

ЛД-21 ИИ

Federal State Budgetary Educational  
institution of higher education "North Ossetian State  
Medical Academy "of the Ministry of Health of the Russian Federation

(FGBOU VO SOGMA MRussian Health Ministry)

**DEPARTMENT OF INTERNAL DISEASES №2**

**Gastroesophageal reflux disease.  
Irritable Bowel Syndrome.**

**METHODOLOGICAL MATERIALS**

main professional educational program of higher education - specialty  
program in the specialty 31.05.01 General Medicine

Methodological materials are intended for teaching 4th year students (7.8 semesters) of the Faculty of General Medicine.GBOU VO SOGMA Min health of Russia on the discipline "Faculty therapy".

**Compilers:**

Associate Professor of the Department of Internal Medicine No. 2, Ph.D. Z.T. Tsabolova

Assistant Department of Internal Diseases No. 2, Ph.D. Gioeva I.Z.

**Reviewers:**

D.V. Bestaev - MD, DSc, Associate Professor, Head of the Department of Internal Medicine No. 3 FGBOU VO SOGMA

R.V. Yenaldiyeva, MD, DSc, Professor of the Department of Internal Diseases No. 1 of the Federal State Budgetary Educational Institution of Higher Education, SOGMA

## **GASTROESOPHAGEAL REFLUX DISEASE**

Gastroesophageal reflux disease (GERD) is a chronic recurrent disease that manifests itself with characteristic clinical signs and is caused by spontaneous, regularly recurring retrograde reflux of acidic gastric and alkaline duodenal contents into the esophagus with damage to its distal parts. It should be noted that GERD is not a synonym for reflux esophagitis, this concept is broader and includes both patients with damage to the esophageal mucosa and patients (more than 50%) with typical symptoms of GERD, who have no visible changes in the mucous membrane during endoscopic examination esophagus.

### **HISTORICAL INFORMATION**

Some of the symptoms of GERD were mentioned in the writings of Avicenna. For the first time, Albert was isolated as an independent disease of the esophagus associated with reflux of the acidic contents of the stomach in 1839, and the first histological description was given by Qunke in 1879. The term "gastroesophageal reflux disease" was proposed by Rossetti (1966). GERD as an independent nosological unit was officially recognized in 1997 at the interdisciplinary congress of gastroenterologists and endoscopists in Genval (Belgium).

### **PREVALENCE**

The prevalence of GERD among the adult population of developed countries reaches 20-40%. However, the low turnover of patients to doctors in milder forms of the disease, the variety of clinical manifestations of GERD, often hiding under the "mask" of other diseases, leads to an underestimation of the true level of morbidity. The tendencies towards an increase in the incidence of GERD were the basis for proclaiming at the 6th European Gastroenterological Week (Birmingham, 1997) the slogan: "XX century - the century of peptic ulcer disease, XXI - century Gastroesophageal reflux disease."

The urgency of the problem of GERD is explained not only by its prevalence, but also caused by serious complications (erosion, peptic ulcer, bleeding, stricture,

development of Barrett's esophagus, esophageal adenocarcinoma). Over the past 20 years, there has been a 3-fold increase in the number of patients with adenocarcinoma of the distal esophagus. Men and women suffer from GERD with the same frequency.

## **PATHOGENESIS**

About 25 years ago, the pathogenesis of GERD was regarded as secondary against the background of an existing hiatal hernia. Even 10 years ago, the pathogenesis seemed to be associated only with weakness and hypotension of the lower esophageal sphincter.

To date, there are two main factors in the pathogenesis of GERD.

The first factor in the pathogenesis of GERD is a decrease in the function of the antireflux barrier, which can develop due to one of 3 reasons:

1. Hernia of the esophageal opening of the diaphragm
2. Decreased pressure in the lower esophageal sphincter
3. Increased number of episodes of spontaneous relaxation

A hiatal hernia is a chronic recurrent disease associated with displacement through the esophageal opening of the diaphragm into the thoracic cavity of the abdominal esophagus, upper stomach, and sometimes intestinal loops. It is necessary to take into account the fact that in 50% of patients it does not cause any clinical manifestations and in the overwhelming majority of cases remains undiagnosed.

Lower esophageal sphincter (LES). At rest, the muscle fibers of the esophagus are in a state of tonic contraction, therefore, at rest, the esophagus is closed in humans. The preserved tone of the LPS is within 15-35 mm Hg. prevents gastric contents from being thrown into the esophagus. The minimum NPS pressure is determined after a meal, the maximum - at night. In a healthy person, during the day, periodically (on average 20-30 times) there is a spontaneous relaxation of the NPS. This short-term, usually no more than 20 seconds, relaxation of the LPS causes the so-called physiological reflux, which does not lead to the development of the

disease. It is believed that the role of these relaxations in physiological conditions is the release of the stomach from the swallowed air.

The pathophysiological mechanisms of the onset of spontaneous or transient relaxation of the LPS are not yet fully understood. Perhaps this depends on the violation of the cholinergic effect or on the enhancement of the inhibitory effect of nitric oxide.

Immediate causes of a decrease in the tone of the LPS most often turn out to be dysregulation of the tone of the LPS (in particular, parasympathetic) and only in rare cases (for example, with scleroderma) organic damage to its smooth muscle fibers.

Many biologically active substances and gastrointestinal peptides decrease (secretin, somatostatin, progesterone, serotonin, dopamine, alpha-blockers, beta-adrenergic agonists) or increase (gastrin, histamine, vasopressin, alpha-adrenergic agonists) the tone of the LPS.

*The following factors contribute to a decrease in the tone of the LPS:*

1. Consumption of products containing caffeine (coffee, tea, Coca-Cola), as well as medications that contain caffeine (citramone, cofetamine, etc.)
2. Drinking alcohol. In this case, not only the tone of the LPS decreases, but also the damaging effect of alcohol on the mucous membrane of the esophagus and the sphincter itself appears
3. Taking certain medications (calcium antagonists, papaverine, no-spa, nitrates, baralgin, anticholinergics, analgesics, theophylline)
4. Effects of nicotine when smoking
5. The tone of the NPS is reduced by some food products - fats, chocolate, citrus fruits, tomatoes)
6. Pregnancy

Even in healthy people, the LPS periodically relaxes to zero pressure. In healthy people, transient relaxation of the LPS occurs, perhaps once an hour. In patients with GERD, long-term transient relaxation can be observed several times within an hour.

At the same time, in some of the patients with GERD, the basal tone of the LPS remains normal. In such cases, the occurrence of gastroesophageal reflux can be facilitated by an increase in intragastric pressure, which is associated with a violation of the motor-evacuation function of the stomach. The increase in intragastric pressure explains the high incidence of gastroesophageal reflux in obese people as well as in pregnant women. Other studies highlight the role of the diaphragm as an antireflux barrier. In these works, it was suggested that the legs of the diaphragm press on the esophagus during inhalation, while during exhalation, the LPS itself is the antireflux barrier.

Thus, GERD develops primarily due to impaired motor activity of the esophagus. The second factor in the pathogenesis of GERD is a decrease in the clearance of the esophagus, which consists of:

- a) chemical - a decrease in the content of hydrocarbons in saliva and a decrease in the production of saliva as such;
- b) volumetric - both due to the suppression of secondary peristalsis, and in connection with a decrease in the tone of the wall of the thoracic esophagus.

Based on this factor of pathogenesis, it follows that the development of gastroesophageal reflux occurs as a result of esophageal dysmotility and dysfunction of the salivary glands (the amount and composition of saliva in healthy people is regulated by the esophagosalivary reflex, which is disturbed in the elderly and with esophagitis). Insufficient salivation is possible with organic and functional diseases of the central nervous system, endocrine diseases (toxic goiter, hypothyroidism), scleroderma, with radiation therapy of tumors in the head and neck region.

The listed violations create conditions for prolonged contact of hydrochloric acid and pepsin, sometimes bile acids with the mucous membrane of the esophagus, which causes its damage.

Thus, the severity of the disease will depend on the damaging properties of refluxate and the characteristics of the esophageal mucosa, which consist in the inability to resist this damaging effect.

The esophagus is constantly cleansed by swallowing saliva, eating and drinking, secretion of the glands of the submucosa of the esophagus, and gravity. When the antireflux barrier is disrupted and stomach contents enter the esophageal lumen, the rate of esophageal clearance determines the duration of acid exposure.

