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Факультет VI по підготовці іноземних студентів

ЗАТВЕРДЖЕНО
на засіданні кафедри внутрішньої медицини №3
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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

Пептична виразка шлунка та дванадцятипалої кишки

Харків 2016

KHARKOV NATIONAL MEDICAL UNIVERSITY DEPARTMENT OF INTERNAL MEDICINE N3

METHODOLOGICAL RECOMMENDATIONS FOR STUDENTS

"Peptic ulcer"

Kharkiv 2016

Practical class "Peptic ulcer", 5 hours

PU of the stomach and duodenum in many countries remains one of the most topical problems of gastroenterology. It is associated with its high prevalence (10-15% of entire adult population), a prevailing debut of disease in young anв average age, a high level of occurrence of relapses and complications. Results of the basic researches of last years and clinical supervision of patients after introduction of essentially new kinds of therapy have completely changed existing conceptions not only about the reasons and mechanisms of occurrence PU, but also about an opportunity for treatment for PU.

The educational purposes:

— to teach students to distinguish the basic symptoms and syndromes of PU;
— to acquaint students with the methods of physical examination of PU;
— to acquaint students with the methods of researches which are applied to the diagnostics of PU; 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 assays independently;
— to teach students to distinguish and diagnose the complications of PU;
— to teach students to administer therapy for PU.

What should the student know?

— the frequency of PU occurrence;
— the etiological factors of PU;
— the pathogenesis of PU;
— the clinical syndromes of PU
— the general and alarm symptoms of PU;
— the physical symptoms of PU;
— the methods for physical examination of patients with PU;
— the diagnostics of PU;
— the diagnostic opportunities of esophagogastroduodenoscopy with PU, the indications and contra-indications;
— morphological study of stomach mucosa in PU;
— the technique of intragastric pH-metry, clinical estimation of results;
— the methods of diagnostics of H. pylori;
— radiological methods of diagnostics of PU;
— complications of PU;
— treatment of PU (lifestyle, diet, medication).

What should the student be able to do?

— to define the clinical and physical syndromes in PU;
— to interpret the results of biochemical and immunenzyme assays;
— to interpret the data of esophagogastroduodenoscopy;
— to interpret the data of intragastric pH-metry;
— to interpret data of radiological methods of diagnostics in PU;
— to institute the therapy for the patients with PU.

The list of practical skills which the student should acquire:

inspection of the belly;
examination of the belly;
superficial palpation of the belly;
deep methodical sliding palpation of the organs of a belly cavity according to Obrazthov-

Strazhesko;
symptoms of peritoneum irritation;
review of skin and mucous membranes;

Topics content

PEPTIC ULCER

Burning epigastric pain exacerbated by fasting and improved with meals is a symptom complex associated with peptic ulcer disease (PUD). An *ulcer* is defined as disruption of the mucosal integrity of the stomach and/or duodenum leading to a local defect or excavation due to active inflammation. Ulcers occur within the stomach and/or duodenum and are often chronic in nature

The clinical manifestations of acid peptic disease do not always predict the various morphologic presentations found at endoscopy. Indeed, gastritis or an ulcer may be silent and recognized only when it presents abruptly with a complication, most commonly perforation or hemorrhage, or incidentally after a diagnostic test is performed for other reasons. Nevertheless, the typical presentation of acid peptic disease is with recurrent episodes of pain. The pain is almost invariably located in the epigastrium and may radiate to the back or, less commonly, to the thorax or other regions of the abdomen . Some patients describe the pain as burning or piercing, whereas others describe it as an uncomfortable feeling of emptiness of the stomach, referred to as *painful hunger*. Indeed, the pain may improve with ingestion of food, only to return in the postprandial period. The timing of the pain in relation to meals and the soothing effects of food, however, are quite nonspecific and may also occur in patients with functional dyspepsia without ulcer. Nocturnal epigastric pain that awakens patients several hours after a late meal is more likely to represent ulcer pain.

Besides the pain during symptomatic episodes, patients may complain of retrosternal burning (heartburn) or acidic regurgitation into the throat, symptoms reflecting associated gastroesophageal reflux, which is aggravated by hyperacidity or delayed gastric emptying. Nausea and vomiting may also occur but are quite nonspecific. The presence of significant diarrhea should raise the possibility of Zollinger-Ellison syndrome, but diarrhea also may result from heavy use of magnesium-containing antacids. In untreated patients, symptoms tend to be intermittent, with flares of daily pain lasting 2 to 8 weeks, separated by prolonged asymptomatic intervals. During periods of remission, patients may feel well and may be able to eat even heavy or spicy meals without apparent discomfort.

Epidemiology

The prevalence of peptic ulcer is decreasing in many Western communities as a result of widespread use of *H. pylori* eradication therapy but it remains high in developing countries. The male to female ratio for duodenal ulcer varies from 5:1 to 2:1, whilst that for gastric ulcer is 2:1 or less. Duodenal ulcers (DUs) are estimated to occur in 6–15% of the Western population. Gastric ulcers (GUs) tend to occur later in life than duodenal lesions, with a peak incidence reported in the sixth decade. More than half of GUs occur in males and are less common than DUs, perhaps due to the higher likelihood of GUs being silent and presenting only after a complication develops. Autopsy studies suggest a similar incidence of DUs and GUs.

