

The role of psychosomatic factors in the formation of diseases of the digestive system

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The mystery of the relationship between psyche and soma is an inexhaustible source of scientific research, in which the knowledge and efforts of specialists of various profiles are integrated for solving specific medical and social problems [5].

The problem of the ratio of "mental" and "somatic" has long been one of the key in medical science. The functioning of the gastrointestinal tract (GIT) system is closely related to the mental state of a person. The general pathology of a person is presented in an abstract form by two kinds of diseases located in the form of a continuum between the poles of mental and somatic disorders. Between these two poles is a clinically polymorphic group of psychosomatic disorders, which, in fact, reflects the real pathology. Modern researchers most often distinguish among psychosomatic disorders psychosomatic reactions and psychosomatic diseases [7].

In the outgoing American psychotherapist and psychoanalyst of Hungarian origin, who became one of the founding fathers of the psychosomatic direction, F. Alexander led a group of psychosomatic diseases, which is now considered a classic [1]. F. Alexander from the 30's. He worked at the University of Chicago, so for this group later, and got the name "Chicago Seven", or "holy seven" — Holy Seven. It has been almost a century, and the Chicago seven still lives in the lexicon of doctors and psychoanalysts. According to F. Alexander in it included:

- 1) Gastric and duodenal ulcers
- 2) Ulcerative colitis
- 3) Neurodermatitis
- 4) Bronchial asthma
- 5) Arterial hypertension
- 6) Hyperfunction of the thyroid gland
- 7) Rheumatoid arthritis

Since that time, much has changed, and the list of psychosomatic diseases has also changed. To date, it has been supplemented and significantly expanded: panic disorders and sleep disorders, oncological diseases, myocardial infarction, irritable bowel syndrome (IBS), sexual disorders, obesity, anorexia nervosa, bulimia — these and many other disorders also have reason to be considered psychosomatic.

Academician A.B. Smulevich (one of the leading scientists and clinicians with a worldwide reputation in the field of psychiatry and psychosomatics) gives the following definition of psychosomatic disorders: "Psychosomatic disorders are a group of disease states that arise on the basis of the interaction of mental and somatic factors and manifested by the somatization of mental disorders, mental disorders that reflect a reaction to a physical disease, or the development of somatic pathology under the influence of psychogenic factors "[6].

There are three types of etiological factors of psychosomatic disorders:

- hereditary-constitutional — personality-typological features with characterological traits of asthenia, hypochondria, hysteroid, depressive, paranoid, etc.;

- psychoemotional, or psychogenic, — acute or chronic external influences affecting the mental sphere: massive (catastrophic), situational acute, situational prolonged, prolonged with persistent mental overexertion (exhausting);

- organic — premorbid organic pathology: prenatal and postnatal injuries, chronic sluggish infections, hypoxic-hypoxemic conditions (especially in the vertebrobasilar basin). In this case, a person is immersed in his illness, and the scope of his mental activity is largely related to the experiences that he feels about this disease.

Psychosomatic disorders include:

- disease with a basic psychosomatic component (peptic ulcer of duodenum, ulcerative colitis, etc.);

- organ neuroses — somatized mental disorders;

- nosogeny — pathological psychogenic reactions to somatic disease;

- somatogeny — mental disorders that occur in a number of serious diseases and are considered in unity with them.

Psychosomatic disorders are the cause of complaints in 36–71% of patients who turn to doctors for violations of the digestive system. However, medical assistance to this contingent of patients at this time is often insufficient. Psychosomatic conditions occurring in the gastroenterological clinic are an actual problem of our time. With diseases of the digestive system, secondary psychopathological manifestations are absent only in 10.3% of patients. Individual, fragmentary asthenic disorders are noted in 22.1% of patients, and in 67.3% — more complex psychopathological conditions [3].

According to ICD-10, the following subgroups are classified as somatoform disorders:

- somatization disorder;

- undifferentiated somatoform disorder;

- hypochondriacal disorder;

- somatoform autonomic dysfunction;

- chronic somatoform pain disorder;

- other somatoform disorders;

- somatoform disorder, unspecified [2].