Esophageal resistance. First and foremost, there are no protective mucous layers in the esophagus. The only physical barrier is the underlying water layer, through which protons can freely enter the epithelial cells. Strong connections between squamous epithelial cells serve as a partial barrier to proton diffusion. However, these compounds are not completely impermeable and if the concentration gradient is large enough (i.e. the pH is low enough), penetration occurs.

The resistance of the esophageal mucosa is due to the defense system, which consists of three main parts:

- a) preepithelial protection (salivary glands, glands of the submucosa of the esophagus), including mucin, bicarbonates, epidermal growth factor;
- b) epithelial protection - normal regeneration of the esophageal mucosa;
- c) postepithelial protection (normal blood flow and normal tissue acid-base balance).

Recently, numerous studies have confirmed the presence of a certain relationship between diseases associated with *H. pylori* and GERD. Attention was drawn to the fact that after successful eradication of *H. pylori* infection, the frequency of peptic ulcer disease decreases, and the number of patients with GERD, on the contrary, increases significantly - approximately 2 times.

There is evidence of the presence in the stomach of special bacteria called Hiatus Hernia, which are capable of causing a decrease in the tone of the lower esophageal sphincter and its periodic relaxation.

Thus, based on the foregoing about the pathogenesis of GERD, it should be noted that most authors currently consider GERD as a disease primarily caused by impaired motility of the esophagus and stomach, decreased LPS tone and esophageal clearance, which is accompanied by an imbalance between aggressive

factors of gastric or duodenal contents. and factors of protection with a clear predominance of factors of aggression.

### **CLASSIFICATION**

According to the modern classification, endoscopically positive GERD and endoscopically negative GERD are distinguished.

Of greatest interest for practice is the Savary-Miller classification, which provides for the allocation of 4 degrees of severity of esophagitis. Zero degree corresponds to the intact mucous membrane of the esophagus.

Grade I - individual non-fused erosion and / or erythema of the distal esophagus, occupying less than 10% of the mucous membrane surface of the distal esophagus.

II degree - confluent erosion, capturing up to 50% of the mucous membrane surface of the distal esophagus.

III degree - the presence of circularly located confluent erosions that occupy almost the entire surface of the esophageal mucosa, as well as the formation of peptic ulcers of the esophagus.

IV degree - chronic ulcer of the esophagus, stenosis, development of the columnar epithelium of the esophageal mucosa (Barrett's esophagus).

Histological signs of esophagitis are hyperplasia of the basal zone, elongation of the papillae, dilatation of venules, and leukocyte infiltration of the epithelium.

In 1997, at the 6th European Gastroenterological Week, a new classification of GERD was presented, which is based not on the degree of severity, but on the degree of prevalence of the lesion (hyperemia, erosion).

Grade A - lesion of the mucous membrane within the folds of the mucous membrane, while the size of each lesion does not exceed 5 mm.

Grade B - the size of at least one lesion site exceeds 5 mm; lesion within one fold, but two folds are not connected.

Grade C - areas of mucosal lesion are connected between the tops of two or more folds, but less than 75% of the esophagus circumference is involved in the process.

Grade D - lesions cover at least 75% of the esophagus circumference.



## CLINIC

The clinical manifestations of GERD are varied. They range from usually heartburn to the development of esophageal adenocarcinoma.

O.O. Castell figuratively views GERD as a kind of "iceberg". Most patients (70-80%) have mild and only sporadically arising symptoms, for which they do not seek medical help, self-medicating with antacids on the advice of friends ("telephone reflux"). This is the underwater part of the iceberg. Its middle, above-water part is composed of patients with reflux esophagitis with more pronounced or persistent symptoms, but without complications, who need regular treatment - "outpatient refluxes" (20-25%). The tip of the "iceberg" is a small group of patients (2-5%) who developed complications (peptic ulcer, bleeding, stricture) - "hospital refluxes".

The usual way to classify the clinical spectrum of the disease is to divide patients into groups with typical and atypical symptoms, as well as complications of GERD.

**Typical Symptoms.** Among the main symptoms, heartburn is central - burning retrosternal or epigastric pain extending upward from the xiphoid process. Heartburn occurs in half of GERD patients. Heartburn in GERD has some features: it can be almost constant during the day, however, the pathognomonic symptom for GERD is its clear dependence on body position, and it occurs either when bending or at night in a horizontal position.

Belching is an involuntary sudden ejection of air or a mixture of air with gastric contents into the mouth from the esophagus or stomach.

Regurgitation is the belching of food and air. One common development mechanism is inherent in these symptoms - insufficiency of the lower esophageal sphincter.

Drooling is a sudden sensation of too much salty fluid in your mouth. The symptom is caused by parasympathetic stimulation of the salivary glands, causing hypersecretion of saliva saturated with baking soda.

Dysphagia.

Odinophagia (pain when swallowing) is rare in uncomplicated GERD and suggests the possibility of infectious esophagitis, such as candidiasis or herpes simplex.

Atypical symptoms. The extraesophageal manifestations of the disease include the following clinical symptoms:

1. In 20-60% of cases, GERD is the cause of chest pain, creating a "coronary mask" of GERD. Pains often resemble angina pectoris.
2. Pulmonary symptoms - cough, shortness of breath, often occurring in the supine position, bronchial asthma, which is more often observed in the practice of pediatricians.

The term "reflux-induced asthma" has now been coined. According to the literature, 80% of patients with bronchial asthma have manifestations of GERD.

Very often, repeated pneumonia (Mendelssohn's syndrome) may occur, arising from aspiration of gastric contents, which can be complicated by atelectasis, asbestosis of the lung.

3. Laryngeal symptoms. With high casting, refluxate can flow into the larynx, an otolaryngological mask develops, manifested by a rough, barking cough, sore throat and small voice.
4. Hiccups. It is often a pronounced sign of the disease, caused by excitation of the phrenic nerve, irritation and contraction of the diaphragm, sometimes it is constantly painful. Persistent, indomitable vomiting in healthy people can be caused by undiagnosed GERD.
5. Dental syndrome is manifested by damage to the teeth due to the destruction of tooth enamel by aggressive gastric contents.

## **DIAGNOSTICS**

Anamnesis is one of the most important components of a comprehensive examination of patients with esophageal pathology. The questioning should be of great importance, since you can make the correct diagnosis if you know the

complaints well, and not just the results of his examination. The history should not be a mechanistic method of gathering information. It requires a high level of professionalism and culture from the doctor, as well as intuitive caution in order to avoid iatrogenic injuries.

GERD is currently being verified using the following diagnostic tests:

1) X-ray examination. A standard barium esophagogram, usually done in conjunction with a complete series of upper GI images, is a quick and inexpensive way to assess the anatomical condition of the esophagus and stomach. At the same time, it is possible to safely exclude a peptic ulcer with localization distal to the esophagus. It is also possible to detect the presence of unexpected defects such as esophageal diverticula or paraesophageal hernia. The main disadvantage of barium esophagoscopy is that it is often normal with existing GERD, even with inflammation of the distal esophagus. This method can detect deep ulcers of the esophagus, but small erosions are often missed.

2) Esophagogastroduodenoscopy is one of the main and most sensitive method used to detect damage to the esophageal mucosa. Moderate esophagitis is easily detected. The diagnosis is confirmed by endoscopic biopsy. However, esophagoscopy does not make it possible to diagnose GERD in the absence of changes in the esophageal mucosa, as well as to assess the frequency and duration of pathological casts.

3) Daily monitoring of intraesophageal pH. With endoscopically negative form of GERD, the main instrumental method to confirm the diagnosis is daily monitoring of intraesophageal pH.

With its help, episodes of gastroesophageal reflux are recognized, manifested by a drop in pH below 4.0, their total frequency and duration are calculated. When decoding the pH readings in the esophagus, the following parameters are assessed:

but. The total time during which the pH drops below 4.0. This indicator is also assessed in the vertical and horizontal position of the body;

b. The total number of refluxes per day;

in. The number of refluxes is more than 5 minutes each.

