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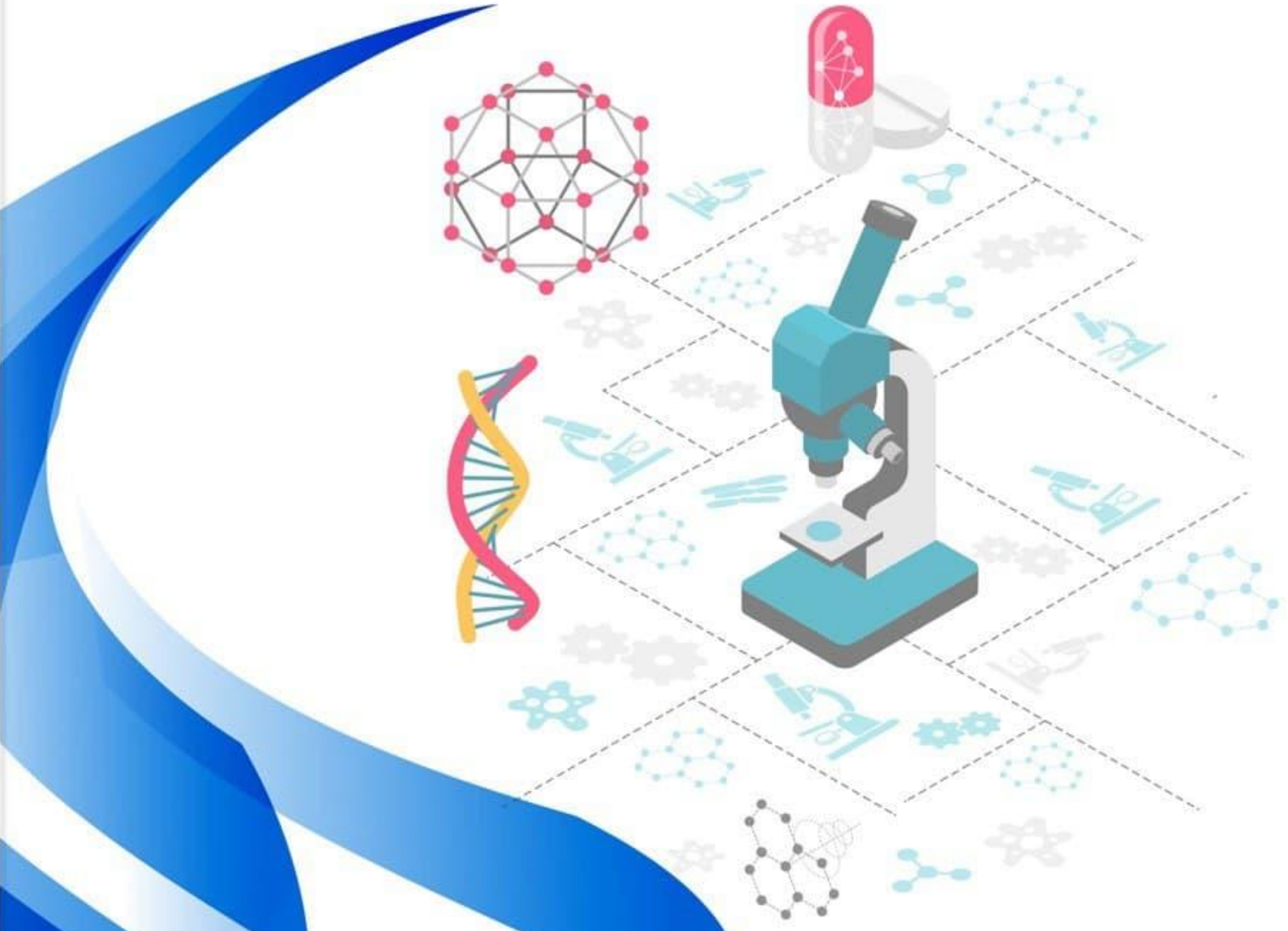

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Features of etiopathogenesis, clinical diagnostic criteria of gastroesophageal reflux disease and its pulmonary manifestations

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Summary. Gastroesophageal reflux disease is one of the most common diseases in modern medicine. A characteristic feature of this disease is that, along with the main symptoms (heartburn, pain behind the sternum and / or in the epigastric region), there may be secondary symptoms associated with impaired motility of the upper gastrointestinal tract, including the esophagus, and / or hypersensitivity stomach to distension (feeling of heaviness, fullness, bloating and rapid satiety in the epigastric region that occurs during or after eating), as well as extraesophageal (atypical) symptoms that aggravate the condition of patients with bronchopulmonary lesions, including asthma, as well as patients suffering from laryngitis, sinusitis and other ailments that worsen the quality of life. The article highlights the features of pathogenesis,

Keywords: gastroesophageal reflux, bronchial obstruction, bronchial asthma, reflux, bronchodilators.