Pathology

Duodenal Ulcers

DUs occur most often in the first portion of duodenum (>95%), with ~90% located within 3 cm of the pylorus. They are usually 1 cm in diameter but can occasionally reach 3–6 cm (giant ulcer). Ulcers are sharply demarcated, with depth at times reaching the muscularis propria. The

base of the ulcer often consists of a zone of eosinophilic necrosis with surrounding fibrosis. Malignant DUs are extremely rare.

Gastric Ulcers

In contrast to DUs, GUs can represent a malignancy. Benign GUs are most often found distal to the junction between the antrum and the acid secretory mucosa. Benign GUs are quite rare in the gastric fundus and are histologically similar to DUs. Benign GUs associated with *H. pylori* are also associated with antral gastritis. In contrast, NSAID-related GUs are not accompanied by chronic active gastritis but may instead have evidence of a chemical gastropathy, typified by foveolar hyperplasia, edema of the lamina propria and epithelial regeneration in the absence of *H. pylori*. Extension of smooth-muscle fibers into the upper portions of the mucosa, where they are not typically found, may also occur.

Pathophysiology

Duodenal Ulcers

H. pylori and NSAID-induced injury account for the majority of DUs. Many acid secretory abnormalities have been described in DU patients. Of these, average basal and nocturnal gastric acid secretion appears to be increased in DU patients as compared to controls; however, the level of overlap between DU patients and control subjects is substantial. The reason for this altered secretory process is unclear, but *H. pylori* infection may contribute. Accelerated gastric emptying of liquids has been noted in some DU patients, but its role in DU formation, if any, is unclear. Bicarbonate secretion is significantly decreased in the duodenal bulb of patients with an active DU as compared to control subjects. *H. pylori* infection may also play a role in this process (see below).

Gastric Ulcers

As in DUs, the majority of GUs can be attributed to either *H. pylori* or NSAID-induced mucosal damage. GUs that occur in the prepyloric area or those in the body associated with a DU or a duodenal scar are similar in pathogenesis to DUs. Gastric acid output (basal and stimulated) tends to be normal or decreased in GU patients. When GUs develop in the presence of minimal acid levels, impairment of mucosal defense factors may be present.

Abnormalities in resting and stimulated pyloric sphincter pressure with a concomitant increase in duodenal gastric reflux have been implicated in some GU patients. Although bile acids, lysolecithin, and pancreatic enzymes may injure gastric mucosa, a definite role for these in GU pathogenesis has not been established. Delayed gastric emptying of solids has been described in GU patients but has not been reported consistently.

H. pylori and Acid Peptic Disorders

Gastric infection with the bacterium *H. pylori* accounts for the majority of PUD. This organism also plays a role in the development of gastric mucosal-associated lymphoid tissue (MALT) lymphoma and gastric adenocarcinoma. Although the entire genome of *H. pylori* has been sequenced, it is still not clear how this organism, which resides in the stomach, causes ulceration in the duodenum, or whether its eradication will lead to a decrease in gastric cancer.

The Bacterium

The bacterium is a gram-negative microaerophilic rod found most commonly in the deeper portions of the mucous gel coating the gastric mucosa or between the mucous layer and the

gastric epithelium. It may attach to gastric epithelium but under normal circumstances does not appear to invade cells. It is strategically designed to live within the aggressive environment of the stomach. Initially, *H. pylori* resides in the antrum but, over time, migrates toward the more proximal segments of the stomach. The organism is capable of transforming into a coccoid form, which represents a dormant state that may facilitate survival in adverse conditions. The genome of *H. pylori* (1.65 million base pairs) encodes ~1500 proteins. Among this multitude of proteins there are factors that are essential determinants of *H. pylori*–mediated pathogenesis and colonization, such as the outer membrane protein (Hop proteins), urease, and the vacuolating cytotoxin (Vac A). The first step in infection by *H. pylori* is dependent on the bacteria's motility and its ability to produce urease. Urease produces ammonia from urea, an essential step in alkalinizing the surrounding pH. Additional bacterial factors include catalase, lipase, adhesins, platelet-activating factor, and pic B (induces cytokines). Multiple strains of *H. pylori* exist and are characterized by their ability to express several of these factors (Cag A, Vac A, etc.). It is possible that the different diseases related to *H. pylori* infection can be attributed to different strains of the organism with distinct pathogenic features.

Epidemiology

The prevalence of *H. pylori* varies throughout the world and depends largely on the overall standard of living in the region. In developing parts of the world, 80% of the population may be infected by the age of 20, whereas the prevalence is 20–50% in industrialized countries. Two factors that predispose to higher colonization rates include poor socioeconomic status and less education. These factors, not race, are responsible for the rate of *H. pylori* infection in blacks and Hispanic Americans being double the rate seen in whites of comparable age. Other risk factors for *H. pylori* infection are (1) birth or residence in a developing country, (2) domestic crowding, (3) unsanitary living conditions, (4) unclean food or water, and (5) exposure to gastric contents of an infected individual.

Transmission of *H. pylori* occurs from person to person, following an oral-oral or fecal-oral route. The risk of *H. pylori* infection is declining in developing countries. The rate of infection in the United States has fallen by >50% when compared to 30 years ago.