In a pH-metric study, gastroesophageal reflux is usually understood to mean episodes in which the pH in the esophagus drops below 4.0 units. Normal values in the terminal esophagus are 6.0-8.0 units. Gastroesophageal reflux also occurs in healthy people, however, the duration of reflux should not exceed 5 minutes, and the total decrease in pH less than 4.0 units and below should not exceed 4.5% of the total recording time. Therefore, the presence of pathological refluxes is indicated by:

- acidification of the esophagus, lasting more than 5 minutes;
- decrease in pH less than 4.0 units for a time exceeding 4.5% of the total recording time.

Reflux is considered moderately expressed lasting 6-10 minutes, sharply expressed - more than 10 minutes.

### **ADDITIONAL METHODS FOR DIAGNOSING GERD**

Additional methods are the Bernstein test, the Stepenko test. When conducting an acid perfusion test or L.B. Bernshtein and L.A. Baker's (1958) patient is in a seated position. The probe is inserted through the nose into the middle part of the esophagus (30 cm from the wings of the nose). At a rate of 100-200 drops per minute, 15 ml of 0.1 M hydrochloric acid are injected. The occurrence of pain, heartburn, or a feeling of chest constriction and their subsiding after the introduction of saline is regarded as a positive sign. For reliability, the test is repeated twice. The sensitivity and specificity of this test is about 80%.

A more physiological test is the Stepenko test, in which, instead of hydrochloric acid, the patient is injected with his own gastric juice.

### **COMPLICATIONS OF GERD**

Complications of GERD include bleeding, peptic ulcers and esophageal strictures, and the development of Barrett's esophagus.

### **TREATMENT**

Taking into account all the links of pathogenesis, the treatment of GERD should be complex and should be based on the following principles: a) decrease in the volume of gastric contents; b) increasing the tone of the NPS; c) improvement of esophageal clearance; d) protection of the esophageal mucosa from damage.

Treatment for GERD patients begins with general interventions called "lifestyle changes". They include dietary recommendations - frequent and fractional meals. It is necessary to exclude "snacking" at night, to lie down after eating. After eating, avoid leaning forward and do not lie down. The last meal should be no later than 3-4 hours before bedtime. It is recommended to refuse to use coffee, chocolate and foods rich in fat (whole milk, cream, fatty fish, goose, duck, pork, fatty beef, cakes, pastries, peppermint, pepper), which reduce the tone of the NPS. An unconditional benefit is provided by patients quitting smoking and taking alcoholic beverages. You should also, if possible, avoid taking medications that promote gastroesophageal reflux (nitrates, theophylline, adrenomimetics, calcium channel blockers). You should sleep with a high headboard, that is, raise the head horses of the bed by 10-15 cm. The exclusion of a strictly horizontal position during sleep allows you to reduce the number of reflux episodes and their duration, since esophageal cleansing increases due to the action of gravity.

Since gastroesophageal reflux is promoted by some exercise and a certain position of the body, lifting weights, physical exercises associated with torso bending and abdominal tension are contraindicated in patients with GERD. In obese patients, normalization of body weight gives a good effect.

However, such measures are often not effective enough, especially in the presence of esophagitis. In most of these cases, drug therapy plays a decisive role in treatment.

Antacids. The most famous drugs that have long been used in the treatment of GERD are antacids. After the introduction into practice of powerful antisecretory drugs, in particular H<sub>2</sub>-blockers, interest in antacids dropped for a while, as they were declared to be insufficiently effective. However, in recent years, attention to

this drug group has increased again, as it turned out that avoiding antacids does not improve the results of treatment.

It turned out that in terms of the rate of symptomatic effect (the speed of disappearance of pain and heartburn), antacids are noticeably superior to antisecretory drugs, which determines the popularity of antacids in patients with GERD.

Currently, preference is given to antacids containing aluminum and magnesium hydroxide (maalox, phosphalugel, etc.), as well as alginic acid (topaal, topalkan). Alginic acid prolongs the action of antacids in GERD. Topalkan is prescribed 2 tablets 3 times a day 40 minutes after meals and at night.

Pathogenetically justified in all cases is the use of prokinetic drugs. The pharmacological action of drugs in this group is to enhance gastric motility and eliminate delayed gastric evacuation, increase the tone of the LPS, reduce gastroesophageal refluxes and the time of contact of gastric contents with the esophageal mucosa, improve esophageal cleansing. The most effective drugs in this group are motilium and coordinax (cisapride, prepulsid, peristil). Motilium is prescribed 1 tablet (10 mg) 3 times a day 15-20 minutes before meals. It is important to remember that the intake of motilium cannot be combined in time with the intake of antacids, since an acidic environment is necessary for its absorption.

According to various authors, the use of cisapride at a dose of 10 mg 3-4 times a day for 6-12 weeks gave a positive effect.

Antisecretory drugs. Traditional stepwise treatment of GERD implies the initial appointment of histamine receptor blockers as secretion inhibitors, and, if they are ineffective, proton pump inhibitors.

Peripheral anticholinergics, despite their antisecretory activity, are contraindicated in patients with GERD, since they reduce the tone of the LPS.

H<sub>2</sub>-Histamine blockers occupy an important place in the complex treatment of patients with GERD. Currently available 5 grades H<sub>2</sub>-blockers: cimetidine (first generation), ranitidine (second generation), famotidine (third generation),

nizatidine (acid) (fourth generation) and roxatidine (fifth generation). The most widely used drugs are from the groups ranitidine (ranisan, zantac, ranitin) and famotidine (kvamatel, ulfamid, famosan, gastrosidine). Daily doses of H<sub>2</sub>-blockers in the treatment of GERD and, in particular, in the treatment of reflux esophagitis should be at least 450-600 mg for ranitidine and 60-80 mg for famotidine.

***Proton pump blockers...*** Proton pump blockers are currently considered the most powerful antisecretory drugs. Currently, four chemical varieties of this group of drugs are known: omeprazole, pantoprazole, lansoprazole, rabeprazole.

In the treatment of patients with GERD, omeprazole (losek, losek-maps, mopral, zoltum) has proven itself well. At a dose of 20-40 mg / day, it promotes the rapid disappearance of the subjective symptoms of the disease and the healing of erosions, especially in cases resistant to therapy with H<sub>2</sub> blockers<sup>2</sup>-receptors. Maintenance therapy with omeprazole at a dose of 10 or 20 mg per day prevents recurrence of reflux esophagitis in most patients.

Recently, a new dosage form of omeprazole, losec-maps, has been introduced into practice. Its advantage is the absence of allergens of fillers (gelatin, lactose), a special capsule coating that makes it easier to swallow.

**To date, several different drug therapy regimens have been proposed.**

**The most common are (A.A. Sheptulin):**

**one.** The scheme of "step-by-step increasing therapy", which involves the appointment at different stages of the disease, drugs of various strengths and their combinations. So, the first place in treatment is given to lifestyle changes and, if necessary, taking antacids. If clinical symptoms persist at the second stage of treatment, prokinetics or H<sub>2</sub>-blockers of histamine receptors. If such therapy is ineffective, then at the third stage of treatment, proton pump inhibitors or a combination of H<sub>2</sub>-blockers and prokinetics;

2. The scheme of "gradually decreasing therapy" assumes from the very beginning the appointment of proton pump inhibitors with the subsequent transition after the

achievement of a clinical effect on the intake of H<sub>2</sub>-blockers or prokinetics. The use of such a scheme is justified in patients with a severe course of the disease and pronounced erosive and ulcerative changes in the mucous membrane of the esophagus.

Options for drug therapy, taking into account the stage of development of GERD (P.Ya. Grigoriev):

1. In case of gastroesophageal reflux without esophagitis, motilium or cisapride 10 mg 3 times a day in combination with antacids 15 ml 3 times a day 1 hour after meals and the fourth time before bedtime is prescribed for 10 days.

2. In case of reflux esophagitis of the first degree of severity, H blockers are prescribed: for 6 weeks - ranitidine 150 mg 2 times a day or famotidine 20 mg 2 times a day. After 6 weeks, with the onset of remission, drug therapy is discontinued.

3. In case of reflux esophagitis of the second severity, 300 mg of ranitidine or 40 mg of famotidine 2 times a day or 20 mg of omeprazole after lunch (14-15 hours) are prescribed for 6 weeks. After 6 weeks, treatment is discontinued if remission occurs.

4. In case of reflux esophagitis of the third severity, omeprazole 20 mg 2 times a day is prescribed for 4 weeks, and then, in the absence of symptoms, continue taking omeprazole 20 mg per day for up to 8 weeks. After that, they switch to taking blockers H<sub>2</sub>-receptors in a maintenance half dose for a year.

