Chronic obstructive pulmonary disease

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ABSTRACT

Over the past 15-20 years, there has been a significant increase in the incidence of chronic obstructive pulmonary disease (COPD) in various countries of the world. At the same time, a situation has arisen when practitioners and specialists dealing with the problem of COPD know more about how to treat this disease than about what is the point of investing in the very concept of COPD. This disease is characterized by incompletely reversible airflow limitation. This limitation is usually progressive and is associated with an abnormal reaction of the lungs to pathogenic particles and gases.

Keywords: Smoking, Obstructive Bronchitis, Complications, Men.

Until recently, the abbreviation COPD was deciphered as “chronic obstructive pulmonary disease” and was interpreted as a collective concept that includes chronic environmentally mediated diseases of the respiratory system with predominant involvement of the distal respiratory tract with partially reversible bronchial obstruction, characterized by progression and increasing chronic respiratory failure. According to the first edition of the federal program, COPD is a group of pulmonary diseases, heterogeneous in nature, which are united by an obstructive type of respiratory function disorder[9]. It defines COPD as “...a disease characterized by partially irreversible airflow limitation. Epidemiology. According to the WHO, the prevalence of COPD among men is 9.34:1000 , among women - 7.33:1000, among patients, people over 40 years of age predominate. In Uzbekistan, there are about 1 million patients with COPD (official statistics), but in reality their number may exceed 11 million people (data from epidemiological studies)[3,5]. In the total sample, COPD was detected in 14.49% of 2063 examined men and women, without division by sex (30-39 years old - 10.76%, 40-49 years old - 10.89%, 50-59 years old - 15, 88%, 60 years and older 21.30%). Chronic obstructive pulmonary disease was detected in 18.72% of 903 examined men and 11.21% of 1160 examined women. It is interesting that when analyzing the respiratory history of the examined, it was revealed that out of the number of people with the diagnosis of chronic obstructive pulmonary disease established by us during the epidemiological study, only 31 people (2 people in the age group of 40-49 years, 8 people in the 50- 59 years old, 21 people aged 60 years and older) were registered with a dispensary with a disease of the respiratory system (chronic obstructive bronchitis, chronic obstructive pulmonary

disease) [17]. At the same time, all cases of previously established diagnoses were classified as moderate and severe course of the disease. Previously diagnosed individuals represent 1.5% of the total sample of individuals examined by us, or 10.37% of the number of individuals diagnosed with COPD during an epidemiological study. This indicates that there is a pronounced underdiagnosis of chronic obstructive pulmonary disease at the outpatient stage and, as a rule, only cases with moderate and severe COPD are recorded. The literature has accumulated enough data to talk about the influence of genetic, physiological, social, environmental, cultural and other characteristics on the course of the disease. For a long time, at the mention of COPD, most doctors had an image of an elderly man who smokes, suffers from cough and shortness of breath, and regularly suffers seasonal exacerbations of chronic bronchitis. Recently, however, the stereotype of a COPD patient has begun to change. This diagnosis is increasingly being made to middle-aged women who smoke moderately, and in some countries do not smoke at all, who have contact with bioorganic fuel combustion products. One of the most important risk factors for the development of COPD is smoking (see table). It used to be more common among men. The Human Smoker Index (HCI) is the main indicator used to calculate the frequency of tobacco smoking . It is calculated as follows: the number of cigarettes smoked per day x the number of months in a year that a person smoked. There are data, including domestic medicine, that allow using this indicator to assess the likelihood of developing COPD[4]. * HIC > 120 - smoking leads to chronic obstructive bronchitis. * HCI > 160 - smoking poses a risk for COPD. * HCI > 240 - smoking inevitably leads to the development of COPD. HCI also indirectly depends on the length of smoking, while the zone that causes guaranteed harm to the body is considered to be HCI in the range from 60 to 720. The results of our study showed a fairly high prevalence of smoking in all age groups among men and to a lesser extent among women. In the general sample, according to our data, 49.37% of men smoke, 22.8% have smoked before, and 27.83% have never smoked. At the same time, in the general sample of women , smoking is common in 14.17% of cases, 8.86% have smoked before and 76.97% have never smoked. Many authors note that the combined effect of tobacco smoke and industrial pollutants is the most harmful. The potentiating effect of smoking and industrial dust is due to the common pathogenetic mechanism of influence on the lung tissue: tobacco smoke, like fibrogenic dust, increases the formation of ROS in the lungs. The established risk factors for COPD include belonging to the male sex (features of the profession, habits, and others). Probable (possible) risk factors for the disease include allergic predisposition and increased reactivity of the bronchi, adverse climatic conditions, chronic diseases of the upper respiratory tract, frequent acute respiratory diseases, a history of acute bronchitis and pneumonia, family predisposition and other factors. The previous acute bronchitis, acute respiratory diseases, pneumonia, chronic tonsillitis, pharyngitis, sinusitis also matter. Of the genetic factors, α1-antitrypsin (AAT) deficiency is the only well-studied genetic pathology leading to the development of COPD. In smokers with this genetic defect, the development and progression of emphysema and the formation of bronchiectasis occur much faster . Although AAT deficiency is relevant to a small population (eg, less than 1% of patients with COPD are born with AAT deficiency in the United States), it illustrates the interplay between genes and environmental factors that lead to COPD. Along with this, it is worth mentioning the syndromes of Marfan , Ehlers - Danlos - diffuse diseases of the connective tissue, in which emphysema occurs in about every tenth patient. Pathogenesis. In the pathogenesis of COPD, the most important role is played by the suppression of cellular and humoral immunity - local destruction of immunoglobulins, a decrease in the level of interferon, lysozyme, lactoferrin , inhibition of the phagocytic activity of neutrophils and alveolar macrophages, active production of histamine and other pro-inflammatory mediators, oxidative stress, impaired mucociliary clearance. Normally , mucociliary clearance is provided by the work of the ciliated