Gastroenterology is the closest to all therapeutic disciplines due to psychiatry, since the digestive tract is a vulnerable area for the emergence of various psychosomatic diseases. It is believed that the type of people with a special gastrointestinal lability, in which not only a painful experience, but any (positive or negative) emotions impose an appreciable imprint on the functions of the digestive system, is quite common.

Organ neuroses in gastroenterology — functional disorders of the digestive system in combination with borderline mental pathology:

- gastralgia — without a connection with food intake, an obligatory connection with emotional factors and fatigue, is characterized by imagery and distinct objectivity;

- psychogenic nausea and vomiting;

- esophagospasm ;

- com at throat (globus hystericus);

- aerophagia — resistant, paroxysmal, often loud belching of the air;

- psychogenic halitosis — a false sensation of a bad breath from the patient;

- dysgeusia — a neurogenic disorder of taste, which is not dependent on food and does not have an organic nature of bitterness in the mouth;

- glossodynia — a violation of the sensitivity of the tongue, manifested by burning, pressure or pricking in the tongue and surrounding areas;

- psychogenic diarrhea — imperative urges for defecation can occur in the most inappropriate situation with the development of the state of anxious expectation of the recurrence of these phenomena ("bear disease", "diarrhea");

- constipation with a neurogenic component — increased concern for the act of defecation and the emergence of anxiety in the event of its delay, fixing attention on the frequency, quantity and quality of their feces.

In December 2014 on conciliation conference in Rome's new criteria were adopted in the whole in the fall 2015 g — first published. Official presentation of the IV Rome criteria c was held 22 May 2016 on relevant symposium in the 52nd American gastroenterological week (St. San Diego, United States). Completely all materials of the Roman criteria IV are published in large two-volume manual, and main articles — in a specialized issue of the journal Gastroenterology (Vol. 150, No 6, May 2016) [1]. Experts of the Rome IV consensus made changes, for which the results of multiple studies conducted over a period of ten years served. Naturally, in view of the scale of the amendments, a large number of nuances, emphasis was placed on the most significant corrections:

- The term "functional" will no longer sound, since this is the most fundamental "reform" of the very approach to pathology. Now correctly use the following terminology: "violations of cerebro-intestinal interaction." Although it is much more difficult to pronounce this phrase, but it contains the

meaning of the real pathogenesis of arising disorders, the mechanisms that occur in the human body are displayed in more detail.

□ Officially, the involvement of microbes and certain food products in the etiologic factors of the occurrence of cerebro-vascular interaction disorders was confirmed.

□ Hypersensitive reflux is the new official medical term for patients with impaired cerebro-vascular interaction (the nature of functional disorders, with clinical manifestations of heartburn). In addition, now you can use in medical practice such names of syndromes as "chronic nausea syndrome", "chronic vomiting syndrome".

□ Opioid-induced constipation, opioid-induced hyperalgesia, cannabinoid vomiting syndrome — have also been included in new terminology, despite the fact that "functionality of origin" raises some doubts. But, on the other hand, the new sounded approach of "disturbing cerebro-vascular interaction" is much closer in meaning, in cases of using narcotic drugs, rather than "functional disorders".

□ "Violation of the central perception of gastrointestinal pain" replaced the usual "functional abdominal pain."

□ Sphincter of Oddi dysfunction (SD), for the most part, it is now exclude organic pathology, but — still accounts for malformations, enzymatic disorders as the basis of pathology. Changes are also made to the approaches of therapy.

□ From the "irritable bowel syndrome" excluded the concept of "discomfort", which did not convey a diagnostic meaning, and rarely disoriented the patients themselves. Now this concept is meant specifically the pain at the time of e def katsii.

□ "Syndrome of the intersection of functional disorders" — the simultaneous flow of several functional states, or the transition from one to another. Such a term was officially approved, which will greatly facilitate the "medical language" both between colleagues and in a conversation with the patient.

One of the sections presented by the Fourth Rome Criteria is called the "Biopsychosocial Model of Functional Digestive Disorders". It shows that the development of a functional disorder is influenced by genetic factors and the environment, neuropsychiatric disorders and changes in the physiology of the digestive tract (Fig. 1) [9].



Fig. 1. Biopsychosocial model of functional digestive disorders.