Pathophysiology

H. pylori infection is virtually always associated with a chronic active gastritis, but only 10–15% of infected individuals develop frank peptic ulceration. The basis for this difference is unknown. Initial studies suggested that >90% of all DUs were associated with *H. pylori*, but *H. pylori* is present in only 30–60% of individuals with GUs and 50–70% of patients with DUs. The pathophysiology of ulcers not associated with *H. pylori* or NSAID ingestion [or the rare Zollinger-Ellison syndrome (ZES)] is becoming more relevant as the incidence of *H. pylori* is dropping, particularly in the Western world (see below).

The particular end result of *H. pylori* infection (gastritis, PUD, gastric MALT lymphoma, gastric cancer) is determined by a complex interplay between bacterial and host factors.

1. Bacterial factors: *H. pylori* is able to facilitate gastric residence, induce mucosal injury, and avoid host defense. Different strains of *H. pylori* produce different virulence factors. A specific region of the bacterial genome, the pathogenicity island, encodes the virulence factors Cag A and pic B. Vac A also contributes to pathogenicity, though it is not encoded within the pathogenicity island. These virulence factors, in conjunction with additional bacterial constituents, can cause mucosal damage. Urease, which allows the bacteria to reside in the acidic stomach, generates NH_3, which can damage epithelial cells. The bacteria produce surface factors that are chemotactic for neutrophils and monocytes, which in turn contribute to epithelial cell injury (see

below). *H. pylori* makes proteases and phospholipases that break down the glycoprotein lipid complex of the mucous gel, thus reducing the efficacy of this first line of mucosal defense. *H. pylori* expresses adhesins, which facilitate attachment of the bacteria to gastric epithelial cells. Although lipopolysaccharide (LPS) of gram-negative bacteria often plays an important role in the infection, *H. pylori* LPS has low immunologic activity compared to that of other organisms. It may promote a smoldering chronic inflammation.

2. Host factors: The inflammatory response to *H. pylori* includes recruitment of neutrophils, lymphocytes (T and B), macrophages, and plasma cells. The pathogen leads to local injury by binding to class II MHC molecules expressed on gastric epithelial cells, leading to cell death (*apoptosis*). Moreover, bacterial strains that encode cag-PAI can introduce Cag A into the host cells, leading to further cell injury and activation of cellular pathways involved in cytokine production. Elevated concentrations of multiple cytokines are found in the gastric epithelium of *H. pylori*–infected individuals, including interleukin (IL) 1/, IL-2, IL-6, IL-8, tumor necrosis factor (TNF) and interferon (IFN). *H. pylori* infection also leads to both a mucosal and a systemic humoral response, which does not lead to eradication of the bacteria but further compounds epithelial cell injury. Additional mechanisms by which *H. pylori* may cause epithelial cell injury include (1) activated neutrophil-mediated production of reactive oxygen or nitrogen species and enhanced epithelial cell turnover and (2) apoptosis related to interaction with T cells (T helper 1, or T_H1, cells) and IFN.

The reason for *H. pylori*–mediated duodenal ulceration remains unclear. One potential explanation is that gastric metaplasia in the duodenum of DU patients permits *H. pylori* to bind to it and produce local injury secondary to the host response. Another hypothesis is that *H. pylori* antral infection could lead to increased acid production, increased duodenal acid, and mucosal injury. Basal and stimulated [meal, gastrin-releasing peptide (GRP)] gastrin release are increased in *H. pylori*–infected individuals, and somatostatin-secreting D cells may be decreased. *H. pylori* infection might induce increased acid secretion through both direct and indirect actions of *H. pylori* and proinflammatory cytokines (IL-8, TNF, and IL-1) on G, D, and parietal cells. *H. pylori* infection has also been associated with decreased duodenal mucosal bicarbonate production. Data supporting and contradicting each of these interesting theories have been demonstrated. Thus, the mechanism by which *H. pylori* infection of the stomach leads to duodenal ulceration remains to be established.

In summary, the final effect of *H. pylori* on the gastrointestinal tract is variable and determined by microbial and host factors. The type and distribution of gastritis correlate with the ultimate gastric and duodenal pathology observed. Specifically, the presence of antral-predominant gastritis is associated with DU formation; gastritis involving primarily the corpus predisposes to the development of GUs, gastric atrophy, and ultimately gastric carcinoma

NSAID-Induced Disease

Epidemiology

NSAIDs represent a group of the most commonly used medications in the world. Side effects and complications due to NSAIDs are considered the most common drug-related toxicities. The spectrum of NSAID-induced morbidity ranges from nausea and dyspepsia (prevalence reported as high as 50–60%) to a serious gastrointestinal complication such as endoscopy-documented peptic ulceration (15–30% of individuals taking NSAIDs regularly) complicated by bleeding or perforation in as many as 1.5% of users per year. About 20,000 patients die each year from serious gastrointestinal complications from NSAIDs. Unfortunately, dyspeptic symptoms do not correlate with NSAID-induced pathology. Over 80% of patients with serious NSAID-related complications did not have preceding dyspepsia. In view of the lack of warning signs, it is important to identify patients who are at increased risk for morbidity and mortality related to NSAID usage. Even 75 mg/d of aspirin may lead to serious gastrointestinal ulceration; thus, no dose of NSAID is completely safe. Established risk factors include advanced age, history of

ulcer, concomitant use of glucocorticoids, high-dose NSAIDs, multiple NSAIDs, concomitant use of anticoagulants, and serious or multisystem disease. Possible risk factors include concomitant infection with *H. pylori*, cigarette smoking, and alcohol consumption.