epithelium. Cigarette smoke, AAT deficiency, toxins of microorganisms cause the destruction and decrease in the number of ciliated cells, a decrease in the activity of cilia. In response to this, hyperproduction of mucus by goblet cells and glands of the submucosal layer occurs, which has a negative effect. The rheology of bronchial mucus is changing: its viscosity and adhesiveness increase , elasticity decreases, which also contributes to the deterioration of mucociliary clearance, mucostasis , and hence the development of microbial colonization, impaired bronchial patency, and an increase in respiratory failure. Stagnation of bronchial contents leads to a violation of the ventilation and respiratory function of the lungs, and inevitable infection leads to the development of endobronchial or bronchopulmonary inflammation. In addition, a viscous secret, in addition to inhibiting ciliary activity, can cause bronchial obstruction due to the accumulation of mucus in the airways. In severe cases, ventilation disorders are accompanied by the development of atelectasis. Tracheobronchial mucus under normal conditions has a bactericidal effect, as it contains immunoglobulins and nonspecific protective factors (lysozyme, transferrin , opsonins, etc.). Inflammation of the respiratory organs, as a rule, is accompanied by a compensatory increase in mucus formation . The composition of the tracheobronchial secret also changes: the water content decreases and the concentration of mucins (neutral and acidic glycoproteins) increases, which leads to an increase in sputum viscosity. It is noted that the higher the viscosity of the mucus, the lower the speed of its movement along the respiratory tract. An increase in the viscosity of bronchial secretion contributes to increased adhesion (sticking) of pathogenic microorganisms to the mucous membranes of the respiratory tract, which creates favorable conditions for their reproduction. A change in the composition of mucus is also accompanied by a decrease in the bactericidal properties of bronchial secretions due to a decrease in the concentration of secretory immunoglobulin A in it. In turn, infectious agents and their toxins have an adverse effect on the mucous membranes of the respiratory tract. Consequently, a violation of the drainage function of the bronchial tree can lead not only to ventilation disorders, but also to a decrease in local immunological protection of the respiratory tract with a high risk of developing a protracted course of the inflammatory process and contribute to its chronicity[12]. < 70 %, characterizing the restriction of expiratory airflow. The separating sign that allows assessing the severity (stage) of COPD as mild (stage I), moderate (stage II), severe (stage I II) and extremely severe (stage IV) is the value of the FEV1 indicator (determined after the appointment of bronchodilators) . Stage I: mild. FEV1/FVC < 70 %. At this stage, the patient may not notice that his lung function is impaired. Obstructive disorders are expressed slightly - the value of FEV 1 > 80% of the proper values. Usually, but not always, COPD presents with chronic cough and sputum production. Therefore, only in 25% of cases the disease is diagnosed in a timely manner (data from the European Respiratory Society), that is, at this stage of COPD development. Stage II: moderate course. FEV1/FVC < 70 %. This stage, in which patients seek medical help due to shortness of breath or an exacerbation of the disease, is characterized by an increase in obstructive disorders (FEV1 is 50-80% of the expected values). There is an increase in the symptoms of the disease and shortness of breath that appears during exercise. Stage III: severe. FEV1/FVC < 70 %. It is characterized by a further increase in airflow limitation (FEV1 is 30-50% of the expected values), an increase in shortness of breath, and frequent exacerbations. Stage IV: extremely severe course. FEV1/FVC < 70 %. At this stage, the quality of life deteriorates markedly, and exacerbations can be life-threatening. The disease acquires a disabling course. It is characterized by extremely severe bronchial obstruction (FEV1 < 30 % of predicted values or < 50% in the presence of respiratory failure)[7,9]. The late diagnosis of COPD and delayed treatment are often facilitated by the lack of attention to their health of smokers and the peculiarity of the clinical course of this disease. COPD can manifest itself for many years with only one symptom - a cough, which