Hereditary factors can exert influence in several ways. A genetically determined low level of interleukin-10 (IL-10) in some patients IBS has an effect on the sensitivity of the mucous membrane of the stomach and intestines. Genetic polymorphism of serotonin reuptake enzymes (5-HT — 5-hydroxytryptamine) can alter its level or influence the effect of drugs blocking 5-HT. Genetic polymorphism also affects a specific protein that affects the central nervous system (CNS) and local nervous regulation at the level of the intestine, and $\alpha 2$ -adrenoceptors that affect motor function. At the present time mechanisms of hereditary CNS influence on functional gastrointestinal disorders (FGID) are being studied [10].

Psychosocial factors are not criteria for diagnosing FGID, but they affect the axis "brain-gut", determine the patient's behavior and, ultimately, clinical features. There are four main areas of influence of psychosocial factors:

Psychological stress exacerbates symptoms usually FGID and rarely causes a similar volume in previously healthy people.

Psychosocial factors change the patient's behavior, which is manifested by increased appeal for medical help. Although patients with FFRC, unlike those with functional pathology, present many complaints and are concerned about their health, the results of their examination are within reference values.

FGID have psychosocial consequences. Chronic pathology, long unpleasant sensations and pains reduce the patient's working capacity and quality of life, complicate their interpersonal relationships in the family and at work.

Psychosocial impact on the disease, namely emotional distress and inadequate consciousness, leads by feedback mechanism to the strengthening and strengthening of symptoms. Patients with severe symptoms begin to show painful pessimism, catastrophism, hypervigilance (increased attention to unpleasant sensations), anxiety for their inner sensations, the threshold of pain perception decreases, self-esteem becomes understated. In such cases it is required behavioral (direction in the psychology of man and animals, literally — the science of behavior) intervention.

Motor disorders are not able to explain the occurrence of a number of symptoms of FGID: functional pain in the chest, probably associated with the esophagus, epigastric pain syndrome, IBS, functional abdominal pain syndrome (SFAB).

Visceral hypersensitivity (hypersensitivity) allows to explain such manifestations of FGID. Such patients have a low pain threshold of sensitivity (visceral hyperalgesia), which is proved with balloon stretching of the bowel, or have increased sensitivity (allodynia). Visceral hypersensitivity may gradually increase in patients with FGID and in this case is called sensitization, or increased pain sensitivity to repeated stimuli. In this case, repeated inflating of the balloon in the gut causes a progressive increase in pain. Hypersensitivity and sensitization may result from damage to the receptors of the sensitivity of the intestinal mucosa and the muscle-intestinal plexus resulting from inflammation. Another possible cause is degranulation mast cells that are closely related to the intestinal nerves, or an increase in serotonin activity, which may be due to exposure to a bacterial flora or pathological infection. It is possible to increase excitability as a result of central sensitization. As a result, the mechanism of central inhibitory regulation of visceral afferent impulses, which under normal conditions reduces pain, can be violated.

Immune dysregulation, inflammation and violation of barrier function may contribute to the onset of symptoms, but only in recent years it has been shown that in half of IBS patients the activity of inflammatory CO and proinflammatory cells cytokines. In connection with studies of postinfection IBS and functional dyspepsia (FD), interest has increased in the permeability of the intestinal membrane in places of tight joints, intestinal flora and impaired immune function. This is consistent with the data that a third of patients with IBS or dyspepsia associate the onset of the disease with acute intestinal infection.

The role of the disturbance of the bacterial flora of the intestine in the appearance of the FGID requires further study. There is evidence that in response to the administration of *Bifidobacter infantis*, the initial IL-10 / IL-12 ratio, which is characteristic for the presence of an inflammatory response and which occurs in IBS, is normalized. These data are supported by a moderate positive effect of probiotics and antibiotics on symptoms in IBS. FGID depend on food, diet, which in turn is on and yayut intracolonic microflora.

There are bi-directional interactions of the "brain-gut" axis. External influences (appearance, smell), as well as internal perceptions (emotions, thoughts) through the central nervous system (CNS) and other parts of the brain affect gastrointestinal sensitivity, motility, secretion and inflammation. In

turn, viscerotopic effects are perceived by the brain and have an effect on the sensation of pain, mood and behavior of a person. Positron emission tomography, functional magnetic resonance imaging and other brain research methods have established a connection between the expansion of the intestine and the activity of certain parts of the brain, and the results in patients with IBS differed from those in the control group of healthy people. Currently, the treatment of patients with FGID is often based on the effect on the same enteral and central brain receptors. The actives include 5-HT and its derivatives, enkephalins, opioids agonists, substance P, calcitonin gene-dependent polypeptide, cholecystokinin, corticotropin-p antagonists and hormone leasing.