Relevance. Gastroesophageal reflux disease (GERD) is a chronic, relapsing disease caused by the presence of pathological reflux from the duodeno-gastric zone to the upper digestive tract with or without esophagitis. GERD is one of the most common pathologies of the gastrointestinal tract [3].

Suppose. To study the scientific literature on the etiology, pathogenesis, course and treatment of bronchopulmonary manifestations of GERD, as well as in comorbid conditions of GERD and BA.

Currently, GERD is considered as a chronic, most common acid-dependent disease with a high level of recurrence, which is based on various factors (impaired motor function of the esophagus and stomach, prolonged and recurrent effects of gastric and duodenal contents on the mucosa of the esophagus, neurotrophic and humoral disorders), leading to the appearance of inflammatory and degenerative lesions of the esophagus [6, 7].

GERD is the most common disease of the esophagus. According to some reports, GERD affects about 20% of the population. 50% of the population is prone to heartburn at least once a month and 5-7% of the population is prone to it every day. According to studies, 59% of 10491 examined patients with BA are subject to typical symptoms of GERD, however, the primacy of GERD or BA in this conosology remains not fully understood. [2].

The prevalence of GERD in Russia varies from 11.3 to 23.6%[14] In recent years, the prevalence of GERD has been steadily increasing, it has received the greatest distribution in Western Europe and North America. The prevalence of GERD

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in the population varies in the range of 18-40%. According to the large ProGERD study, 4.8% of patients with GERD also have asthma. Another study provides evidence that AD is the 3rd most common extraesophageal manifestation of GERD (9.3%) [4].

Bronchial asthma is a chronic inflammatory disease of the upper respiratory tract caused by bronchial hyperreactivity and manifested by typical symptoms. According to the Ministry of Health of Russia, there is an increase in the incidence of asthma by more than 30%. The relationship between GERD and asthma has been studied for quite a long time; the first studies were carried out in 1892, when an asthma attack was recorded after eating. Further observations showed that the combination of these pathologies is observed in 34-89% of patients, while in 24% of cases reflux is not clinically detected. Most of these patients have a hiatal hernia. The quality of life of this group of patients is reduced by 30-50%. [20]

According to research by Vorotnikova et al. in the examined groups of patients, broncho-obstructive syndrome is combined on average in 43.9% of cases with GERD: with BA - in 75.3%, with pneumonia in 53%, with obstructive bronchitis in 51.5% of cases. In severe BA, GERD was detected 3.4 times more often in boys, with a prolonged course of pneumonia with biofeedback, 1.9 times more often in girls. Inflammatory diseases of the digestive system (gastritis, gastroduodenitis) in BA were detected in 40.6% of patients. In the combined course of BOS and GERD, the aggravated premorbid background in children was: preeclampsia (31.8%), threatened miscarriage (20.8%), intrauterine hypoxia of the fetus (22.2%), violation of the diet and day of the child (45.7%).[10]]

Patients with overweight and obesity are more prone to transient relaxation of the LES muscles, and the esophageal mucosa of such patients is exposed to reflux for a longer time. As a result of the study, extraesophageal symptoms of GERD more often prevail in such patients [27]

In international literature, there is such a term as laryngopharyngeal reflux (LFR), although the concept itself does not reflect the full picture of the disease, since it essentially means a non-existent reflux from the larynx to the pharynx, but this abbreviation has become part of the practice of many doctors. LPR is considered as a pathological condition, which is reflected by inflammation of the mucous membrane of the upper respiratory tract and gastrointestinal tract, due to direct and indirect effects of gastroduodenal refluxate, which can provoke changes in the mucous membranes. There are two theories of LPR - reflux and reflex.

The reflux theory assumes a direct effect of refluxate (hydrochloric acid, pepsin, etc.) on the pharyngeal and laryngeal epithelium.

The reflex theory suggests stimulation of the vagus nerve and laryngeal chemoreflex due to afferent stimulation of the superior laryngeal nerve.