patients do not attach importance to, which is why treatment begins late, when shortness of breath already appears, leading them to the doctor[2]. The second explanation for the absence of bronchial obstruction in the initial stages of COPD is the insufficient resolution of the devices used to study the function of external respiration. Risk factors for COPD Probability of significance of factors External factors Internal factors Established Smoking Occupational hazards Deficiency (cadmium, silicon) of α1-antitrypsin High Air pollution (SO2, NO2, O3) Occupational hazards Low socioeconomic status Passive smoking in childhood Prematurity High IgE level Bronchial hyperreactivity Familial nature of the disease Possible adenovirus infection Vitamin C deficiency Early diagnosis of COPD is one of the most difficult problems in respiratory medicine. Unfortunately , today there is no simple test that would have 100% sensitivity and specificity. The most important method in the diagnosis of COPD is the determination of the function of external respiration (RF), which is of the greatest diagnostic value, in which some basic volume and speed indicators are measured (vital capacity of the lungs, forced vital capacity of the lungs, forced expiratory volume in the first second, forced expiratory flow in 75, 50 and 25% levels. These indicators form a functional diagnosis of COPD and determine the severity of the disease, its progression and prognosis. It should be noted that chronic obstructive pulmonary disease occurs much earlier than ventilation disorders appear, and, therefore, in this situation, it is no longer possible to do without the study of immunopathogenesis - immunological testing with the determination of factors of cellular, humoral immunity, cytokine profile indicators as the basis for early diagnosis of the disease[1]. Studies conducted at the Samara State Medical University proved the significant role of occupational hazards in the development of COPD, suggested that occupational bronchitis (chronic dust bronchitis, chronic bronchitis of toxic-chemical etiology) and chronic obstructive pulmonary disease are identical. Treatment. The goals of COPD treatment are to reduce the rate of progression of the disease, leading to an increase in bronchial obstruction (BO) and respiratory failure (RD), reduce the frequency and duration of exacerbations, increase exercise tolerance and improve the quality of life. Smoking cessation is known to reduce chronic cough, sputum production, and dyspnea, but in both men and women, smoking more cigarettes per day and starting smoking early increases the risk of these symptoms persisting for several more years. after smoking cessation. Based on the results of a prospective randomized multicentre lung health study (Lung Health Study) smoking cessation in smokers with early symptoms of bronchial obstruction and reduced expiratory flows leads to an end to the fall in FEV1. At the end of the first year, in the group of patients receiving nicotine replacement therapy, FEV1 increased (by an average of 47 ml, or 2% of predicted), while in the control group it continued to fall. Pharmacotherapy of COPD, of course, should be comprehensive, and it is necessary to educate patients on the correct use of drugs, drug treatment is determined by the stage of the disease, the severity of symptoms, the severity of bronchial obstruction, the presence of respiratory or right ventricular failure, concomitant diseases. Of the drugs, bronchodilators constitute the basic therapy, since it is bronchial obstruction that plays a primary role in the pathogenesis and progression of COPD. The use of bronchodilators can reduce the severity of shortness of breath and other symptoms of COPD in about 40% of patients and increase exercise tolerance. The choice of one or another group of bronchodilators (M - anticholinergics , B2-agonists and methylxanthines), their combinations is made for each specific patient individually. M- anticholinergics block muscarinic receptors in the smooth muscles of the tracheobronchial tree and suppress reflex bronchoconstriction , and also prevent acetylcholine-mediated stimulation of sensory fibers of the vagus nerve when exposed to various factors, thereby providing bronchodilatory and preventive effects.[6,11] Of this group, ipratropium bromide and tiotropium bromide (prolonged drug) have been widely used . Ipratropium bromide is a quaternary isopropyl derivative of atropine.