Ways to treatment, proposed by the Fourth Rome criteria. Twelve steps to reach a patient:

The patient should be satisfied with his doctor. Positive perception of the patient's physicians is based on his medical humanism, professional competence, interest in the psychosocial factors that led to the disease. It is necessary to look for the root causes of the disorder. The information that the physician represents must be reliable, accessible and not overloaded with special medical terms. Communication with the patient should include non-verbal contacts from the physician: a confidential eye-to-eye view, a soft and gentle tone of voice. With the patient there should be trusting, intimate, partner interpersonal relationships, the patient should be with the doctor on one side of the barricade.

Collect an anamnesis without a directive and instructive attitude. The focus should be on the patient, his thoughts, feelings and impressions.

Determine the immediate cause of this patient's treatment. Assess verbal and non-verbal information from the patient. The following possible reasons for direct treatment should be established:

- a) the emergence of new or increased factors (changes in diet, the appearance of other diseases, side effects from new drugs);
- b) personal problems or stressful situations in the family (death of a loved one or other grief, abuse of alcohol, drugs, etc.);
- c) strengthening and the emergence of mental disorders (anxiety, depression);
- d) difficulties with the implementation of current work;
- e) hidden causes (abuse of drugs or laxatives, litigation or claims for disability).

4. It is necessary to carry out the research carefully, taking into account its informativeness, cost and effectiveness. A well-conducted study has a therapeutic effect.

5. Determine how sick a sign is with the nature of your disease.

6. Find out how the patient understands his symptoms (illness chart), and explain them thoroughly, taking into account the patient's opinion.

7. Determine what the patient expects from the treatment, and explain its possibilities.

8. Demonstrate the relationship of the disease between stress factors and symptoms that correspond to the patient's views. Many patients can not or do not tend to associate stressors with the disease, but most patients understand that the progression of the disease affects their emotional status.

9. Set solid limits in the treatment of the disease.

10. Involve the patient in the process of treatment, let the patient understand that the result of treatment largely depends on him.

11. Give recommendations that are in the interests of the patient.

12. Help the patient establish a relationship with you or with a family doctor.

It is recommended to treat the disease taking into account the degree of its severity. Patients with mild symptoms may not seek medical help or turn to a family (district) doctor. Such patients are about 40%. The clinical picture in them mainly includes manifestations of gastrointestinal dysfunction (vomiting, diarrhea, constipation, etc.), minimal or minor pain, no comorbid pathology, no mental disorders. The quality of life suffers insignificantly. Patients lead a normal lifestyle. Treatment should be conducted in the following areas:

Education. The patient should explain that FGID is a disease that reacts excessively to all kinds of food changes, hormonal profile, drugs and stressful effects. Pain occurs due to spasm or stretching of the bowel, which is excessively sensitive. Violation of the motor function of the gut leads not only to pain, but also to a number of other symptoms: nausea, vomiting, diarrhea. The physician should emphasize that both physiological and psychological factors contribute to the development of symptoms that disturb the patient.

Reassurance. The physician should eliminate the patient's concern and concern and instill confidence in the result of treatment and a favorable prognosis of the disease. It should be borne in mind that if the doctor does this hurriedly, after a superficial survey and examination, without obtaining the results of various studies, the patient may not accept the recommendation.

Diet and medicine. Food that causes pain and discomfort (for example, sweets, coffee, fatty foods, alcohol), as well as medicines with a similar effect, should be "calculated" and, if possible, eliminated. In IBS recommended FODMAP restricted diet products causing fermentation oligoo-, di-, monosaccharides and polyols. It is often enough to follow dietary recommendations.