Pathophysiology

Prostaglandins play a critical role in maintaining gastroduodenal mucosal integrity and repair. It therefore follows that interruption of prostaglandin synthesis can impair mucosal defense and repair, thus facilitating mucosal injury via a systemic mechanism. Systemically administered NSAIDs may lead to mucosal injury due to prostaglandin depletion, ischemia. Injury to the mucosa also occurs as a result of the topical encounter with NSAIDs. Aspirin and many NSAIDs are weak acids that remain in a nonionized lipophilic form when found within the acid environment of the stomach. Under these conditions, NSAIDs migrate across lipid membranes of epithelial cells, leading to cell injury once trapped intracellularly in an ionized form. Topical NSAIDs can also alter the surface mucous layer, permitting back diffusion of H^+ and pepsin, leading to further epithelial cell damage. Moreover, enteric-coated or buffered preparations are also associated with risk of peptic ulceration. The interplay between *H. pylori* and NSAIDs in the pathogenesis of PUD is complex. Meta-analysis supports the conclusion that each of these aggressive factors are independent and synergistic risk factors for PUD and its complications, such as gastrointestinal bleeding.

Pathogenetic Factors Unrelated to H. pylori and NSAIDs in Acid Peptic Disease

Cigarette smoking has been implicated in the pathogenesis of PUD. Not only have smokers been found to have ulcers more frequently than do nonsmokers, but smoking appears to decrease healing rates, impair response to therapy, and increase ulcer-related complications such as perforation. The mechanism responsible for increased ulcer diathesis in smokers is unknown. Theories have included altered gastric emptying, decreased proximal duodenal bicarbonate production, increased risk for *H. pylori* infection, and cigarette-induced generation of noxious mucosal free radicals. Despite these interesting theories, the mechanism for the cigarette-induced peptic ulcer diathesis has not been established.

Genetic predisposition may play a role in ulcer development. First-degree relatives of DU patients are three times as likely to develop an ulcer; however, the potential role of *H. pylori* infection in contacts is a major consideration. Increased frequency of blood group O and of the nonsecretor status have also been implicated as genetic risk factors for peptic diathesis. However, *H. pylori* preferentially binds to group O antigens. The role of genetic predisposition in common PUD has not been established.

Psychological stress has been thought to contribute to PUD, but studies examining the role of psychological factors in its pathogenesis have generated conflicting results. Although PUD is associated with certain personality traits (neuroticism), these same traits are also present in individuals with nonulcer dyspepsia (NUD) and other functional and organic disorders. Although more work in this area is needed, no typical PUD personality has been found.

Diet has also been thought to play a role in peptic diseases. Certain foods can cause dyspepsia, but no convincing studies indicate an association between ulcer formation and a specific diet. This is also true for beverages containing alcohol and caffeine. Specific chronic disorders have been associated with PUD. Those with a strong association are (1) systemic mastocytosis, (2) chronic pulmonary disease, (3) chronic renal failure, (4) cirrhosis, (5) nephrolithiasis, and (6) $_1$-antitrypsin deficiency. Those with a possible association are (1) hyperparathyroidism, (2) coronary artery disease, (3) polycythemia vera, and (4) chronic pancreatitis.

Multiple factors play a role in the pathogenesis of PUD. The two predominant causes are *H. pylori* infection and NSAID ingestion. PUD not related to *H. pylori* or NSAIDs is increasing. Other less common causes of PUD are infection, drugs, basophilia in myeloproliferative disease, duodenal obstruction, infiltrating disease, ischemia, radiation therapy, sarcoidosis, Crohn's disease, idiopathic hypersecretory state. These etiologic agents should be considered as the incidence of *H. pylori* is decreasing. Independent of the inciting or injurious agent, peptic ulcers develop as a result of an imbalance between mucosal protection/repair and aggressive factors. Gastric acid plays an essential role in mucosal injury.

Clinical presentation

History

Abdominal pain is common to many gastrointestinal disorders, including DU and GU, but has a poor predictive value for the presence of either DU or GU. Up to 10% of patients with NSAID-induced mucosal disease can present with a complication (bleeding, perforation, and obstruction) without antecedent symptoms. Despite this poor correlation, a careful history and physical examination are essential components of the approach to a patient suspected of having peptic ulcers.

Epigastric pain described as a burning or gnawing discomfort can be present in both DU and GU. The discomfort is also described as an ill-defined, aching sensation or as hunger pain. The typical pain pattern in DU occurs 90 min to 3 h after a meal and is frequently relieved by antacids or food. Pain that awakes the patient from sleep (between midnight and 3 A.M.) is the most discriminating symptom, with two-thirds of DU patients describing this complaint. Unfortunately, this symptom is also present in one-third of patients with NUD. The pain pattern in GU patients may be different from that in DU patients, where discomfort may actually be precipitated by food. Nausea and weight loss occur more commonly in GU patients. Endoscopy detects ulcers in <30% of patients who have dyspepsia.

The mechanism for development of abdominal pain in ulcer patients is unknown. Several possible explanations include acid-induced activation of chemical receptors in the duodenum, enhanced duodenal sensitivity to bile acids and pepsin, or altered gastroduodenal motility.