5. In case of reflux esophagitis of the fourth degree of severity, omeprazole 20 mg 2 times a day is prescribed for 8 weeks, and when remission occurs, they switch to continuous intake of H<sub>2</sub>-blockers.

6... Considering that one of the main reasons leading to an increase in spontaneous relaxation of the LPS is an increase in the level of neurotization, patients with GERD, along with standard therapy, are shown the appointment of Eglonil 50 mg 3 times a day or Grandaxin 50 mg 2 times a day. The use of these drugs improves the prognosis of the disease.



Anti-relapse treatment. The most difficult problems in the treatment of GERD are the high frequency of its recurrence and, accordingly, the need for maintenance treatment. It has now been established that stopping treatment immediately after healing of the erosion of the esophageal mucosa is fraught with a rapid relapse of the disease. According to foreign authors, relapse of GERD symptoms occurs in 50% of patients 6 months after stopping treatment, in 87-90% after 12 months. This necessitates a long-term maintenance intake of antacids up to 1-2 years, H<sub>2</sub>-blockers, omeprazole or cisapride.

Currently, there are several options for anti-relapse treatment for GERD:

- H<sub>2</sub>-blockers in a full daily dose 2 times a day (ranitidine 150 mg or famotidine 20 mg 2 times a day);
- omeprazole 20 mg in the morning on an empty stomach;
- cisapride (coordinax) or motilium at half the dose compared to the dose used during the exacerbation;
- long-term treatment with non-absorbable antacids (maalox, phosphalugel).

Reasons for the ineffectiveness of GERD treatment:

- incorrect diagnosis of GERD;
- insufficient suppression of secretion;
- the defeat is associated with the intake of other medications;
- the presence of Zollinger-Ellison syndrome;
- violation of the evacuation of stomach contents.

## **SURGERY**

Indications for surgical treatment are:

- failure of conservative treatment within 6 months, regardless of the presence or absence of a hiatus hernia;
  - complications of GERD (strictures, repeated bleeding, deep peptic ulcers, resistant to drug treatment);
- Barrett's esophagus (due to the danger of malignancy)

## **IRRITATED INESTINAL SYNDROME**

Among functional bowel diseases, irritable bowel syndrome (IBS) is rightfully ranked first. Millions of people around the world suffer from some form of this disease.

The urgency of the IBS problem is determined, firstly, by its prevalence (from 14-22 to 30-48%), and in women it occurs 2-4 times more often than in men, and the age peak falls on the period from 30 to 40 years ... According to the British authors, at least one symptom corresponding to the "Roman criteria" of IBS is detected in 47% of women and 27% of men; two symptoms characteristic of IBS - in 24 and 11%, respectively; three or more symptoms - in 13 and 5%.

When assessing the incidence and prevalence of IBS, we are faced with the "iceberg" phenomenon. Due to the delicate nature of complaints, about  $\frac{2}{3}$  of patients consider it not quite convenient to bother the doctor with such problems, preferring to be treated on their own with the help of enemas, laxatives, etc.

Secondly, the urgency of this problem is associated with a significant decrease in the quality of life of patients. Comparison of the quality of life of patients with IBS, as well as patients with diabetes mellitus, acute myocardial infarction, arterial hypertension and depression showed that in persons with IBS, the quality of life is comparable to that of patients with depression and is the lowest among all surveyed groups. ...

Thirdly, it is necessary to point out the lack of effectiveness of treatment. Long-term clinical remission can be achieved only in 10% of patients, and in 30% of patients, a significant improvement in well-being is observed. Thus, about 60% of patients, despite the treatment, continue to experience abdominal pain, excess gas and unstable stool.

Fourthly, the cost of the disease is an important problem. The annual cost of screening and treating patients with IBS in the United States is \$ 25 billion.

Before 1988, IBS was described under various names such as spastic colitis, mucous colic, nervous colic, nervous diarrhea, irritable bowel, functional distress syndrome. These names reflected various symptoms of the disease and did not reflect a common understanding of the problem.

In 1988, in Rome, the International Group for the Study of the Functional Pathology of the Gastrointestinal Tract for the first time officially approved the term "irritable bowel syndrome", gave its definition and developed the criteria for making a diagnosis, later called the "Roman criteria for IBS". In 1999, the criteria were supplemented and the "Rome SRK II Criteria" was adopted.

Since the syndrome, as it is well known, occurs in a wide variety of diseases, then IBS, according to a number of authors, cannot logically be considered an independent nosological form, but should be interpreted as a collective concept.

However, the "Encyclopedic Dictionary of Medical Terms", along with the specified interpretation of this concept, allows the use of the term "syndrome" to denote a specific nosological form. An example of such a designation "syndrome" can be, in particular, the Zollinger-Ellison syndrome (gastrin-producing tumor of the pancreas). The phrase "IBS" refers to the second use of the term "syndrome".

IBS is not a collective concept, but an independent nosological form with features of etiology and pathogenesis.

According to international consensus, IBS is defined as a complex of functional (i.e., not associated with organic lesion of the intestine) disorders, the main clinical symptom of which is abdominal pain and / or abdominal discomfort, for a total duration of at least 12 (not necessarily consecutive) weeks over the last 12 months,

which are combined with at least two of the following three signs: a decrease in symptoms after a bowel movement; and / or abnormal stool frequency (constipation, diarrhea, or alternation); and / or a change in stool consistency.

### **ETIOLOGY**

Despite its widespread occurrence, the true causes of the onset of the disease are not completely clear, but the significance of a number of factors in its occurrence can be considered established. According to the modern concept, IBS is considered as a biopsychosocial disease, in the development of which both the patient's personality traits and predisposing factors play an important role. Personal characteristics can be genetically determined or formed under the influence of the environment. A premorbid personality with this pathology is characterized by a number of features. In particular, it was noted that such patients are characterized by a higher level of anxiety, depression, and sleep disorders. Future patients before illness are assessed as overly conscientious persons, very punctual, obligatory persons who have reached certain heights in their profession.

The fact that symptoms of IBS in identical twins are more common than in fraternal twins may indicate a certain role of hereditary predisposition to the development of the disease.

Much attention is paid to the possible role of psychoemotional stress in the onset of IBS, because the direct dependence of the onset of IBS symptoms on stressful situations has been proven. This disorder makes its debut after a traumatic situation that is significant for the personality, being, in fact, a somatized reaction of the body to stress. It is generally accepted that IBS is a classic example of psychosomatic illness, representing the response of a particular personality to key experiences. In ICD-10, this syndrome belongs to the heading "Somatoform dysfunction of the nervous system of the lower part of the gastrointestinal tract." At the same time, a traumatic situation can be transferred in childhood (loss of one of the parents, sexual harassment), a few weeks or months before the onset of the

disease (divorce), or it can become chronic, persisting for a long time (serious illness of someone close).

The onset of the disease itself can lead to the appearance of certain mental disorders in terms of pathological reactions to the very fact of the disease, and, in addition, social restrictions are important due to the nature of this type of suffering. It is shown that in the process of this psychosomatic illness, the response of the personality to stress changes: its intrapunitive (self-punishing) type turns into extrapunitive (blaming others), which leads to an accelerated formation of secondary psychosomatosis and a special pathological (psychosomatic) personality formation.

Thus, personality traits combined with predisposing factors can lead to symptoms of IBS, symptoms of mental illness, and the development of painful behavior.

## **PATHOGENESIS**

To explain the mechanism of development of visceral hypersensitivity and impaired motility, concepts are proposed about the leading role of the central and autonomic nervous systems in the development of the disease in the form of changes in the neurohumoral regulation of the functional state of the intestine, including its reactions to stress, as well as the involvement of serotonergic mechanisms in the process.

The following factors support the involvement of the central nervous system:

- in IBS, centrally acting drugs (antidepressants), as well as psychotherapeutic methods of treatment (psychotherapy, hypnosis) are quite effective;
- there are no symptoms of the disease during sleep, when the activity of the central nervous system is minimal;
- in patients with IBS, other functional and psychosomatic disorders are very often found in the development of which the central nervous system is involved.

Specially conducted electrophysiological studies have shown the presence of disorders of intestinal motility in patients with IBS, arising in response to the effects of various stimuli.

