprazole, lansoprazole, rabeprazole, esomeprazole and pantoprazole. Long-term use of proton pump inhibitors, particularly at high doses, may increase your risk of hip, wrist and spine fractures. Ask your doctor whether a calcium supplement may reduce this risk.

Medications to reduce acid production. Acid blockers — also called histamine (H-2) blockers — reduce the amount of acid released into your digestive tract, which relieves gastritis pain and promotes healing. They include ranitidine, famotidine, cimetidine and nizatidine.

Antacids that neutralize stomach acid. Your doctor may include an antacid in your drug regimen. Antacids neutralize existing stomach acid and can provide rapid pain relief. Side effects can include constipation or diarrhea, depending on the main ingredients.

Treatment is primarily supportive, and antacids in either liquid or tablet form may be sufficient to treat cases of mild gastritis. Antacids may also be used if the gastritis is associated with an ulcer. Gastritis caused by NSAIDs usage may be treated by taking the drug with food, decreasing the dose, or discontinuing the drug. Excess stomach acid production may be treated with drugs such as a histamine receptor antagonist or a proton pump inhibitor. Medications that coat and protect the stomach lining may also be used. Gastritis due to alcohol consumption is usually mild and treated by counseling the individual to either stop or decrease the amount of alcohol consumed. Individuals with symptoms aggravated by caffeine consumption are instructed to limit coffee, tea, and caffeinated beverages. Should the individual be deficient in vitamin B_{12}, shots must be received on a monthly basis. A blood transfusion may be required if severe bleeding has occurred. Endoscopic surgery to stop the bleeding (hemostasis) or surgery to remove part of the stomach (subtotal gastrectomy) is indicated in rare instances.

The control of initial level of knowledge

1. The patient complains of heartburn, eructation, heavy feeling in epigastrium which appear after emotional overstrain. What could cause such clinical picture?

A. Chronic gastritis
B. Functional dyspepsia
C. Stomach ulcer
D. Duodenal ulcer
E. GERD

2. The 32 year old man, complains of weakness, heartbeat after meal. Objectively: a skin and mucosal of usual color. pulse rate is 78/min., blood pressure is 120/70 mm Hg. Tones of heart are rhythmic, sonorous. The liver and spleen are not enlarged. Than the given complaints are caused?

A. Chronic cholecystitis
B. Chronic gastritis
C. FD
D. Gastric ulcer
E. Chronic pancreatitis

3. The woman, 35 years, complains of heartburn and pain while the swallowing. Which of the researches results are the most informative?

A. Colonoskopy
B. pH-metry
C. Ultrasound research
D. X-ray of stomach
E. Esophagogastroduodenoscopy

4. The 24 year old patient complains of pain in the chest during sleep which is occasionally accompanied by heartburn. Abdomen is soft, painless. The liver and a spleen are not enlarged. Which of the researches is the most informative?

A. ECG
B. pH-metry
C. Esophagogastroduodenoscopy
D. X-ray of stomach
E. Ultrasound research

5. The 29 year old patient complains of weakness, air eructation. Which previous diagnosis is the most probable?

A. GERD
B. Type A chronic gastritis
C. Type B chronic gastritis
D. FD
E. Stomach ulcer

6. The 20 year old employee has pains in epigastrium which are accompanied by heartburn. Work is connected with nervous overstrain. Which of the listed methods the most informative for diagnostics:

A. Factious research of gastric juice
B. X-ray of stomach
C. Fibroesophagogastroduodenoscopy
D. pH-metry
E. Duodenal sounding

7. The 35 year old patient complains of pains in epigastrium after eating, heartburn and eructation. A pathology was not revealed during fibroesophagogastroduodenoscopy. What is the most credible diagnosis?

A. FD
B. Chronic gastritis
C. Stomach ulcer
D. Chronic duodenitis
E. GERD

8. The 22 year old patient complains of weakness, sensation of lump in a throat, pain in epigastrium and hiccups. Your preliminary diagnosis?

A. GERD
B. Esophageal reflux
C. FD
D. Chronic esophagitis
E. Stomach cancer

9. The 19 year old patient with the increased weight complains of pain in epigastrium and heartburn at night. Which of research is the most expedient?

A. ECG
B. Factious research of gastric juice
C. Ultrasound research
D. X-ray of epy stomach
E. Esophagogastroduodenoscopy

10. The 31 year old patient complains of intensive pain which amplifies after emotional overstrain, does not pass after meal. Think, if it is possible, what disease it can be first of all?

