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***Guidelines for conducting a practical lesson with 6th year students of  
the Faculty of Medicine on the topic:***

**DIFFERENTIAL DIAGNOSIS IN INTESTINAL DYSPEPSIA  
(the duration of the lesson is 8 hours, the second lesson is 4 hours)**

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## Guidelines for conducting a practical lesson with 6th year students of the Faculty of Medicine on the topic: DIFFERENTIAL DIAGNOSIS IN INTESTINAL DYSPEPSIA

### Purpose of the lesson:

in the process of clinical analysis of the patient to increase the level (quality) of knowledge and skills of students in the diagnosis (differential diagnosis), the formulation of the diagnosis of irritable bowel syndrome and dysbacteriosis.

### Motivation for the relevance of the topic:

Diseases of the small intestine with severe malabsorption and inflammatory diseases of the colon are relatively rare. The most common forms of intestinal pathology are functional diseases in which intestinal motility is impaired. With the help of absorption tests in some patients, it is possible to detect violations of membrane digestion and absorption, but the morphological structure of the mucous membrane of the small and large intestines is not changed in them. Therefore, they never have severe disorders of intestinal digestion and absorption. Irritable bowel syndrome (IBS) is a very common condition in gastroenterological practice. Its frequency among the population of developed European countries averages 15-20%. The nature of functional disorders, which is not always correctly understood, and their sometimes erroneous interpretation as a serious organic disease, sometimes lead to unnecessary re-conducting of various instrumental studies, the appointment of enhanced drug therapy, which often turns out to be insufficiently effective.

Many intestinal diseases are manifested by characteristic symptoms, noticing which, from the very beginning, you can choose the shortest path to diagnosis. Acquaintance with modern functional and instrumental research methods shows how detailed and thorough the final diagnosis can be, which is the key to successful treatment of the patient.

### Determining the level of preparation of students:

The second level of knowledge: methods of control - a written survey (20 min). The student must know the essence of the disease, the definition and classification of irritable bowel syndrome, the etiology and pathogenesis of irritable bowel syndrome, the main risk factors, the clinical manifestations of the main variants - with a predominance of pain and flatulence, with a predominance of constipation, with a predominance of diarrhea, differential diagnosis with inflammatory bowel diseases; the student must be able to - possess propaedeutic skills, independently identify the main pathological syndromes in enterology, make a preliminary diagnosis according to the accepted classification, determine the required amount of research and be able to interpret the data of additional research methods (general blood test, b / x blood test, coprogram, fecal analysis for dysbacteriosis, bacterial culture of feces, results of rectomanoscopy, irrigoscopy, colonoscopy).

Report of student curators in the ward: when reporting a patient, students should pay special attention to the following manifestations of the disease. IBS is a stable set of functional disorders lasting at least 12 weeks over the past 12 months, manifested by pain and / or discomfort in the abdomen, which disappear after defecation, are accompanied by changes in the frequency and consistency of stools and are combined for 25% of the disease time with at least two persistent symptoms of impaired bowel function - changes in stool frequency, fecal consistency, the act of defecation itself (imperative urge, tenesmus, feeling of incomplete emptying of the intestine, additional efforts during defecation), mucus with feces, flatulence.

The general condition of patients with IBS: suffers little and does not correspond to the abundance of various somatic complaints. Typical clinical symptoms of IBS include:

1. Chair less than 3 times a week.
2. Chair more often 3 times a day.
3. Hard consistency of feces ("sheep").
4. Liquid or mushy feces.
5. Tension during the act of defecation.
6. Imperative urge to defecate.
7. Feeling of incomplete emptying of the bowels.
8. Mucus discharge during defecation.
9. Feeling of bloating and fullness in the abdomen.

The IBS variant with a predominance of diarrhea is characterized by a combination of signs 2, 4, 6 in the absence of signs 1, 3, 5. In turn, the IBS variant with a predominance of constipation is characterized by a combination of signs 1, 3, 5 in the absence of signs 2, 4, 6.

In the diarrhea-predominant variant, patients complain of intermittent watery diarrhea lasting for weeks, months, or years. It is most pronounced, it happens in the morning, often after a meal. Such pronounced clinical manifestations have received in the literature the name "morning onslaught syndrome" (or "morning storm"). At the same time, after three to four times the discharge of unformed feces (as a rule, not more than 200 grams per day), the patient's condition remains satisfactory for the remaining day. Spontaneous remission is possible, the duration of which varies.