Variation in the intensity or distribution of the abdominal pain, as well as the onset of associated symptoms such as nausea and/or vomiting, may be indicative of an ulcer complication. Dyspepsia that becomes constant, is no longer relieved by food or antacids, or radiates to the back may indicate a penetrating ulcer (pancreas). Sudden onset of severe, generalized abdominal pain may indicate perforation. Pain worsening with meals, nausea, and vomiting of undigested food suggest gastric outlet obstruction. Tarry stools or coffee-ground emesis indicate bleeding.

Physical examination

Epigastric tenderness is the most frequent finding in patients with GU or DU. Pain may be found to the right of the midline in 20% of patients. Unfortunately, the predictive value of this finding is rather low. Physical examination is critically important for discovering evidence of ulcer complication. Tachycardia and orthostasis suggest dehydration secondary to vomiting or active gastrointestinal blood loss. A severely tender, boardlike abdomen suggests a perforation. Presence of a succussion splash indicates retained fluid in the stomach, suggesting gastric outlet obstruction.

Diagnosis

In view of the poor predictive value of abdominal pain for the presence of a gastroduodenal ulcer and the multiple disease processes that can mimic this disease, the clinician is often confronted with having to establish the presence of an ulcer. Documentation of an ulcer requires either a radiographic (barium study) or an endoscopic procedure. However, a large percentage of patients with symptoms suggestive of an ulcer have NUD; empirical therapy is appropriate for individuals who are otherwise healthy and <45, before embarking on a diagnostic evaluation.

Barium studies of the proximal gastrointestinal tract are still commonly used as a first test for documenting an ulcer. The sensitivity of older single-contrast barium meals for detecting a DU is as high as 80%, with a double-contrast study providing detection rates as high as 90%. Sensitivity for detection is decreased in small ulcers (<0.5 cm), presence of previous scarring, or in postoperative patients. A DU appears as a well-demarcated crater, most often seen in the bulb. A GU may represent benign or malignant disease. Typically, a benign GU also appears as a discrete crater with radiating mucosal folds originating from the ulcer margin. Ulcers >3 cm in size or those associated with a mass are more often malignant. Unfortunately, up to 8% of GUs that appear to be benign by radiographic appearance are malignant by endoscopy or surgery. Radiographic studies that show a GU must be followed by endoscopy and biopsy.

Endoscopy provides the most sensitive and specific approach for examining the upper gastrointestinal tract. In addition to permitting direct visualization of the mucosa, endoscopy facilitates photographic documentation of a mucosal defect and tissue biopsy to rule out malignancy (GU) or *H. pylori*. Endoscopic examination is particularly helpful in identifying lesions too small to detect by radiographic examination, for evaluation of atypical radiographic abnormalities, or to determine if an ulcer is a source of blood loss.

For diagnosing *H. pylori* several biopsy urease tests have been developed (PyloriTek, Clotest, Hpfast, Pronto Dry) that have a sensitivity and specificity of >90–95%. Several noninvasive methods for detecting this organism have been developed. Three types of studies routinely used include serologic testing, the ^{13}C- or ^{14}C-urea breath test, and the fecal *H. pylori* (Hp) antigen test. A urinary Hp antigen test, as well as a refined monoclonal antibody stool antigen test, appears promising. Occasionally, specialized testing such as serum gastrin and gastric acid analysis or sham feeding may be needed in individuals with complicated or refractory PUD. Screening for aspirin or NSAIDs (blood or urine) may also be necessary in refractory *H. pylori*–negative PUD patients.

Histologic examination of gastric mucosal biopsies, which is the standard procedure when endoscopy is initially performed for diagnosis, is quite sensitive and specific for *H. pylori.* However, the accuracy of this technique may also be affected by sampling error, improper orientation of the specimen, technical issues, and recent therapy with proton pump inhibitors (PPIs).

A second option is *serology,* which is a relatively simple, inexpensive test that has reduced predictive value in areas where the prevalence of *H. pylori* is low. Serology is not helpful to verify whether *H. pylori* has been eradicated with antibiotics because it may take many months or even years for *H. pylori* antibodies to fall to undetectable levels.

A third option is a *stool antigen test,* which is more accurate than serology. This test is capable of detecting *H. pylori* infection in only 1 week after PPIs are discontinued.

Finally, the *carbon*-13 (^{13}C)–urea breath test, which relies on the detection of *H. pylori* urease activity, is a noninvasive and relatively simple test, but it is more expensive than stool or blood testing. Although the test becomes negative as soon as *H. pylori* is eradicated, a minimum interval of 4 to 6 weeks after antibiotic treatment is recommended to reduce false-negative results.

Differential diagnosis

The list of gastrointestinal and nongastrointestinal disorders that can mimic ulceration of the stomach or duodenum is quite extensive. The most commonly encountered diagnosis among patients seen for upper abdominal discomfort is nonulcer dyspepsia (NUD) or functional dyspepsia, refers to a group of heterogeneous disorders typified by upper abdominal pain without the presence of an ulcer. Up to 60% of patients seeking medical care for dyspepsia have a negative diagnostic evaluation. The etiology of NUD is not established, and the potential role of *H. pylori* in NUD remains controversial.

Several additional disease processes that may present with "ulcer-like" symptoms include proximal gastrointestinal tumors, gastroesophageal reflux, vascular disease, pancreaticobiliary disease (biliary colic, chronic pancreatitis), and gastroduodenal Crohn's disease.