Moderate symptoms. Only a small part of these patients seek primary medical or specialized gastroenterological care with mild symptoms, resulting in a periodic decline in social activity. As a result, such patients are 30–35% of the total number of patients with FGID. Patients may note a close relationship of the onset of symptoms with dietary errors, travel or overexertion. Moderate abdominal pain and psychological distress in this group of patients is more pronounced than in the group with mild symptoms. Patients with moderate symptoms have comorbid somatic, neurological or psychiatric problems and seek help from various specialists. These patients p It is recommended to following th tactics:

Monitoring of symptoms. The patient should keep a diary for 1 to 2 weeks, in which time and severity of symptoms should be recorded, as well as possible provoking factors. The diary can help to identify them. The doctor can analyze the diary and identify dietary and psychosocial factors that

provoke an increase in symptoms. Such keeping a diary involves the patient in the process of treatment and, with the improvement, increases the confidence in successful control of the disease.

Symptomatic pharmacotherapy. Treat for symptoms that lead to distress or disrupt daily work. The choice of the drug is determined by the main symptoms. In general, medicines should be considered as an addition to the diet and lifestyle, and their appointment should be carried out with exacerbation of the disease.

Psychotherapy. Psychotherapy should be administered to patients with moderate or severe gastrointestinal manifestations of the disease and with pain. Psychotherapy is most effective in the connection of increased symptomatology under the influence of stress factors. Psychotherapy includes the following options: cognitive-behavioral therapy, relaxation, hypnosis and combined techniques. Psychotherapy can reduce anxiety, maintain a healthy lifestyle, increase the responsibility and control of the patient for treatment, and increases tolerance to pain.

Severe symptomatology. Only a small proportion of FGID patients have severe or symptom-resistant symptoms. Such patients usually have psychosocial disorders, including fear, personality disorders, as a result of which their performance is impaired. At least 10% of these patients are not able to work, as before the onset of the disease. Sometimes this is preceded by the loss of loved ones or acts of violence, poor social or psychological adaptation, strong emotional upheavals. These patients often turn to the gastroenterologist and want to "cure" their numerous disorders. They may reject the role of psychosocial factors in their illness and are often resistant to psychotherapy or pharmacotherapy aimed at eliminating gastrointestinal symptoms, or have a strong protest against treatment.

Development of tactics of treatment. Such patients need a long-term follow-up of a physician (gastroenterologist or therapist, general practitioner) for periodic short visits. In general, a physician should: 1) carry out diagnostic studies and objective treatment-based medical measures before the patient begins to demand them; 2) establish a realistic goal of treatment, for example, improving the quality of life, rather than completely eliminating pain or cure; 3) to share the responsibility for the result of treatment with the patient, involving him in this process; 4) shift the center of gravity of the goal of treatment from cure to existence with a chronic disease.

Referral to the center for pain management. In this center, specialists of various specialties carry out rehabilitation of the most serious patients

Treatment with antidepressants. Tricyclic antidepressants (TCAs), for example, desipramine and amitriptyline, and newer serotonin and noradrenaline reuptake inhibitors (SSRIs) are important in controlling pain through central analgesia, as well as a reduction in associated depressive symptoms. Selective serotonin reuptake inhibitors (SSRIs) may play an auxiliary role, they are less effective for the treatment of pain, but can reduce associated anxiety and depression. Antidepressants should be given to patients with chronic pain and reduced performance, concomitant symptoms of large, somatoform or masked depression, symptoms of anxiety or panic attacks. Even without depressive symptoms, these

drugs can help if the pain dominates or is the main problem. A poor clinical effect may be the result of an inadequate or incorrectly selected dose, taking into account the therapeutic and side effects. The duration of treatment should be at least 3–4 weeks. When the effect is obtained, treatment lasts for up to a year, and then the dose gradually decreases [4].

Now in the arsenal of the doctor there are more than 500 psychotropic drugs. For successful therapy of psychosomatic disorders, the drug must meet the following requirements:

- have a wide range of psychotropic activities, effectively affect anxious, phobic, affective (depressive), hypochondriacal, somatovegetative symptoms;
- have a limited number of side effects with minimal negative impact on mental activity and physical functions;
- to cause positive somatotropic effects (therapeutic effect on concomitant somatic pathology);
- have minimal behavioral toxicity (minor or no sedation — drowsiness throughout the day, disturbance of concentration and attention, etc.);
- minimally interact with drugs of somatotropic action.