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Data on the clinical interaction of GERD and AD are ambiguous. There is information that the frequency of asthma attacks in patients with GERD is the same as in patients without it, but the frequency of nighttime attacks with a combination of these pathologies is an order of magnitude higher. Arame et al (2010) believe that GER is not only a trigger for asthma attacks, but also one of the pathogenetic links in the development of asthma in children. According to the study by Apenchenko et al (2018), children with a combination of BA and GER show a less burdened heredity for BA, as well as a lower sensitivity of scratch tests to household allergens, which indicates a mixed nature of BA in such children. The severity of the clinic of respiratory failure and bronchial obstruction is more susceptible to children with a combination of asthma and GERD compared to children without GERD.[5]

However, the theory of the reverse effect of respiratory tract pathologies on the upper digestive tract remains doubtful. However, there is evidence that damage to the upper respiratory tract can lead to a decrease in the tone of the lower esophageal sphincter, contributing to the onset or progression of GERD. At the heart of this is a lack of coordination between breathing and swallowing. Such conditions are usually observed in patients with chronic lung diseases. However, in such cases, patients swallow during or before inspiration, which increases the risk of aspiration. Also, hypoxia and the load on the respiratory muscles in CLD leads to a decrease in intrathoracic and an increase in intra-abdominal pressure, which in turn leads to the development of GERD. It is known that patients receiving chronic asthma therapy develop symptoms of GERD over time. Anti-asthma drugs such as theophyllines, sympathomimetics lower the tone of the CHD and LES, provoking the development or worsening of GERD, which in turn negatively affects the level of bronchial obstruction, forming a vicious circle.[24]

There are several additional factors that provoke the development of GERD against the background of BA:

- Cough - can cause reflex relaxation of the LES

- Displacement of the legs of the diaphragm - the legs of the diaphragm are involved in the formation of the esophageal-gastric barrier, which is caused by pulmonary hyperinflation. Dysfunction of the legs of the diaphragm appears with a strained cough and asthma attacks, which provokes relaxation of the LES.

- Hernia of the esophageal opening of the diaphragm is another provocateur of GERD and occurs in patients with BA more often than in healthy people. E. Mays et al. revealed the presence of HH in 64% of patients suffering from BA and 19% in the control group. S. Sontag et al. revealed HH in 58% of persons suffering from BA.

- Lifestyle and food culture - S.Sontag et al. It was noted that in 60% of patients with asthma and 44% of patients in the control group who took food before bed, there was anxiety and awakening due to the onset of symptoms of GER [30]

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In a study conducted in asthmatic patients with GERD, direct pH was evaluated, where it was noted that 119 of 151 (78.8%) cases of asthma symptoms and 76 of 84 (90.5%) cough episodes were associated with reflux. The etiology of the combination of these pathologies lies in the common origin of the esophagus and bronchial tree during embryogenesis, as well as the common innervation by the vagus nerve [8].

Thus, taking into account the above, we can conclude that there is a strong relationship between GERD and AD.

Clinical manifestations of gastroesophageal reflux disease (GERD) are quite numerous. According to studies, GERD as an independent disease is quite rare, often accompanied by such diseases as coronary heart disease, diabetes mellitus, COPD, diseases of the gastrointestinal tract, etc., which makes its timely diagnosis quite difficult. GERD is one of the most common pathologies in the structure of diseases of the gastrointestinal tract, but the negotiability of patients is less than 1/3 of cases. Gastroesophageal reflux, the throwing of stomach contents into the esophagus, is a physiological phenomenon that occurs periodically in healthy people, for example, when changing body position or when eating a large meal. The threshold value for the occurrence of episodes of GER is up to 50 times a day, lasting no more than 1 hour. [23,17].

Clinically, manifestations of GERD are divided into esophageal (typical) and extraesophageal. Esophageal manifestations of GERD include: heartburn, belching, feeling of a lump in the throat, difficulty swallowing, pain when swallowing, pain in the epigastrium and behind the sternum, nausea, bitterness in the mouth, hiccups, vomiting, etc. [thirteen]

Extraesophageal manifestations include:

1.Bronchopulmonary (cough, shortness of breath, suffocation, respiratory failure)

2. ENT syndromes (pain in the throat and ears, hoarseness and loss of voice);

3. Cardiological (retrosternal pain);

4.Dental (stomatitis, gingivitis, tooth enamel erosion)