In the variant with a predominance of constipation in some patients, a long-term (for several days) absence of defecation is replaced by the so-called constipation diarrhea, followed by repeated stool retention. In other patients, the act of defecation is quite regular, but is accompanied by a feeling of incomplete emptying of the intestine, and the stool resembles sheep's feces or takes on a ribbon shape. Many patients, due to prolonged and systematic retention of stool, which causes a painful general condition, begin to abuse laxatives.

Patients with a predominance of pain and flatulence (spastic variant) experience intermittent spastic abdominal pain, usually without irradiation, most often in the sigmoid colon, which decrease after passing gases or feces. They complain of bloating, usually not diagnosed by a doctor. Pain is described by patients as "vague", "burning", "dull", "aching", "constant", "dagger". Episodes of acute, unbearable pain can occur against the background of constant, aching pain. Others develop heartburn, bloating, lower back pain, weakness, lightheadedness, and palpitations, and sometimes the pain can be localized in the right upper quadrant of the abdomen or in the epigastric region, simulating the pathology of the biliary tract and gastric ulcer.

Despite such a variety of complaints from patients, objective signs of the disease are minimal.

The microflora of the TC of a healthy person performs a number of important functions in the life of the human body, maintaining its homeostasis. The most significant of them:

1. Ensuring the colonization resistance of the macroorganism due to the antagonistic relationship between the obligate microflora (mainly bifidobacteria and lactobacilli) and opportunistic microorganisms.
2. The production of substances with antibiotic properties, as well as organic acids that shift the pH level to the acid side (up to 5.3–5.8), which prevents the growth and reproduction of putrefactive and gas-forming microflora.
3. Detoxifying effect on endogenous and exogenous toxins due to their absorption ("natural biosorbent") and their removal from the body (metals, phenols, various poisons of plant, animal and microbial origin).
4. Participation in the synthesis of vitamins (K and B-complex, folate, nicotinic acid), the absorption of vitamin D and calcium salts, the production of cytokines and the synthesis of amino acids.
5. Stimulation of the lymphatic apparatus with an impact on various parts of the tissue and humoral immune system, including the synthesis of immunoglobulins, interferon, as well as maintaining the functional activity of non-specific protective factors, which provides immunological protection of the macroorganism.
6. Production of biologically active substances that stimulate metabolic processes in the body (enzymes, mediators, histamine, etc.), participation in the recycling of bile acids of cholesterol, steroid hormones. Under the influence of microbial enzymes in the distal ileum, bile acids are deconjugated and primary bile acids are converted into secondary bile acids. Under physiological conditions, 80 to 95% of bile acids are reabsorbed. The rest are excreted in the faeces as bacterial metabolites. The latter contribute to the normal formation of fecal masses: they inhibit the absorption of water and thereby prevent excessive dehydration of feces. Excessive bacterial colonization of the small intestine leads to premature deconjugation of bile acids and secretory diarrhea.
7. Enzymatic breakdown of nutrients not digested in the small intestine, including dietary fiber, with the formation of amines, phenols, etc.
8. Morphokinetic (trophic) action that enhances the physiological activity of the digestive tract. None of the functions of the large intestine can be realized without the participation of its resident microflora.

Intestinal dysbacteriosis is a change in the qualitative and quantitative composition of the bacterial flora, due to a dynamic violation of the intestinal microecology as a result of a breakdown in adaptation, a violation of the protective and compensatory mechanisms of the body.

Intestinal dysbiosis is very common. It is detected in 75-90% of cases of acute and chronic gastroenterological diseases.

Clinical picture of dysbacteriosis

- ☐ Diarrhea - loose stools can occur 4-6 or more times, in some cases the consistency of feces is mushy, pieces of undigested food are found in the feces. Diarrhea is not a mandatory symptom of intestinal dysbacteriosis. In many patients, diarrhea is absent, there may only be an unstable stool.
- ☐ Flatulence is a fairly constant symptom of dysbacteriosis.
- ☐ Pain in the abdomen of a non-permanent, indefinite nature, as a rule, of moderate intensity.
- ☐ The syndrome of malabsorption develops with a long and severe course of dysbacteriosis.
- ☐ Bloating, rumbling on palpation of the terminal segment of the ileum and less often - the caecum.

Small intestine dysbiosis ("bacteria overgrowth syndrome") is diagnosed by direct inoculation of duodenal or (better) jejunal contents on bacterial media, obtained using a special small intestine probe. An increase in the total number of microorganisms (more than 10<sup>5</sup> / ml of intestinal contents) living in the small intestine confirms the diagnosis of small intestine dysbiosis. There are other diagnostic methods: a breath test with lactulose labeled with H<sub>2</sub>, tests with 14Sxylose and 14C-glycocholate.