After a single application of 40 mcg (2 inhalations) of ipratropium bromide, the effect begins after 20-40 minutes, reaches a maximum after 60 minutes and lasts for 5-6 hours. The drug in doses that have a bronchodilatory effect does not penetrate the central nervous system, inhibits the secretion of the salivary glands to a lesser extent, does not affect the motor activity of the ciliated epithelium of the trachea and does not change blood pressure and heart rate[13]. Tiotropium bromide binds to M1-, M3- and, to a lesser extent, M2-subtypes of cholinergic receptors : the half-life of the connection with M1- and M3-receptors in tiotropium bromide is 14.6 and 34.7 hours, respectively, for M2-receptors - only 3 .6 hours. Accordingly, the duration of the connection of tiotropium bromide with cholinergic receptors allows you to use it 1 time per day. Having low systemic absorption from the respiratory tract (half-life does not exceed 1 hour), it practically does not cause atropine -like side effects. 2-agonists quickly act on bronchial obstruction, improving the well-being of patients in a short time. With prolonged use | | 2-agonists develop resistance to them, after a break in taking the drugs, their bronchodilatory effect is restored. A decrease in the effectiveness of 2-adrenergic stimulants and, as a result, a deterioration in bronchial patency are associated with desensitization of 2-adrenergic receptors and a decrease in their density due to prolonged exposure to agonists, as well as with the development of "rebound syndrome", characterized by severe bronchospasm . "Rebound syndrome" is caused by blockade of 2-adrenergic receptors of the bronchi by metabolic products and a violation of the drainage function of the bronchial tree due to the development of the "lung closure" syndrome. Contraindications to the use of 2-agonists in COPD are hypersensitivity to any component of the drug, tachyarrhythmias , heart defects, aortic stenosis, hypertrophic cardiomyopathy , decompensated diabetes mellitus, thyrotoxicosis, glaucoma, threatening abortion. This group of drugs should be used with particular caution in elderly patients with concomitant heart disease. Methylxanthines are added to therapy with insufficient effectiveness of the first two groups of drugs, they reduce systemic pulmonary hypertension and increase the work of the respiratory muscles. In mild COPD, inhaled short-acting bronchodilators “on demand” (2 -agonists and M- anticholinergics) are used. Ipratropium bromide is prescribed 40 mcg (2 doses) 4 times a day, fenoterol - 100-200 mcg up to 4 times a day. M - anticholinergic drugs are first-line drugs in the treatment of COPD, their appointment is mandatory for all degrees of severity of the disease. In moderate, severe and extremely severe cases, long-term and regular treatment with bronchodilators is a priority . The advantage is given to long-acting bronchodilators : tiotropium bromide 1 time per day, 18 mcg through handihaler , long-acting 2-agnosites 2 times a day. In patients with severe and extremely severe COPD , bronchodilatory therapy is carried out with special solutions (fenoterol and ipratropium bromide) through a nebulizer . Of the drugs of the xanthine series, only prolonged theophyllines are used. In patients with FEV1 < 50 % of predicted value (severe and extremely severe stages of COPD) and recurrent exacerbations (3 times or more in the last 3 years), metered-dose inhaled glucocorticosteroids (budesonide) are used along with bronchodilator therapy. Mucolytics (mucoregulators , mucokinetics) are indicated for a very limited group of patients with stable COPD and are used in the presence of viscous sputum; they do not significantly affect the course of the disease. For the prevention of COPD exacerbation, long-term use of mucolytics (N - acetylcysteine , ambroxol) is promising[11,17]. With increased shortness of breath, an increase in the amount of sputum and its purulent nature, antibiotic therapy is prescribed. The main etiologically significant microorganisms of infectious exacerbations of COPD are Streptococcus (Str .) pneumoniae , Haemophilus (H.) influenzae , Moraxella (M.) catarrhalis , less often - Staphylococcus (S.) aureus , bacteria of the family Enterobacteriaceae . With this in mind, the selected drug must have sufficient activity against these pathogens. Based on the clinical situation in exacerbations of COPD, an approximate determination of the microbial spectrum is possible. With a mild exacerbation,