5. Anemic (hypochromic IDA)

6. Abdominal (feeling of rapid satiety, heaviness, flatulence). [fifteen]

In our time, the classic manifestations of GERD are fading into the background and more and more patients with extraesophageal symptoms are encountered. In patients with GERD, with untimely treatment, aspiration pneumonia, bronchial asthma, and COPD may develop. In a survey conducted by Ermolenko et al. The main complaints presented by the patients were belching, choking after eating, pain and heaviness in the epigastric region, dysphagia, nausea, cough and shortness of breath. [eleven]

Kryukov et al. cite a clear clinical case in which the patient for many years was worried about the typical symptoms of GERD, to which the patient did not pay

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attention and was not treated. Erosive esophagitis was diagnosed on endoscopy. After some time, the typical complaints were joined by shortness of breath, dry paroxysmal cough. The patient consulted a pulmonologist. Treatment of BA did not show the desired effect. After that, the patient was referred to a gastroenterologist, where a connection between reflux and AD symptoms was established [21].

In a study by Rustamova et al. 150 patients with BA II-IV severity were examined. According to the study, against the background of BA, most patients did not pay attention to malaise from gastroenterological diseases. With a deeper questioning, epigastric pain and / or belching was observed in 60% of patients, a sensation of a lump in the throat and belching in 50%, nausea in 40% of patients. Also, BA patients with endoscopically confirmed pathology of the digestive tract have 3 or more gastroenterological symptoms. [26]

There is evidence of an association between the severity of symptoms in patients with asthma and the presence of GERD. So, in the presence of reflux esophagitis, the course of BA is more severe than in patients with endoscopic absence of esophagitis. The most common symptoms are belching, chest pain, heartburn, drooling during sleep, heartburn, and coughing. [28]

In the article by Asadullaeva et al. data of examination of 104 patients with GERD are given. Patient complaints were studied. Among them were: belching with air (86.7%), belching with sour (78.8%), heartburn (76.9%), epigastric pain (62.5%), burning sensation behind the sternum and pain (70.1 %), difficulty swallowing (25%), nausea (19.2%) cough (26.9%), burning sensation in the mouth (8.6%), constipation (61.5%), desire to clear the throat (24%) , nocturnal cough (11.5%) hoarseness (9.6%). At the same time, the connection of these complaints with other concomitant pathologies of the gastrointestinal tract, cardiovascular system and the respiratory system. There were also symptoms atypical for GERD, such as shortness of breath (36.5%) and headaches (26.9%). The authors explain the low incidence of symptoms such as cough and bitterness in the mouth by the fact that they occur more often in more advanced stages of the disease, and the subjects apparently suffered from milder stages.

Diagnosis of gastroesophageal reflux disease (GERD) is carried out on the basis of complaints, data from laboratory and instrumental research methods.

For the diagnosis of GERD, the GerdQ questionnaire is used - a questionnaire for therapists and primary care workers. The questionnaire consists of 6 questions and 3 groups. Complaints are evaluated for the last week before the survey (Table 1).

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BUT.	**1. How often do you feel heartburn (burning in the chest)?**			
	0 days(0 points)	1 day(1 point)	2-3 days(2 points)	4-7 days(3 points)
	2. How often have you noted that the contents of the stomach (liquid or food) again enter the pharynx or oral cavity (belching)?			
	0 days(0 points)	1 day(1 point)	2-3 days(2 points)	4-7 days(3 points)
AT.	**3. How often did you feel pain in the center of your upper abdomen?**			
	0 days(3 points)	1 day(2 points)	2-3 days(1 point)	4-7 days(0 points)
	4. How often did you feel nauseous?			
	0 days(3 points)	1 day(2 points)	2-3 days(1 point)	4-7 days(0 points)
WITH.	**5. How often did heartburn and/or belching prevent you from getting a good night's sleep?**			
	0 days(0 points)	1 day(1 point)	2-3 days(2 points)	4-7 days(3 points)
	6. How often for heartburn and/or belching did you additionally take other medications other than those recommended by your doctor?			
	0 days(0 points)	1 day(1 point)	2-3 days(2 points)	4-7 days(3 points)

Table 1

With a score of 8 or more, the diagnosis of GERD is established, and the patient is referred to a specialist.

Group C is evaluated separately, as it strongly affects the patient's quality of life. A score greater than 3 is assessed as severe GERD, less than 3 as moderate GERD. With a score of 8-10, the probability of developing erosive esophagitis is 48.5%, from 11 to 18 points - 60.7%. The questionnaire cannot be the only diagnostic method and has a reliability of about 60-70%.[one]. It is also claimed that this questionnaire is not effective in relation to GER with low acidity or its absence [12].