The intestinal motor function is disturbed under the control of numerous regulatory influences (central, peripheral, enteric nervous systems and gastrointestinal peptides), which determine the normal tone and contractile activity of the intestinal wall.

In irritable bowel syndrome, the sensitivity of the receptors of the colon wall to stretching is increased, and therefore pain and discomfort occur in them with a lower threshold of excitability than in healthy people, i.e. visceral hyperalgesia develops. According to modern concepts, visceral hyperalgesia in patients with IBS is associated with the fact that peripheral stimuli (for example, stretching of the intestinal wall) cause hyperextension (overexcitation) of spinal neurons, followed by the formation of pain.

The condition for the formation of increased visceral sensitivity is often the presence of so-called sensitizing factors (for example, psychoemotional stress, intestinal infection, physical trauma). These factors, causing changes in the motor function of the intestine, contribute to the activation of spinal neurons and further lead to the development of the phenomenon of increased spinal excitability, when stimuli of ordinary strength (for example, stretching of the intestine with a small amount of gas) cause an increased reaction, manifested by pain. At the same time, in patients with IBS, the descending process, i.e., due to the influence of the cerebral cortex, suppression of pain perception, may be disrupted.

Of a certain importance in the development of IBS are the dietary habits of patients (low content of ballast substances in the diet, refusal of a full breakfast, etc.), a sedentary lifestyle, some physiological conditions (pregnancy), gynecological diseases.

Acute intestinal infections (ACI) can contribute to the formation of IBS. It is known that some people who have undergone dysentery and other AEI do not fully recover: they remain in pain, abdominal discomfort, and stool disturbance. In half of the patients, the onset of IBS was preceded by AEI, mainly shigellosis. Getting rid of the patient from AEI cannot guarantee against recurrence of IBS. In the pathogenesis of chronic intestinal disease, high bacterial contamination of the

small intestine, dysbiosis of the large intestine and damage to the enteric nervous system by OCI antigens are important against the background of a decrease in the body's immune defense.

The development of IBS after OCI is facilitated by the applied antibiotic therapy. Antibacterial drugs suppress not only the growth of pathogenic microorganisms, but also the normal intestinal microflora. As a result, saprophytic microbes multiply, acquiring pathogenic properties with high drug resistance. These are, first of all, staphylococci, proteus, yeast fungi, enterococci, *Pseudomonas aeruginosa*, *Klebsiella*.

Thus, chronic mental stress, stresses with a change in the balance of mediators and the sensitivity threshold of visceral receptors, which determine the motor-evacuation function of the intestine and the perception of pain, a decrease in tolerance to food substances, a hereditary predisposition, and previous acute intestinal infections can be a trigger mechanism in the development of IBS.

### **CLINICAL PICTURE**

All clinical manifestations of IBS can be conditionally divided into three groups: intestinal, related to other parts of the gastrointestinal tract, and non-gastroenterological. The classification of intestinal complaints includes the well-known "Rome criteria" of the second revision. However, the clinical symptoms of IBS that meet the "Rome II criteria" cannot be considered pathognomonic only for this disease. They are also found in many organic diseases, in particular, intestinal tumors, Crohn's disease, ulcerative colitis, chronic pancreatitis, etc.

Depending on the nature and combination of clinical symptoms, there are three main variants of IBS: 1) a variant proceeding mainly with diarrhea; 2) mainly with constipation; 3) mainly with abdominal pain and flatulence.

However, with any of these options, the leading symptom of the disease is abdominal pain. The main mechanisms for the development of abdominal pain are due to visceral hyperalgesia and impaired intestinal motility.

The pain can be of varying intensity: from dull aching to burning, stabbing, cramping (some women associate pain in the intestines with pain during childbirth). The pain can be localized in any part of the abdomen, more often in the iliac regions, as a rule, it does not radiate.

Abdominal pain usually worsens after eating, in women - during menstruation; decreases after defecation, passing gas, taking antispasmodics.

In parallel with pain (and sometimes without pain), a feeling of overstretching, overflow, and bloating is disturbing.

Clinical signs of IBS are necessarily complemented by such an indicator as the frequency of bowel movements, which allows differentiating the disease into IBS with a predominance of diarrhea and IBS with a predominance of constipation (although in many patients these symptoms alternate). To facilitate diagnosis, a table of IBS-specific symptoms can be used.

### ***Clinical signs and symptoms of IBS***

1. Chair less than 3 times a week
2. Stool more than 3 times a week
3. Solid consistency of feces
4. Loose or mushy stools
5. Straining during the act of defecation
6. Imperative urge to defecate
7. Feeling of incomplete bowel movement
8. Discharge of mucus during bowel movements
9. Feeling bloated and full

IBS with a predominance of diarrhea is characterized by a combination of signs 2, 4, 6 in the absence of signs 1, 3, 5. Otherwise, in the presence of signs 1, 3, 5 and in the absence of signs 2, 4, 6, they speak of IBS with a predominance of constipation.

An important place in the structure of IBS is occupied by the variant of the disease, proceeding with a predominance of diarrhea (sometimes this variant of IBS is



referred to as functional diarrhea). According to the largest Hungarian clinician I. Magyar, functional diarrhea accounts for 6 cases of chronic diarrhea out of 10. The variant with a predominance of diarrhea occurs in about 30% of patients with IBS. The relevance of the IBS variant with a predominance of diarrhea is also determined by the fact that such patients are often misdiagnosed as "dysbiosis", "chronic spastic colitis", "chronic pancreatitis", etc., and pathogenetically based therapy is prescribed (in particular, enzyme preparations ).

The clinical picture of diarrhea in IBS has its own distinctive features that make it possible to suspect the functional nature of the disease even with careful questioning of the patient. It is important that diarrhea is absent at night, but occurs in the morning, usually after breakfast (as a result of stimulation of intestinal motility due to the gastrointestinal reflex). Stool happens 2-4 times in a short period, often accompanied by an imperative urge and a feeling of incomplete emptying of the intestines.

Since increased intestinal peristalsis in patients with IBS is usually combined with increased gas production, the urge to defecate in such patients is imperative, which is reflected in the name "morning storm syndrome". It has long been noted that in patients with IBS, symptoms appear, as a rule, only during wakefulness. If pain and diarrhea occur at night and wake the patient up, the diagnosis of IBS is unlikely.

Often, during the first act of defecation, the stool is denser than during subsequent ones, in which its volume decreases, but it becomes more liquid.

In the clinical picture of IBS, there is often a discrepancy between the abundance of complaints presented and a good general condition, the absence of signs of disease progression. When questioning patients, one can note a variety of clinical symptoms, an abundance of so-called extraintestinal complaints, indicating manifestations of neurocirculatory dystonia (migraine-type headaches, a feeling of coma when swallowing, dissatisfaction with inhalation, inability to sleep on the left side, vasospastic reactions, urinary disorders, etc. ), the relationship of

diarrhea with neuropsychic factors, as well as a high frequency of anxiety-hypochondriac and depressive reactions.

An equally important condition aimed at preventing gross errors in diagnosis is the observance of the rules: do not refer to patients with IBS as those who have symptoms that are often found in inflammatory, vascular and neoplastic diseases of the intestine. The authors of Roman Criteria II called these signs "alarm symptoms", which include fever, unmotivated weight loss, dysphagia, vomiting with blood (hematemesis) or black tarry stools (melena), the appearance of scarlet blood in the stool (hematochezia), anemia, leukocytosis, increased ESR, the onset of the disease in people over 50 years old, cancer and inflammatory bowel disease in relatives, nighttime symptoms, the detection of which makes the diagnosis of IBS unlikely.

Among the symptoms characteristic of lesions of other organs of the gastrointestinal tract, signs of functional dyspepsia are more common (according to different authors, up to 87%) - a feeling of fullness in the stomach, belching, heartburn, nausea, vomiting, flatulence, which is explained by a similar value of disturbances in the motility of the digestive tract in the pathogenesis of both diseases.

Non-gastroenterological manifestations of IBS often play a major role in a decrease in the quality of life. Patients with IBS often complain of a headache (like a migraine), pain in the sacrum, a feeling of coma when swallowing, dissatisfaction with inhalation, vasospastic reactions, urinary disturbances, drowsiness. IBS is also characterized by a long history of the disease, a changeable nature of complaints, a relationship between the deterioration of well-being with psychoemotional factors. The prolonged course of IBS can lead to the development of strategies for certain social restrictions: patients stop attending theaters, cinemas, do not use the metro, avoid crowded places, try to choose those routes where there are public toilets. A distinct socio-psychological position of self-isolation is being formed.