Complications

Gastrointestinal Bleeding

Gastrointestinal bleeding is the most common complication observed in PUD. It occurs in ~15% of patients and more often in individuals >60 years old. The higher incidence in the elderly is likely due to the increased use of NSAIDs in this group. Up to 20% of patients with ulcer-related hemorrhage bleed without any preceding warning signs or symptoms.

Perforation

The second most common ulcer-related complication is perforation, being reported in as many as 6–7% of PUD patients. As in the case of bleeding, the incidence of perforation in the elderly appears to be increasing secondary to increased use of NSAIDs. *Penetration* is a form of perforation in which the ulcer bed tunnels into an adjacent organ. DUs tend to penetrate posteriorly into the pancreas, leading to pancreatitis, whereas GUs tend to penetrate into the left hepatic lobe. Gastrocolic fistulas associated with GUs have also been described.

Gastric Outlet Obstruction

Gastric outlet obstruction is the least common ulcer-related complication, occurring in 1–2% of patients. A patient may have relative obstruction secondary to ulcer-related inflammation and edema in the peripyloric region. This process often resolves with ulcer healing. A fixed, mechanical obstruction secondary to scar formation in the peripyloric areas is also possible. The latter requires endoscopic (balloon dilation) or surgical intervention. Signs and symptoms relative to mechanical obstruction may develop insidiously. New onset of early satiety, nausea, vomiting, increase of postprandial abdominal pain, and weight loss should make gastric outlet obstruction a possible diagnosis.

Treatment

Treatment of peptic ulcers varies depending on the etiology and clinical presentation. The initial management of a stable patient with dyspepsia differs from the management of an unstable patient with upper GI hemorrhage.

Treatment options include empiric antisecretory therapy, empiric triple therapy for *H pylori* infection, endoscopy followed by appropriate therapy based on findings, and *H pylori* serology followed by triple therapy for patients who are infected. Breath testing for active *H pylori* infection may be used.

Endoscopy is required to document healing of gastric ulcers and to rule out gastric cancer. This

usually is performed 6-8 weeks after the initial diagnosis of PUD. Documentation of *H pylori* cure with a noninvasive test, such as the urea breath test or fecal antigen test, is appropriate in patients with complicated ulcers.
Given the current understanding of the pathogenesis of PUD, most patients with PUD are treated successfully with cure of *H pylori* infection and/or avoidance of NSAIDs, along with the appropriate use of antisecretory therapy.

Acid suppression
Two classes of acid-suppressing medications currently in use are histamine-2 receptor antagonists (H2RAs) and proton pump inhibitors (PPIs).[35] Both classes are available in intravenous and oral preparations. Examples of H2RAs include ranitidine, cimetidine, famotidine, and nizatidine. Examples of PPIs include omeprazole, pantoprazole, lansoprazole, and rabeprazole.

H pylori Infection
PPI-based triple therapy regimens for *H pylori* consist of a PPI, amoxicillin, and clarithromycin for 7-14 days. A longer duration of treatment (14 d vs 7 d) appears to be more effective and is currently the recommended treatment. Amoxicillin should be replaced with metronidazole in penicillin-allergic patients only, because of the high rate of metronidazole resistance. In patients with complicated ulcers caused by *H pylori*, treatment with a PPI beyond the 14-day course of antibiotics and until the confirmation of the eradication of *H pylori* is recommended.
PPI-based triple therapies are a 14-day regimen as shown below:
Omeprazole: 20 mg PO bid
or
Lansoprazole: 30 mg PO bid
or
Rabeprazole: 20 mg PO bid
or
Esomeprazole: 40 mg PO qd
Plus
Clarithromycin: 500 mg PO bid
and
Amoxicillin: 1 g PO bid

Alternative triple-therapy regimens
The alternative triple therapies, also administered for 14 days, are as follows:
Omeprazole: 20 mg PO bid
or
Lansoprazole: 30 mg PO bid
or
Rabeprazole: 20 mg PO bid
or
Esomeprazole: 40 mg PO qd
Plus
Clarithromycin: 500 mg PO bid
and
Metronidazole: 500 mg PO bid

Quadruple therapy
Quadruple therapies for *H pylori* infection are generally reserved for patients in whom the standard course of treatment has failed.
Quadruple treatment includes the following drugs, administered for 14 days:
- PPI, standard dose, or ranitidine 150 mg, PO bid

- Bismuth 525 mg PO qid
- Metronidazole 500 mg PO qid
- Tetracycline 500 mg PO qid

Medical Management of NSAID Ulcers

Active ulcers associated with NSAID use are treated with an appropriate course of PPI therapy and the cessation of NSAIDs. For patients with a known history of ulcer and in whom NSAID use is unavoidable, the lowest possible dose and duration of the NSAID and co-therapy with a PPI or misoprostol are recommended.

Prophylactic regimens that have been shown to dramatically reduce the risk of NSAID-induced gastric and duodenal ulcers include the use of a prostaglandin analog or a PPI according to the following regimens:

- Misoprostol 100-200 mcg PO 4 times per day
- Omeprazole 20-40 mg PO every day
- Lansoprazole 15-30 mg PO every day

Diet

A special diet is not indicated for patients with duodenal ulcers. It is a common-sense approach to avoid any food or beverages that may aggravate symptoms. Although the link between duodenal ulcers and alcohol is inconclusive, moderation of alcohol intake may be recommended for other health reasons.