A. GERD
B. Stomach ulcer
C. Type A chronic gastritis
D. FD
E. Type B chronic gastritis

Correct answers:

1. B
2. C
3. E
4. C
5. D
6. D
7. A
8. C
9. E
10. D

The control of final level of knowledge

1. The patient complains of heartburn, food eructation, periodic pain under xiphoid with increasing at swallowing. A pathology was not revealed during fibroesophagogastroduodenoscopy. What is the most probable reason of this complains?

A. FD
B. Type A chronic gastritis
C. Type B chronic gastritis
D. GERD
E. All set forth above

2. With development of what a syndrome of dyspepsia is connected at FD:

A. Disorders of suction
B. Decline of hydrochloric acid contents
C. Decline of pepsin contents
D. Presence of antibodies to cells of the stomach
E. Disorders of gastroduodenal motility

3. Functional dyspepsia is:

A. Complex of symptoms which includes a painful syndrome at absence of morphological and metabolic changes.
B. Century complex of symptoms, which includes a painful syndrome, sensation of overflow in the upper part of abdomen after eating, which are usual accompanied by others dyspepsia symptoms (vomiting, heartburn, eructation) at absence of morphological and metabolic changes.
C. Complex of symptoms, which includes sensation of overflow in the upper part of the belly after meals, which are usual accompanied by others FD symptoms (nausea, vomiting, heartburn, eructation) at absence of morphological and metabolic changes.
D. Complex of symptoms, which includes dyspepsia symptoms (nausea, vomiting, heartburn, eructation) at absence of morphological and metabolic changes.
E. Complex of symptoms which includes a painful syndrome, sensation of overflow in the upper part of abdomen after meal which are usual accompanied by others dyspepsia symptoms (nausea, vomiting, heartburn, eructation).

4. A pathogenetic mechanisms of development of concern:

A. Duodenostasis
B. Disorders of gastroduodenal motility
C. Gastrostasis
D. Increase of acidity of gastric contents
E. Decline of acidity of gastric contents

5. Name the basic clinical types of FD
A. Ulcer-like, dysmotility variant, nonspecific FD
B. Non-erosive and erosive FD
C. Esophageal and out-esophageal FD
D. Stomach and intestinal
E. All set forth above

6. Prominent feature of clinic FD is:
A. Emotions painting of complaints
B. Strengthening of pain during eating
C. Long and burning character of pain
D. Distribution of pain on a course of esophagus
E. Pain when stomach is empty

7. The basic method of diagnostics FD it is:
A. Psychological tests
B. Research of stomach secretory functions
C. Esophagogastroduodenoscopy
D. pH-monitoring
E. X-ray
8. FD is characterized by:
A. Gullet ulcer
B. Stomach ulcer
C. Anaemia
D. Absence of morphological changes of stomach
E. Metaplazija epithelium of cardium a department of a stomach

9. Differential diagnosis should be spent with:
A. GERD
B. Stomach ulcer
C. Chronic gastritis
D. Stomach cancer
E. With all the listed diseases

10. For treatment of FD can be effective:
A. Platsebo
B. Blocators of H2 - receptors of histamine
C. Prokinetics
D. M - cholinolitics
E. All listed

Correct answers:

1.	A	6.	A
2.	E	7.	C
3.	B	8.	D
4.	B	9.	E
5.	A	10.	A

Case-based questions

1. A patient of 37 years old complains of pain in epigastrium, more often during while sleeping, or after emotional overload, heartburn. These symptoms amplify after eating. Objectively: A belly is painless while palpation, the liver and spleen are not enlarged. What diagnosis is most probable?

A. Stomach cancer
B. Stomach ulcer
C. Chronic gastritis
D. Chronic cholecystitis
E. FD

2. The 21 year old pregnant patient (pregnancy of 30 weeks) complains of constant heartburn, eructation, sleeplessness, frequent migraines. Before pregnancy she was healthy. What is the most probable reason of given disorders?

A. By declining of anti-reflux barrier function
B. By the decline of hover of esophagus
C. FD
D. By stomach evacuation disorders
E. By inability of mucous membrane of esophagus to resist to action of stomach contained which is thrown out into esophagus

3. The patient, suffering from bronchial asthma, complains of attacks of asthma which arise at slopes of the trunk or in horizontal position, and feeling of fast saturation after meals, weights and swelling in epigastrium. These disorders have been regarded by him as attacks of bronchial asthma, but usual means of knocking over of attacks have not given results. Than is it possible to explain the given phenomenon?

A. Getting to means which are applied
B. By a necessity to increase a doze of means which were used as usual
C. Used by a presence of the incorporated pathology
D. By a necessity to change means for knocking over of attacks
E. By a necessity to add one more means

4. The patient complains of heartburn and eructation, irritability, periodic pain in epigastrium of moderate intensity without irradiation which disappears after meals. At esophagogastroduodenoscopy - without pathology. For what disease it is characterized?