According to modern concepts, the state of mind of patients with IBS is borderline, it already differs from the norm, but this is not yet an obvious psychopathy. Patients with IBS are characterized by hysterical, aggressive reactions, depression, cancerophobia, obsession, fear, hypochondriacal manifestations, and suicide.

According to the prevailing psychopathic picture, the following variants of this syndrome are distinguished: melancholic, depressive-anxious, depressive-hypochondriac, depressive-phobic and schiziform.

In the melancholic version, there is a classic melancholy with depressive resignation to fate, dull doom, "joyless humility", while the disease is perceived as a real given for "sins", wrong actions in the past. That is why patients do not conduct any active fight against the disease.

The depressive-anxious type of IBS is characterized by situational and somatogenic anxiety, which increases during periods of exacerbation of the underlying disease or the appearance of some of its symptoms in an unacceptable situation (for example, the appearance of diarrhea during a trip to the subway). The inability to find a way out of situations significantly increases the anxiety and, as it were, translates it into the category of hysterical reactions that outwardly resemble hysterical attacks.

The depressive-hypochondriacal variant is, as it were, a logical continuation of the previous one. Against the background of depression and anxiety, ideas arise - at first, rather vague and rather suspicions or conjectural guesses, and it is possible that one has not only IBS, "but also a disease of a different genesis, prognostically more severe and, possibly, incurable.

The depressive-phobic variant is, as it were, the logical conclusion of the hypochondriacal orientation of the patients of the previous group. Hypochondria here has a point of application in the form of the formation of clear and specific phobias (carcinophobia). Awareness of the "presence" of an oncological disease intensifies the activity of patients in the search for new and "urgently needed" methods of treatment so much that their anxiety, which is now realized in "search

activity", is somewhat reduced, which is manifested by some improvement in the somatic state in IBS.

The schiziform variant of IBS deserves special attention, since it is it that causes significant difficulties in the differential diagnosis of this condition and sluggish schizophrenia. Carcinophobic obsession affects not only the gastrointestinal tract, but more often other organs and systems. In addition, the content side of phobias is expanding due to an increase in the repertoire of phobias (fear of contracting AIDS, diabetes mellitus and other illnesses that are not easily treatable, according to patients). In this case, the situationally conditioned anxiety is transformed into a diffuse, "free floating" one. Exacerbations of the mental state lose their causal relationship with the deterioration of the somatic component of IBS.

Thus, IBS, being a typical psychosomatic suffering, occurs under the influence of severe mental trauma in a particular personality. It is characterized by psychopathological heterogeneity, which makes it possible to distinguish its clinical variants that are significant from the diagnostic and therapeutic points of view; therefore, the problem of identifying masked depression or other mental changes in patients with IBS is very urgent.

## **DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS**

A reliable diagnosis of IBS can be considered only after examination, which includes mandatory clinical and biochemical blood tests, complete fecal analysis and fecal occult blood analysis, colonoscopy, supplemented, if necessary, by biopsy of the colon mucosa, and the use of endoscopic methods.

The examination allows you to exclude such diseases as ulcerative colitis and Crohn's disease, microscopic forms of colitis (lymphocytic and collagenous), colon tumors, amyloidosis, laxative abuse.

To exclude the infectious nature of intestinal lesions, microbiological studies are carried out for the presence of intestinal bacteria in the feces (Salmonella, Shigella,

Yersinia, Clostridia, etc.). Extraintestinal changes and damage to the organs of the retroperitoneal space are recognized using ultrasound, CT, angiography.

Since the symptoms of IBS can be secondary to other diseases, it is also recommended to study the functional state of the gastroduodenal zone, biliary tract, and pancreas.

Radiographically, in IBS, signs of colon dyskinesia are found - uneven filling and emptying (sometimes painful), alternation of spastically contracted and dilated sections of the intestine. Often, when such a picture is detected, the radiologist gives a conclusion about the presence of colitis, which is inappropriate: it is possible to talk about the presence of colitis only on the basis of data from a morphological study of a biopsy of the intestinal mucosa in the presence of inflammatory or inflammatory-dystrophic changes due to a specific etiological factor.

Thus, the diagnosis of IBS can only be made after a thorough collection of complaints, anamnesis data and examination of the patient, including mandatory clinical and biochemical blood tests, as well as fluoroscopy, colonoscopy, supplemented by biopsy if indicated.

### **MODERN METHODS FOR TREATMENT OF IBS**

IBS treatment should be comprehensive, aimed at eliminating interrelated central and visceral negative effects. The pharmacotherapy of IBS is quite well developed and usually comes down to the use of various antispasmodics (to relieve pain), laxatives (to eliminate constipation) and antidiarrheal drugs (to combat diarrhea).

For the relief of abdominal pain and dyspeptic syndrome in the complex treatment of diseases of the gastrointestinal tract, smooth muscle relaxants are traditionally used, which include several groups of drugs.

1. Drugs acting at the stage of the nerve impulse / humoral signal conduction (neurotropic antispasmodics): anticholinergic agents.

2. Drugs that act directly on smooth muscle cells (myotropic antispasmodics): sodium channel blockers; calcium channel blockers; donors of nitric oxide (nitrates); phosphodiesterase inhibitors (isoquinoline derivatives).

*Mechanism of action of major muscle relaxants*

<b>Stages of muscle fiber contraction (points of application of drugs)</b>	<b>Drugs that block muscle fiber contraction</b>
Activation of M-cholinergic receptors in muscle fiber	M-anticholinergics: atropine, metacin, platifillin, gastrocepin, buscopan
Na-channel opening and Na <sup>+</sup> entry into the cell	Na channel blockers: meveberine
Ca-channels opening and Ca entry into the cell from the extracellular space	Calcium channel blockers: pinaverium bromide, otylonium bromide
Activated phosphodiesterase, cAMP breakdown, energy supply for muscle fiber contraction	Phosphodiesterase blockers: alverin, drotaverine, papaverine, etc.

The principle of action of anticholinergic drugs is that due to the blockade of M-cholinergic receptors, the action of acetylcholine on muscarinic receptors is eliminated and the process of muscle contraction, mediated by calcium ions, is not triggered. Currently, along with natural ones, synthetic anticholinergics have been synthesized, among which the following drugs are of greatest importance for the relief of abdominal pain caused by spasm of the smooth muscles of the gastrointestinal tract.

Buscopan (hyoscine butyl bromide) is one of the highly selective anticholinergics that selectively suppress the release of acetylcholine in the peripheral endings of muscarinic receptors of types 1 and 3, which are localized mainly in the wall of the gastrointestinal tract, gallbladder and biliary ducts. At the same time, buscopan has a ganglion-blocking effect, suppressing the release of acetylcholine in the spinal

ganglia, and therefore is one of the most powerful antispasmodics. In this case, the drug does not penetrate the blood-brain barrier and is devoid of a pronounced atropine-like systemic effect.

The absorption of buscopan with oral administration is 8-10%, with rectal administration - 3%. At the same time, low absorption does not affect the antispasmodic effect. In connection with blood proteins, 3-11% of the absorbed drug enters. The maximum plasma concentration of buscopan is reached within 1-2 hours after oral administration and is about 4.4 ng / ml, i.e. the therapeutic effect of the drug is provided by its small doses. The evidence of the selectivity of the action of buscopan is the high content of the drug in smooth muscles, exceeding its concentration in the blood plasma. Buscopan is characterized by a rapid onset of antispasmodic action (20-30 minutes after ingestion) and long-term preservation of the effect (for 2-6 hours). The drug is excreted unchanged by the kidneys. The half-life is 4.2 hours.

The drug is available in sugar-coated tablets and suppositories of 10 mg; dispensed without a doctor's prescription. The recommended dose of buscopan is 1-2 tablets or 1-2 suppositories 3-5 times a day.