Clinical symptoms in grades I and II of MC dysbiosis are usually absent. In this period, dysbiosis is mainly a microbiological (laboratory) concept that does not require the use of active methods of correction: restoration of MC

eubiosis is provided by self-regulation mechanisms. With III and IV degrees of dysbiosis, a whole range of clinical manifestations occurs: constipation, diarrhea, persistent flatulence, food and drug allergies, abdominal pain, anemia, coagulopathy, hypo- or hypercholesterolemia, motor dysfunctions, impaired water and mineral metabolism, liver damage (in result of endotoxemia), teeth (caries) and much more. In some cases, dysbiosis can occur without morphological changes in the TC, but it is possible to develop an inflammatory process, the appearance of metastatic foci of inflammation of various localizations, endo- and superinfections. In these cases, MC dysbiosis transforms from a microbiological concept into a clinical microbiological one.

Recently, the clinic is increasingly diagnosing antibiotic-associated diarrhea (ADD), which is a "classic" manifestation of MC dysbiosis, which developed as a result of the suppression of its resident microflora with broad-spectrum antibiotics with the dominance of populations of opportunistic microorganisms. In the pathogenesis of AAD, important importance is attached to violations of the processes of decomposition of carbohydrates with the formation of SCFA and the development of osmotic diarrhea. The idiopathic form of AAD proceeds more favorably - without pronounced phenomena of intoxication, leukocytosis, increased ESR, the presence of pathological impurities in the feces and inflammatory changes in the TC. But in some patients, severe clinical symptoms of pseudomembranous colitis may appear due to the suppression of indigenous microflora and colonization of TC by anaerobic bacteria such as *Pseudomonas aeruginosa* or *Clostridium difficile*, which produces endotoxins A and B. More often than others, clindomycin, cephalosporins, amoxiclav are called as a possible cause for the development of pseudomembranous colitis. .

Clinical symptoms in small bowel dysbiosis ("bacteria overgrowth syndrome") in some cases may be absent, but often a syndrome of recurrent secretory diarrhea develops. With severe microbial contamination of the small intestine, persistent flatulence, discomfort and pain in the abdomen, maldigestion and malabsorption syndromes, steatorrhea and creatorrhea, B12 deficiency anemia, hypocoagulation (vitamin K deficiency) and visual disturbances (vitamin A deficiency) appear. In severe cases, systemic and septic manifestations are possible.

Additional diagnostic methods:

The X-ray picture of IBS is most often manifested by dyskinesia of the sigmoid and descending colon with alternating areas of expansion and narrowing up to 1 cm. Spasm of the sigmoid colon, large haustra and tubular form of the descending colon are often observed. There is uneven filling and emptying of the colon. The relief of the mucous membrane is represented by thin loopy folds resembling a delicate reticulation. Often in the lumen of the intestine - excess mucus. With the introduction of antispasmodic drugs, spastic contractions decrease or disappear, the relief of the mucous membrane becomes normal.

In endoscopic examination, patients with IBS often do not show any changes or note superficial catarrhal phenomena in the rectosigmoid region, which may be associated with dysbacteriosis. The morphological picture is also characterized by the absence of any specific changes.

In the feces of patients with IBS, the absence of inflammatory elements is characteristic.

Almost always, IBS is accompanied by dysbiotic changes characterized by a deficiency of bifidobacteria and lactobacilli, often up to their complete disappearance, an increase in the population level of opportunistic microorganisms (*Klebsiella*, *Proteus*, lactose-negative and hemolyzing *Escherichia*, etc.), which is confirmed by a number of studies.

The key point in the diagnosis of IBS is the initial course of treatment followed by a reassessment of the diagnosis. The purpose of such treatment is to eliminate the symptoms of the disease and verify *ex evantibus* the correctness of the diagnosis, the absence of the need for further search for organic pathology and the implementation of additional diagnostic procedures. As a result of treatment, the patient should be convinced that his condition is improving or at least not worsening, which allows him to make a decision not to conduct further examination with greater confidence and in agreement with the patient.

1st stage of diagnostics - mandatory studies: general analysis of blood, urine, feces; analysis of feces for worm eggs, occult blood, dysbacteriosis; biochemical analyzes (hypo- and dysproteinemia in enteritis) sigmoidoscopy, colonoscopy (if necessary with a biopsy), irrigoscopy.