Laboratory studies include a clinical blood test (increase in leukocytes with a shift to the left, acceleration of ESR), biochemical tests (C-reactive protein, fibrinogen) and sputum analysis (change in color, viscosity, increase in leukocytes, the presence of pathogenic flora). However, laboratory tests are not highly effective in diagnosing GERD.

Of the endoscopic methods, esophagastroduodenoscopy is effective. With EFGDS, cardial insufficiency, erosive esophagitis, mainly in the lower third of the esophagus, as well as pathological gastroesophageal reflux, can be detected. There is also the possibility of diagnosing Barrett's esophagus and hiatal hernia.

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The "gold" standard in the diagnosis of GER is the daily pH-metry of the esophagus. This technique allows you to assess the pH level in the esophagus, its deviations from the norm, the duration of GER and the degree of change in the esophageal mucosa. The advantage of this method is the possibility of its implementation both in stationary and outpatient conditions. [eighteen]. According to some authors, 24-hour pH-metry in patients with BA should be carried out carefully and with preliminary preparation of the subjects, since the introduction of the probe in some cases can provoke asthma attacks. Therefore, it is recommended to carry out the procedure during the period of complete remission; for some patients, it is possible to consult a psychologist before the procedure [16]. The disadvantages of daily pH metering are low sensitivity to weakly acidic and non-acidic refluxes. For diagnosis in such cases, the method of pH-impedancemetry is used. Its sensitivity is 98.8% and specificity is 97.9%. [29]. Currently, the "gold standard" is considered to be 24-hour multichannel intraluminal impedancemetry (CMIM). The method allows assessing the genesis of esophageal manifestations and making or refuting the diagnosis of GERD, as well as prescribing timely treatment. [nineteen]

In addition to these methods, contrast fluoroscopy of the esophagus is also informative, which allows you to indirectly diagnose reflux and differentiate it from other organic diseases of the esophagus.

Diagnosis of GERD associated with AD presents some difficulties. To assess the severity of asthma, spirometry is used to determine FEV1, vital capacity, instantaneous volumetric velocity in% of VC (MOS25, MOS50, MOS75), peak flowmetry, bronchoscopy, etc. In studies conducted by Pozdnyakova et al. 70 hormone-dependent and non-hormone-dependent patients with BA were examined by the above methods. The authors noted a high association between asthma attacks and episodes of acid reflux. Patients with a combination of GERD and asthma have worse esophageal peristalsis and a low antireflux barrier. There was also a dependence of the severity of the lesion of the esophagus on the indicators of the assessment of respiratory function (FEV1, MOS25, MOS50, MOS75).[25]

The approach to the treatment of GERD in combination with respiratory manifestations should be carried out comprehensively and carefully.

Treatment of GERD in patients with BA includes the addition of antisecretory drugs, prokinetics, and antacids to the basic therapy of BA.

Numerous studies have noted an improvement in the quality of life of BA patients with concomitant GERD. In addition to a significant reduction in nocturnal seizures, there is also a positive trend in external respiration [7]

Burkov et al. conducted a study among 162 patients with AD. 86 patients were diagnosed with GERD. 41 of them experienced nocturnal asthma attacks. In the first group of 28 people, in addition to the basic therapy for BA, antisecretory therapy with PPI-Ultop (Omeprazole) 40 mg was performed for 28 days. The remaining 13

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people did not receive Ultop, they received only symptomatic treatment with antacids on demand. In the first group, a decrease in GERD symptoms by day 7 was noted in 19 patients, and by day 28 in 26 patients. Daytime asthma attacks decreased by 24.1%, and nighttime attacks by 51.9%. Changes in the second group of subjects were insignificant. [nine]

Antireflux therapy significantly reduces the severity of asthma symptoms, reduces the need for bronchodilators, and improves respiratory function parameters according to spirography and peak flowmetry. If Helicobacter pylori infection is detected in patients with GERD and BA, it is possible to carry out anti-Helicobacter therapy with two anti-Helicobacter pylori drugs, since the presence of Helicobacter pylori aggravates the course of BA. But at the same time, the penicillin series of antibiotics should be used with caution. The drugs of choice are macrolides, tetracyclines, metronidazole, bismuth preparations [11–13].

It is a bidirectional, integrated approach that gives results in the introduction of this group of patients. Achieving remission during GERD leads to control of asthma.

Conclusion. Thus, gastroesophageal reflux disease with respiratory syndrome is an urgent problem of modern medicine, often detected at the late stages of the disease and requires a careful approach in early diagnosis and complex treatment.

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