A significant advantage of buscopan is its low bioavailability - only a small amount of the drug enters the systemic circulation. For a buscopan, this figure is 1%. The drug is mainly concentrated in the spasmodic areas of the smooth muscles of target organs. Low bioavailability is associated with the minimal severity of the systemic effects of the drug. According to this indicator, buscopan compares favorably with drotaverine (no-shpy), the bioavailability of which is 25-91%, which provides a pronounced systemic effect. Contraindications to taking buscopan are angle-closure glaucoma, prostatic hyperplasia with a tendency to urinary retention, organic stenosis of the gastrointestinal tract, tachycardia, myasthenia gravis, megacolon.

Thus, buscopan is the most powerful, effective, rapidly relieving pain modern antispasmodic, which meets all the requirements for essential drugs, and can be

recommended for widespread use as the drug of first choice in the treatment of spastic abdominal pain.

Since muscarinic receptors of the third type are localized in the muscle cells of the intestine, selective M3 anticholinergic compounds (zamifenapine and darifenacin) are currently synthesized.

Mebeverine hydrochloride (duspatalin) - has two effects. The first of them comes down to blockade of fast sodium channels of the myocyte cell membrane, which disrupts the processes of sodium entry into the cell, slows down the depolarization processes and stops the entry of calcium into the cell through slow channels. As a result, myosin phosphorylation processes decrease and muscle fiber spasm is relieved (antispastic effect). The second effect is due to a decrease in the replenishment of intracellular calcium stores, which leads only to a short-term release of potassium ions from the cell and its hyperpolarization. The latter prevents the development of hypotonia of the muscle wall. This effect of mebeverin compares favorably with the action of other myotropic antispasmodics, which cause prolonged hypotension. The drug is administered orally at 200 mg 2 times a day for 4 weeks.

Pinaverium bromide (dicetel) is a selective blocker of calcium channels of smooth muscles of the gastrointestinal tract. The advantage of dycetel, one of the most effective antispasmodics, is based on the selectivity of action on smooth muscles of the gastrointestinal tract and the absence of systemic anticholinergic effects and systemic vasodilating and cardiotropic action inherent in calcium channel blockers of the nifedipine group. The drug is administered orally, 1 tablet 3-4 times a day, in some cases, the daily dose may be increased to 6 tablets. The drug should be taken with meals with plenty of water. Course treatment - up to 1 month, possibly continued in the form of maintenance doses (1-2 tablets per day) for up to 2-3 months.

In addition to relieving pain, as in dysbiosis, it is advisable to use pro- and prebiotics, which reduce the secretion of water and electrolytes stimulated by



pathogenic microflora, inhibit intestinal motility, thereby improving stool consistency and reducing flatulence.

Hilak forte is a sterile concentrate of metabolic products of normal gram-positive and gram-negative intestinal microflora. It contains lactic acid, milk buffer salts, lactose, amino acids and short-chain volatile fatty acids. A dose of 1 ml corresponds to biosynthetic active substances secreted by 10<sup>10</sup> microorganisms.

Pharmacological properties and action of the drug:

- Restoration of the biological environment in the intestine, necessary for the existence of normal microflora
- Suppression of the growth of pathogenic bacteria
- Stabilization of pH values in the gastrointestinal tract within the physiological norm, which creates unfavorable conditions for the vital activity of pathogenic microorganisms
- Stimulation of the synthesis of B vitamins and vitamin K
- Improving the physiological functions of the gastrointestinal mucosa
- Stimulation of epithelial cell synthesis
- Restoration of disturbed water and electrolyte balance in the lumen of the colon
- Regulation of the processes of secretion of the intestinal mucosa
- Inhibition of intestinal motility
- Improving stool consistency

Dosage regimen: children under 3 years old 15-30 drops, children over 3 years old 20-40 drops, adults 40-60 drops 3 times a day, the duration of treatment is on average 2-4 weeks.

### ***Irritable Bowel Syndrome Constipation Treatment***

In the case of the dominance of constipation in the clinical picture, treatment has two goals: normalizing the consistency of feces and achieving regular bowel movements. Therapy begins with the use of non-drug methods.

With hypomotor dyskinesia of the colon, the diet is built according to the type of "slag load" using dietary fiber. The release of the intestines is facilitated by the use

of foods such as vegetables and fruits, berries, mostly raw (at least 200 g / day), figs, dates, prunes or dried apricots (8-12 berries), bananas and apples, vegetable oil (olive, corn) 1-2 tbsp. tablespoons on an empty stomach, wheat bran (20-60 g per day, add to almost all dishes). They absorb water (1 g of bran binds 18 g of water), contribute to an increase in the number of bacteria in the colon, increasing the mass of feces and, by changing the myoelectric activity of the intestine, balance the propulsive and tonic contractions of the muscles of the colon.

The bran is included in special types of bread - Health, Barvikhinsky, Doktorsky. A daily intake of wheat bran in a daily dose of 30 g shortens the transit time through the colon by 2-3 times.

It should be borne in mind that many patients with IBS do not tolerate cabbage, wheat bran and other foods with a high content of ballast substances, which cause pain and flatulence in them.

Patients should exclude from their diet bread made of high-grade flour, pastry, fatty meats, smoked meats, canned food, spicy dishes, chocolate, strong coffee and tea, limit the use of semolina and rice porridge, noodles, potatoes; products that cause increased gas formation (legumes, cabbage, sorrel, spinach, apple and grape juices) are not recommended, and in case of spastic dyspepsia, also products containing essential oils (turnip, radish, onion, garlic, radish).

It is advisable to drink 1-2 glasses of cold water (or fruit juice) in the morning on an empty stomach with the addition of 1 tbsp. l. honey or xylitol to stimulate the gastrointestinal reflex.

With hypermotor (spastic) dyskinesia of the colon, the diet is more gentle - vegetables are given in boiled form, much attention is paid to vegetable fats. Wheat bran is prescribed in gradually increasing doses (from 2 teaspoons to 3-6 tablespoons), then decreasing, then increasing their amount until the optimal (minimum) dose is established, which will maintain the achieved effect.

Patients with constipation are shown mineral waters. "Essentuki No. 17" is prescribed for constipation with hypomotor dyskinesia, 150-200 ml cold 2-3 times

a day; less mineralized - in the same doses in a warm form, for example, "Essentuki No. 4" with hypermotor dyskinesia.

An equally important task is the drug effect on the motor function of the large intestine. In some doses in a warm form; motor dyskinesia, 150-200 ml in a cold form, 2-3 times a day; less mineralization

Drug therapy is prescribed taking into account the nature of the motor disorders of the colon.

In hypomotor dyskinesia of the colon, preference should be given to prokinetic agents related to 5-HT<sub>4</sub> serotonin receptor agonists. Until recently, the prokinetic cisapride was actively used in the treatment of constipation, but the use of this drug is associated with the development of side effects. Cases of cardiac arrhythmias and sudden death of patients (long QT syndrome) have been described.

Tegaserod is the first of the new generation drugs, an agonist of 5-HT<sub>4</sub> serotonin receptors. By imitating the physiological action of serotonin, tegaserod improves the conduction of nerve impulses in the intestinal wall, normalizing motor activity; it also reduces visceral sensitivity and pain sensitivity, and stimulates the secretion of salt and water into the lumen of the small intestine. It is usually prescribed 6 mg 2 times a day, the duration of treatment is from 4 to 12 weeks.

With spastic dyskinesia, antispasmodics of myotropic action are prescribed, the appointment of anticholinergics (methocinia iodide, pirenzepine) and myotropic antispasmodics (mebeverin, papaverine, drotaverine, pinaveria bromide, meteospazmil, etc.) is justified.

Trimebutin is a drug from the group of endogenous peptides - enkephalins, which act on opioid receptors and restore physiological motor control. Assign 1-2 tablets (100-200 mg) 3 times a day for 3-4 weeks.

Meteospazmil (Alverin and Simethicone) is a low surface pressure polymer that reduces gas in the intestines. The two components of the drug provide a complementary effect on all pathogenetic mechanisms of IBS: they eliminate abdominal pain and flatulence, normalize the frequency and consistency of stools, normalize intestinal motility, and eliminate the transit of gases through the

intestines. Assign 1 capsule 2-3 times a day before meals. The therapeutic effect of the drug becomes especially pronounced approximately 7-10 days after the start of treatment and persists for a long time after the drug is discontinued.

In the complex therapy of constipation, a certain role belongs to drugs with a choleric effect (allochol, chenodeoxycholic and ursodeoxycholic acids).

Compliance with these recommendations often helps to overcome constipation. If this is not achieved, it is necessary to resort to laxatives.