Stage 2 - differential diagnosis of irritable bowel syndrome with inflammatory bowel diseases with clarification of the diagnosis of the underlying disease - chronic colitis and "irritable colon" syndrome (absence of morphological changes in the mucous membrane of the colon), ulcerative colitis (presence of ulcerative necrotic process in mucous membrane of the colon), Crohn's disease (characteristic x-ray picture - "cobblestone pavement", "cord symptom"), ischemic colitis.

In the diagnosis of dysbiosis, TC still retains the importance of the "classic" bacteriological analysis of feces. With strict observance of the rules for collecting, storing and bacteriological examination of feces for dysbiosis (special clean dishes with a lid; immediate referral to a bacteriological laboratory and immediate sowing of feces on bacterial media), the results of a study of feces generally correlate with the species and quantitative composition of the TC microflora. The Litvak-Wilshinsky method is also known with the study of feces in increasing dilutions, subsequent inoculation on bacterial media and quantitative determination of the species composition of the microflora of the TC

Bacteriological examination of faeces for dysbiosis makes it possible to establish the quantitative and species composition of the microflora that currently dominates in the TC, to detect the change of obligate microflora to conditionally pathogenic and to justify the need to correct the identified violations (taking into account the degree of dysbiosis, its etiology and pathogenesis, the species composition of transient microflora). It is important not only to establish the fact of the presence of dysbiosis, but also to isolate its "clinical component" - in the case of the appearance and increase of clinical symptoms that aggravate the symptoms of the underlying disease. Thus, stool analysis remains an informative clinical and microbiological method for diagnosing colonic dysbiosis. The denial of this fact by some authors contradicts clinical logic.

As additional (direct and indirect) diagnostic methods, fecal smear microscopy is also used; biochemical express method for determination of biogenic amines, bile and keto acids, aromatic compounds; determination of VFAs (acetic, aminobutyric, etc.), as well as  $\beta$ -aspartal-glycine and  $\beta$ -aspartal-lysine, 5-aminovaleric and  $\gamma$ -aminobutyric acids (gas-liquid and high-voltage chromatography methods). Methods for the determination of antilysozymes, DNase and RNase activity are proposed. It is important to study the nature of violations of the motor-evacuation function of the TC, creating favorable conditions for the development of dysbiosis, as well as assessing the morphological state of the TC (biopsy).

Preliminary diagnosis: on the basis of leading complaints and clinical manifestations, as well as indicators of additional studies, to establish the presence of functional dyspepsia in the patient in the form of irritable bowel syndrome and / or intestinal dysbacteriosis

#### Differential Diagnosis:

In the differential diagnosis, first of all, the simplest causes of intestinal irritation, which include chronic exposure to dietary factors and drugs, should be excluded. Common food irritants include fatty foods, alcoholic beverages, coffee, gas-producing foods and drinks, large (banquet) meals, changes in eating habits during business trips and travel. Among the drugs, the intestines are irritated by laxatives, antibiotics, preparations of potassium, iron, bile acids, etc.

The physiological conditions of women - the premenstrual period, pregnancy and menopause can occur with symptoms of IBS. Prolonged psycho-emotional and intellectual overstrain, fear, excitement can lead to the development of signs of IBS, which quickly disappear after rest and resolution of the stressful situation.

The most common pathology, accompanied by manifestations of IBS, is congenital fermentopathy - lactase and disaccharidase deficiency, the simplest way to diagnose which is an exclusion diet that does not contain milk and its products, sorbitol (chewing gum), the assimilation of which requires lactase or disaccharidase.

Organic bowel diseases - colorectal cancer, polyposis, diverticulosis, Crohn's disease, ulcerative colitis, mastocytosis, intestinal infections, parasitic infections, malabsorption syndrome, short bowel syndrome, dolichosigma, celiac disease, tuberculosis are necessarily included in the range of differential diagnostic search. Neuroendocrine tumors of the gastrointestinal tract, primarily gastrinomas, carcinoid syndrome and VIP-omas in the first stages can proceed under the guise of diarrheal or painful forms of IBS. Gynecological diseases (most often endometriosis and plastic cicatricial peritonitis) may have a clinical picture typical of IBS. Among endocrine diseases, thyrotoxicosis and diabetes mellitus with autonomous diabetic enteropathy most often proceed according to the type of diarrheal form.

#### Clinical diagnosis:

It is formulated according to the accepted classification, indicating the variant, the frequency of exacerbations with the possible addition of intestinal dysbacteriosis and inflammatory diseases of the colon.

Conducting classes in a thematic classroom. Analysis of the features of risk factors, pathogenesis and clinic of inflammatory bowel diseases in a particular patient.

The final part of the lesson: control of acquired knowledge - test control.

Summary.