The control of an initial level of knowledge

1. Which of the listed factors will play the role in etiology of stomach ulcer?

A. alimentary;
B. heredity;
C. all listed;
D. HP;
E. chronic stress.

2 Which of this factors does not define the pathogenesis of stomach ulcer?

A. infringement of cortical-subcrustal mutual relations;
B. infringement of processes of regeneration mucous;
C. disbalance factors of aggression and protection;
D. increased production of the hydrochloric acid;
E. allergic reaction of the slowed down type.

3. How does the painful syndrome change in case of stomach ulcer complicated by bleeding?

A. amplifies;
B. decreases;
C. remains without changes;
D. becomes gripping;
E. loses touch with reception of food and time of day

4. Which hemodynamic changes are observed at a gastroenteric bleeding?

A. bradycardia, ABP decrease;
B. bradycardia, ABP increase;
C. tachycardia, ABP decrease;
D. tachycardia. ABP increase;
E. arrhythmia, ABP does not change.

5. In which of the organs more often penetrates the duodenal ulcer?

A. liver
B. spleen;
C. pancreas;
D. intestines;
E. diaphragm

6. What clinical symptoms are characteristic for development of the ulcer stenosis?
A. loss of appetite;
B. unitary vomiting with blood;
C. vomiting by the food eaten on the eve;
D. nausea, bitterness in a mouth;
E. heartburn, an eructation sour.

7. How does the painful syndrome changes with malignant ulcers?
A. amplifies;
B. decreases;
C. disappears;
D. loses cyclicity, rhythm, seasonal prevalence;
E. does not change.

8. Which group of drugs related to antisecretory?
A. blockers of the H 2-histamine receptors, inhibitors " proton pomp ";
B. metabolics, cytoprotectors;
C. reparants, M-cholinolytics;
D. spasmolytics, enzymes;
E. bismuth's preparations, anabolics.

9. Which of the listed drugs is blocker H 2-rncTaMHHOBbix receptors?
A. omeprszole;
B. methacin;
C. de-nole;
D. quamatel;
E. vicaline.

10. Which of the methods of instrumental research is the most informative at the stomach ulcer?
A. x-ray of organs of the belly cavity;
B. irrigoscopy;
C. FGDS with biopsy;
D. cholecystography;
E. research of gastric juice.

Correct answers:

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

The control of the final level of knowledge

1. Which of the stimulators is the most physiological in recruitment of gastric juice?
A. histamine;
B. insulin;

C. aminophylline;
D. pentagastrine;
E. caffeine

2. Which of the listed diseases is the contra-indication to carrying out of research of gastric juice?
A. gullet stricture;
B. old myocardial infarction;
C. mental diseases;
D. hypertonic disease of II-III stage;
E. all listed variants.

3. What caused the color of vomit at ulcer bleeding?
A. formation salino-sour hematin;
B. impurity of the bile;
C. presence of the food impurity;
D. impurity of the pancreatic juice;
E. all listed variants.

4. In what condition of acidity of the stomach pH 2,1 -5,9 in basal and 2.1-3,0 in stimulated phase of secretion?
A. hyperacidity;
B. hypoacidity;
C. normal acidity;
D. achilia;

5. Whicn of this features does not applies to the attribute of the pyloric ulcer?
A. refractory recurrent clinical course;
B. short and unstable remissions;
C. frequent complications by a bleeding and stenosis;
D. deformation of bulb DG and the gatekeeper;
E. expressed painful and dyspeptic syndromes

6. Bacteria chelicobacter pylory is:
A. acid unstable;
B. acid neutralizing;
C. hydrochloric acid neutral for a metabolism of bacteria;
D. acid resisting;
E. alkali adjective.

7. The indications for urgent hospitalization in surgical branch are stomach ulcer with following complications, except one:
A. punching of the ulcer;
B. penetration of the ulcers;
C. the subcompensated stenosis of the gatekeeper;
D. bleeding from of the ulcer;
E. periduodenitis.

8. The direct radiological attributes of the peptic ulcer is:
A. symptom of "niche";
B. inflammatory shaft;
C. convergence of folds;
D. defect of filling;

E. all set forth above.

9. Occurrence of "noise of splash" is connected with:
A. presence of the functional pylorus stenosis;
B. presence of the organic pylorus stenosis;
C. association of functional and organic pylorus stenoses;
D. hypersecretion of the hydrochloric acid;
E. hyposecretion of the hydrochloric acid.

10. Vomiting by the "coffee grouts" is observed:
A. gastrointestinal bleeding;
B. bilious colic;
C. nephritic colic;
D. pulmonary bleeding;
E. varicose-expanded veins of the gullet.

Correct answers.

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

Case-based questions

1. The patient was admitted to the gastroenterological department with complaints on heavy feeling in epigastrium, arising after meals, nausea, vomiting by food, which is eaten on the eve, general weakness. Suffers from the stomach ulcer about 18 years, it was repeatedly treated. Present deterioration began gradually during a year, has grown thin for 5 kg. With palpation of the belly the constrained morbidity in epigastrium, greater curvature of a stomach is defined on 2 sm below of the omphalus, with percussion in epigastrium -"noise of splash ". What complication of the stomach ulcer has the patient?
A. punching of the ulcer;
B. penetration of the ulcer;
C. pyloroduodenal stenosis;
D. perivisceritis;
E. malignant change.