A. Stomach ulcer
B. Chronic gastritis
C. Chronic pancreatitis
D. FD
E. Dysmotility of gall-bladder

5. The 22 year old patient, whom was established the diagnosis FD, an ulcer-like variant at inspection and treatment in gastroenterology department. What combination of groups of preparations is most effective for treatment?

A. Spasmolytics + Antacids
B. Analgetics + Antacids
C. Antibacterial preparations + Inhibitors proton pomp
D. Hepatoprotection preparations + blocators of H2- receptors of histamine

E. Inhibitors of proton pomp + diosmektit

6. The patient complains of pain which periodically arises in epigastrium during dreaming and heartburn after eating. Objectively: the patient has excessive weight of body. Disorder of which organ is the most possible?
A. Stomach
B. Gall-bladder
C. Pancreas
D. Intestine
E. Esophagus

7. The woman was delivered in clinic with complaints of pain under shoot of the constrained intensity which arises during sleep, accompanied by nausea and sometimes vomiting, disappears after reception antacids. From anamnesis: complaints of heartburn during last year. The stomach takes participation in the certificate of breath, is moderate-painful in epigastrium. There was not revealed any organic pathology during examination. What is the most probable reason of abdominal pain?
A. Heart attack
B. Acute gastritis
C. Acute pancreatitis
D. Bilious colic
E. FD

8. The 48 year old patient complains of periodic pain in epigastrium, without irradiation, heartburn, which amplify after meals, migraine and sleeplessness. After reception of 20 mgs of rabeprazole during first two days these symptoms disappeared. For what disease this clinical picture is typical?
A. Type A chronic gastritis
B. Duodenal ulcer
C. FD
D. Chronic pancreatitis
E. Chronic hepatitis

9. The man complains of sleeplessness caused by night pain in epigastrium, sensation of fast saturation after meals, overflow and swelling of the stomach. It was established the diagnosis - gastric dyspepsia. For which variant of disease this clinical picture is characterized?
A. Ulcer dyspepsia
B. Dysmotility variant
C. Nonspecific variant
D. All listed

10. The patient was revealed a plural erosion of esophagus at esophagogastroduodenoscopy. With what disease their occurrence is connected?
A. GERD, non-erosive form
B. GERD, erosive form
C. Type A chronic gastritis
D. FD
E. Stomach ulcer

Correct answers:

1. E	5. E	9. C
2. C	6. E	10. B
3. C	7. E	
4. D	8. C	

Test questions

1. Definition of FD, CG.
2. The basic clinical syndromes of FD, CG.
3. The characteristics of the painful syndrome of FD, CG.
4. The characteristics of dyspeptic syndrome of FD, CG.
5. Classification of FD and CG.
6. Name the methods of FD and CG diagnosis.
7. Principles of FD and CG treatment.
8. Lifestyle and diet therapy in FD and CG.
9. Medication therapy of FD and CG.
10. Prevention of FD and CG.

Practical tasks

1. Supervise a patient with FD, CG.
2. Interpret received laboratory tests.
3. Give the interpretation of the received results of instrumental methods of investigation.
4. Perform a differential diagnosis of FD, CG.
5. List the complications of FD, CG.
6. Write the recipes concerning the symptomatic therapy of FD, CG.

Clinical examination of the patient

Name of the patient_____
_____

Age____profession_____

Complaints_____
_____
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_____
_____

Anamnesis morbi
_____
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Anamnesis vitae
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The results of physical examination of the patient:
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Preliminary diagnosis:
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_____

The results of additional research methods:
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_____

Substantiation of clinical diagnosis:
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_____

Clinical diagnosis:
Main
diagnosis_____
_____
_____
Concomitant pathology
_____
_____
_____
Complications
_____
_____
_____

Treatment:
1. _____
2. Diet _____
3._____
4._____
5._____

Materials for self-preparation:

1. Davidson's "Principles and Practice of Medicine" 21st edition, Alimentary tract and pancreatic disease, p. 835-919.
2. Current Medical Diagnosis and Treatment, Gastrointestinal disorders, 2014, p. 564-662
3. Harrison's, Principles of Internal Medicine, 19th edition, Gastoenterology and Hepatology, p.257-398

Інформаційні ресурси

сайт кафедри внутрішньої медицини № 3 ХНМУ http://www. vnmed3.kharkiv.ua/, встановлене інформаційно-освітнє середовище Moodle на піддомен сайта http://distance-training. vnmed3.kharkiv.ua

Методична вказівка складена: асистентом А.К. Журавльовою

Методична вказівка переглянута і затверджена на засіданні кафедри: _____

З доповненнями (змінами) _____

Завідувач кафедри Л.В. Журавльова