Chronic constipation does not require daily laxatives. It is advisable to prescribe them once every 3-4 days, periodically taking breaks and changing them every 2 years.

There are a large number of laxatives, which, according to the main direction of their effect and the mechanism of action, are conditionally divided into four groups:

- 1) causing chemical irritation of the receptors of the intestinal mucosa: anthraquinones (derivatives of senna, buckthorn, rhubarb, aloe), diphenols (bisacodyl, sodium thiosulfate), castor oil;
- 2) having osmotic properties: salt (sodium or magnesium sulfate, Karlovy Vary salt), disaccharides (lactulose), polyhydric alcohols (mannitol, sorbitol), macrogol;
- 3) increasing the volume of intestinal contents - ballast substances (agar-agar, methylcellulose, bran, flax seed);
- 4) contributing to the softening of feces (liquid paraffin, vaseline oil, macrogol).

Laxatives that stimulate bowel function and do not contain anthraglycosides include bisacodyl (dulcolax) and sodium picosulfate (guttalax).

Bisacodyl (dulcolax) - a diphenylmethane derivative, increases the secretion of mucus in the colon, accelerates and enhances its peristalsis. Available in 5 mg tablets and 10 mg candles. When taken orally, bisacodyl is in an active form already in the stomach, therefore, its intake, especially with an increase in the dose, is accompanied by spastic pain in the upper abdomen. When used in candles, the laxative effect occurs within 1 hour. This form of the drug is used to quickly

cleanse the intestines when preparing a patient for an urgent operation or instrumental examination. Adults are prescribed 1-2 tablets, or 1 suppository 1-2 times a day. The tablets should be swallowed without chewing and washed down with plenty of water.

Sodium picosulfate (guttalax) gives a similar effect. This preparation is a "prodrug". Sodium picosulfate is converted to the active form of diphenol in the lumen of the colon under the action of bacterial enzymes - sulfatases. The mechanism of action is to stimulate the receptors of the colon mucosa, which is accompanied by an increase in peristaltic activity. The laxative effect usually develops 6-12 hours after taking the drug. The usual dose for adults and children over 10 years old is 10-20 drops (for persistent and severe constipation - up to 30 drops), for children 4-10 years old - 5-10 drops. It is advisable to take the drug at night. The most typical situations in which the optimal use of this drug is constipation in patients on bed rest, temporary constipation associated with a change in the nature of food, emotional stress and uncomfortable conditions for defecation ("constipation of travelers"), painful defecation due to pathological processes in the anus (cracks, hemorrhoids). Guttalax is effective in relieving constipation in cancer patients receiving large doses of opioids (used in a dose of 2.5-15 mg / day).

When choosing a laxative, certain tactics should be followed. Treatment should be started with drugs that increase the volume of intestinal contents (fillers and osmotic laxatives). Among these laxatives, macrogol has an advantage, which, even with prolonged use, does not cause side effects. In case of severe hypotension or atony of the intestine, drugs that increase the volume of contents in the intestine should be combined: macrogol with prokinetics or laxatives that cause chemical irritation of the intestine. In this case, individual dosage is necessary (as little as possible, but as much as necessary; avoid diarrhea). Daily intake of motor stimulants is not necessary. It is advisable to take breaks from taking laxatives to determine if the constipation has passed. Thanks to the combination of motility stimulants with drugs,

### ***Irritable Bowel Syndrome Diarrhea Treatment***

Drugs that normalize bowel function in patients with diarrheal IBS include opiate receptor agonists, cholestyramine, 5-HT<sub>3</sub> receptor antagonists, and kappa receptor agonists.

The best drug for the treatment of diarrheal IBS is currently imodium (loperamide). The daily dose of Imodium in the treatment of IBS is selected individually, averaging 2 capsules per day in adults. A promising form of imodium should be considered Imodium Plus, which, in addition to imodium (at a dose of 2 mg), includes simethicone (at a dose of 125 mg), which effectively adsorbs gases in the intestine.

In recent years, psychotherapeutic methods have become increasingly important in the treatment of patients with IBS (including those with diarrheal syndrome). The most widespread among them are hypnotherapy, relaxation therapy (achieving relaxation and reducing muscle activity using special audio and video programs), cognitive-behavioral therapy, aimed at identifying stress factors and modeling the patient's personal reactions to stress, psychodynamic therapy, designed to provide the patient with psychological assistance in solving interpersonal conflicts that can play an unfavorable role in the development of the disease.

With severe autonomic disorders, as well as the identification of neurotic syndromes, psychotropic drugs are also included in the complex treatment of IBS. The drugs are prescribed in accordance with the psychopathological syndrome: asthenia, depression, hysterical syndrome, autonomic dysfunction.

For patients with severe asthenia, autonomic disorders, low mood, general strengthening agents, multivitamins, nootropics (aminalon, piracetam), psychostimulants, including herbal psychostimulating drugs (ginseng, zamaniha, eleutherococcus, lemongrass) are recommended.

If symptoms of anxiety depression are detected, azafen or amitriptyline is used in combination with phenazepam.

With hysterical syndrome, as well as with obsessive fears, nausea, hiccups, vomiting, ethaperazine gives a good effect.

In case of hypochondriac syndrome with increased irritability, fears, anger, depression, climacteric disorders, persistent sleep disorders, Sonapax 5 mg 2-3 times a day is indicated.

The relief of severe autonomic disorders is facilitated by eglonil 50-100 mg 1-2 times a day orally or intramuscularly 2 ml.

In the treatment of patients with diarrheal IBS, antidepressants are increasingly used. The prescription of antidepressants is recognized as a promising direction in the treatment of patients with IBS. Research results have shown that the use of tricyclic antidepressants (doxepin in a daily dose of 75-150 mg) or serotonin reuptake inhibitors (fluvoxamine in a daily dose of 150-200 mg) reduces the severity of complaints in patients with IBS (including manifestations of depression) and potentiates antidiarrheal effect of imodium.

Despite the fact that drug therapy plays an important role in the treatment of patients with IBS, only 30% of patients manage to achieve complete disappearance of symptoms and the onset of remission, in 60% of patients drug therapy can temporarily weaken the manifestations of the disease, and in 10% of patients it is completely ineffective ... Therefore, active development of new, pathogenetically grounded methods of treatment is underway.

One of the most effective is the scheme based on the combined use of food polysaccharides and acupuncture, but in 40% of cases it does not allow to achieve significant improvement. In addition, the positive effect of this therapy is retained for a year in only 48% of patients.

A technique has been developed for the application of sulphide silt mud from Lake Tambukan in the form of rectal tampons with a temperature of 39 ° C and applications of mud to reflex-segmental zones at a temperature of 40-42 ° C. Electric mud procedures (electrophoresis of a mud solution) are considered less stressful, which give about the same therapeutic effect as "pure" mud, but some patients are better tolerated.

Complex treatment of patients with IBS also includes the use of hardware physiotherapy. Inductothermy is an effective method.

There is also a method of treating functional disorders of the large intestine by exposing the brain to a pulsed current of low frequency and low strength - electrosleep. As a result of this effect, changes in the functional state of the central, autonomic nervous and endocrine systems occur. The disadvantage of this method of treatment is not always good electrical sleep tolerance due to increased reactivity of the nervous system in patients with IBS.

Patients with IBS with a predominance of constipation are recommended to have a local impact of IT (interference currents) on the projection area of the large intestine with a frequency of 0-10 Hz, a current of 20-30 mA; for patients with a predominance of diarrhea, it is advisable to recommend transcerebral exposure to IT using the fronto-mastoid technique with a frequency of 90-100 Hz, a current of 20-30 mA. IT, used according to the transcerebral technique, helps to reduce increased autonomic reactivity, improve the psychological state of patients and eliminate pain syndrome; with a local impact on the projection area of the colon, IT optimizes autonomic tone, balances the action of the sympathetic and parasympathetic components of the ANS, and eliminates immune disorders.

IT have pronounced analgesic, myoneurostimulating, antispasmodic, trophic effects; they excite the neuromuscular structures, cause contraction of the smooth muscles of the internal organs; after the procedure, blood supply and tissue trophism improve, there is a normalizing effect on the ANS. In general, under the influence of IT, the intensity of acute pains decreases, the threshold of pain perception rises, and muscle spasm decreases.