2. The 36 years old man complains of dizziness, the general weakness during 2 days. She suffers from stomach ulcer of a bulb of duodenum about 8 years. Objectively: FB - 22 for 1 minute, pulse - 100 for 1 minute, blood pressure - 95/60 mm hg. The skin and mucous membranes are pale. Which of the researches will be the most authentically confirm a bleeding at this patient?
A. Colonosopy
B. FGDS
C. Proctoscopy
D. Irrigoscopy
E. Roentgenoscopy

3. The 27 year old man was directed to the doctor in occasion of an aggravation of the stomach ulcer. It has been taken the test on presence of pathological flora during gastroscopy. Which agent most likely will be detected?
A. Lamblia
B. Chelicobacterium
C. S. Candidium

D. Staphylococcus
E. Clamydia

4. The 35 years old woman was entered in clinic with complaints of pain in epigastrium which arises in 1-1,5 hours after the meals, heartburn, vomiting which brings simplification. Objectively: glosso is imposed white for a short while, a belly soft, painful in epigastrium. It was observed the positive Mendel's symptom. What diagnosis is the most probable?
A. peptic ulcer of the stomach
B. peptic ulcer duodenum guts
C. GERD
D. functional dyspepsia
E. chronic pancreatitis

5. The ulcer of a bulb of the duodenum for the first time is diagnosed for the young 18 year old man. The test on Helicobacter pylori - positive, pH of gastric juice - 1,0. Which of the plan of treatment is the most expedient in this case?
A. Omeprazole + amoxicillin+clarithromycin
B. De-nole + trichopol+almagel
C. Gastrostat + omeprazole+metacin
D. Omeprazole + oxacillin+atropine
E. De-nole + cimetidine+papaverine

6. The 35 years old man complains of intensive hungry pain in epigastrium, heartburn, regurgitation the sour contents, propensity to locks. The data of FGDS: an ulcer of the bulb of duodenum. What symptom the most authentically testifies to efficiency orders of etiopatogenetic therapies at an early stage of treatment?
A. Decrease of the pain
B. Dissolution of the pain.
C. S. Dissolution of the heartburn
D. Normalization of the defecation
E. Dissolution of the regurgitation symptoms

7. The 32 years old patient suffers from chronic gastroduodenitis during 5 years. Smokes, eats irregularly. Holds a supervising post. During last month there was a hungry night pain. Objectively: local morbidity in epigastrium is defined. Resistance and Mendel's positive symptom in the pyloroduodenal zone. Data FGDS: a ulcer on a forward wall of a duodenal gut. Which of factors is leader in occurrence of this pathology?
A. Smocking
B. Chronic gastroduodenitis in the anamnesis
C. S. Infections by Helicobacter pylori
D. Disruption of the feed and stresses
E. All above-listed

8. At the 25 year old patient were appeared a heartburn, locks, pain in epigastrium which arise in 1,5-2 hours after meals, sometimes at night, in the autumn. The pain amplifies in case of the use of acute, salty, sour food, decreases after application of soda. Is ill {sick} during a year. The sick lowered fatness, language is not imposed, damp. During percussion and palpation of the stomach morbidity in mesogastrium is defined. In this area is defined resistance of the forward belly wall muscles. What diagnosis is the most probable?
A. Autoimmune gastritis
B. Diaphragmatic hernia
C. Peptic ulcer of the duodenum
D. Cholelithic disease

E. Chronic pancreatitis

9. The patient was entered in gastroenterology department with complaints of multiple vomiting with the vomit of "a coffee grouts" color, the general {common} weakness, dizziness. In the anamnesis – the stomach ulcer. During last week it was disturbed a pain in epigastrium after meals, it was not treated. Detect disappearance hurt after vomiting. What is the most probable diagnosis?

A. gastrointestinal bleeding
B. chronic pancreatitis
C. pulmonary bleeding
D. cholelithic disease
E. thrombosis of mesenteric vessels

10. The 37 year old man was delivered in hospital with complaints of pain in epigastrium through 2 days after meals. Objectively: the blood pressure - 110/70 mm hg. Language damp, near a root is covered albesent for a short while. It was defined the morbidity and pressure of muscles in epigastrium. Endoscopy: a chronic ulcer with localization in bulb of duodenum. The doctor ordered to the patient a famotidine, 40 mg a day. With what purpose was famotidine order?

A. Antisecretory action
B. Stimulation reparative processes
C. Decrease of the inflammatory and dystrophic changes
D. Bactericidal effect
E. Increase of the prostaglandins synthesis.

Correct answers

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

Control questions

1. Definition of PU.
2. Etiopathogenetic mechanisms of PU
3. The basic clinical syndromes of PU
4. The characteristic of physical data in PU
5. Peculiarities of the course of stomach ulcers
6. Peculiarities of the course of duodenal ulcers
7. List the methods of diagnostics of PU
8. List the complications of PU
9. Principles of antichelicobacterial therapy
10. Antisecretory therapy for the patient with PU
11. Medication therapy of the Hp-negative ulcers
12. Prevention of PU

Practical tasks

1. Supervise the patients with PU
2. Give the interpretation for the received results of laboratory assays
3. Give the interpretation of the received results of instrumental studies
4. Perform differentiated diagnosis with PU

5. List the complications of PU
6. Write the recipes concerning the treatment of PU

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_____
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_____

Concomitant pathology
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_____

Complications
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_____
_____
_____

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