TCAAs cause excitation of central and peripheral adrenergic receptors. Selective inhibitors of norepinephrine reuptake (mianserin) exert a selective effect on one of the subtypes of noradrenergic receptors — alpha-2-adrenergic receptors. MAO inhibitors block monoamine oxidase, which causes oxidative deamination and inactivation of monoamines (noradrenaline, dopamine, serotonin), with their accumulation in the structures of the brain. Selective serotonin reuptake inhibitors (SSRIs) slow down the re-entry of serotonin from the synaptic cleft into the interior of the presynaptic neuron. In contrast, selective serotonin reuptake stimulators facilitate the capture of serotonin. By double-acting antidepressants, providing the desired effect due to the potentiation of synaptic transmission in the two neurotransmitter systems include selective inhibitors of the reuptake of norepinephrine and serotonin and noradrenergic selective serotonergic antidepressants. Common indications for the use of antidepressants are depressive disorder (dysthymia; psychogenic, symptomatic, organic and somatogenic depression, depression associated with the use of psychoactive substances; depression associated with the female reproductive cycle), anxious-depressive disorders, anxiety and phobic disorders (panic disorder, social phobia). In addition, this list also includes obsessive-compulsive disorders, somatoform and psychosomatic disorders, eating disorders (anorexia nervosa and bulimia nervosa).

The main indications for the appointment of antidepressants in gastroenterology are functional disorders of the digestive tract, chronic diffuse liver diseases, persistent pain syndrome in chronic pancreatitis, obesity, eating disorders. Two recent reviews have once again demonstrated the effectiveness of psychotropic drugs in functional GIT diseases.

Nicholas J. Talley et al. conducted a multicenter, randomized, placebo-controlled study in which antidepressants were used for 12 weeks in patients with FD. Therapy with amitriptyline or escitalopram was more effective than placebo in alleviating the symptoms of FD and in improving the quality of life. According to the analysis protocol, the response rate was highest in amitriptyline: 38 (52%) in the placebo group, 47 (66%) for amitriptyline, and 32 (52%) for escitalopram ($p = 0.09$). Patients who took amitriptyline had greater chances for adequate relief than those who received placebo (OR = 2.1 [95% CI: 1.04-4.36], $p = 0.04$) [11].

Alexander C. Ford et al. made a systematic review and meta-analysis which showed that, psychotropic drugs are more effective than placebo for treating FD. However, this beneficial effect was limited to antipsychotic drugs such as sulpiride and levosulpiride, as well as TCAs such as amitriptyline and imipramine. This review suggests encourage gastroenterologists proper use of these funds and stimulate further RCTs in this field [12].

Thus, psychosomatic disorders in gastroenterological practice are often encountered. They are accompanied by pain and motor sensations. Visceral pain and motor-evacuation disorders of the gastrointestinal tract is a common symptom of functional gastrointestinal disorders, which have a multifactorial etiology. Many patients with these diseases have comorbid behavioral disorders, such as anxiety or depression, and FGID are described as a disorder of the GIT tract-brain axis. Stress is involved in the development and exacerbation of visceral pain disorders. Chronic stress can change the central pattern of pain, as well as the change in motility and permeability in the gastrointestinal tract. Recently, the role of intestinal microflora in bi-directional communication along the axis of the intestine of the brain and subsequent changes in the behavior of patients has been proved. With stress and intestinal microflora can interact through complementary or opposite factors, affect visceral nociceptive relationships. The purpose of multidirectional treatment in FGID should include psychotropic drugs and groups of somatic antipsychotics and antidepressants. The most significant evidence base among these drugs is amitriptyline.

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Psychosomatic disorders are frequent in gastroenterological practice. Visceral pain and motor-evacuation disorders of the gastrointestinal tract is a common symptom of functional gastrointestinal disorders which have a multifactorial etiology. Many patients with these diseases have comorbid behavioral disorders, such as anxiety or depression, and functional gastrointestinal disorders are described as disorders of the “gastrointestinal tract-brain” axis. Chronic stress can change the central pattern of pain, as well as motor activity and permeability of the gastrointestinal tract. The multidirectional treatment for these diseases should include psychotropic drugs and groups of somatic antipsychotics and antidepressants.