the most common clinically significant microorganisms are H.influenzae (non- typable and non- encapsulated forms), S.pneumoniae , M.catarrhalis . With more severe exacerbations and the presence of unfavorable prognostic factors (severe bronchial obstruction, respiratory failure, decompensation of concomitant pathology, etc.), which often require hospitalization in intensive care units, the proportion of the above microorganisms decreases, while the proportion of H.influenzae producing lactamases ; Gram-negative bacteria, in particular various members of the Enterobacteriaceae family . An important requirement for an antimicrobial chemotherapy drug prescribed to patients with exacerbation of COPD is the minimum level of resistance to it of the main etiologically significant microorganisms. Of particular importance is microbial resistance in patients with risk factors (old age, previous antibiotic therapy, the presence of severe comorbidities). The most real problem is the resistance of S^neumoniae to penicillins and macrolides (cross-resistance), as well as an increase in the frequency of H.influenzae and M.catarrhalis strains that produce - lactamase . The destructive effect of lactamase can be overcome through the appointment of protected aminopenicillins (amoxicillin + clavulanic acid). Macrolide preparations are widely used in the treatment of infection -dependent exacerbations of chronic obstructive pulmonary disease. Azithromycin and other macrolides of modern generations have clinically significant activity against H. influenzae , they are a priority in the treatment of acute bronchitis, exacerbation of COPD in young patients without serious concomitant diseases and severe bronchial obstruction. Psychotropic drugs for elderly patients with COPD for depression, anxiety, insomnia should be used with great caution due to their inhibitory effect on the respiratory center. Appointment of adrenergic blockers is contraindicated. In severe forms of COPD and the development of cor pulmonale, there is a need for cardiovascular therapy with the inclusion of vasodilators, angiotensin - converting enzyme inhibitors (data on their effectiveness are rather contradictory), angiotensin II receptor antagonists , diuretics, antiplatelet agents and other groups[14,16]. Patients with chronic respiratory failure are given continuous oxygen therapy , which so far remains the only method that can reduce mortality in an extremely severe stage of COPD. An indication for systematic oxygen therapy is a decrease in PaO2 in the blood to 60 mm Hg. Art., decrease in SaOa < 85 % on a standard 6-minute walk and < 88% at rest. Preference is given to long-term (18 hours per day) low-flow (2-5 l/min) oxygen therapy both in stationary conditions and at home[15]. In severe respiratory failure, helium-oxygen mixtures are used. For home oxygen therapy, oxygen concentrators are used, as well as devices for non-invasive ventilation of the lungs with negative and positive pressure on inhalation and exhalation. At all stages of the process, physical training programs are highly effective, increasing exercise tolerance and reducing shortness of breath and fatigue. Training of the respiratory muscles is achieved with the help of individually selected breathing exercises. Perhaps the use of transcutaneous electrical stimulation of the diaphragm. In case of severe polycythemic syndrome (H b > 155 g/l), it is recommended to carry out erythrocytepheresis with the removal of 500600 ml of deplasmized erythrocyte mass[17]. In the event that erythrocytepheresis is technically impracticable, phlebotomy can be performed in a volume of 800 ml with adequate replacement with isotonic sodium chloride solution. In recent years, surgical methods of treatment have begun to be used, primarily the reduction of lung volume, which leads to a decrease in dyspnea and an improvement in lung function.

Prevention. In order to prevent exacerbation of COPD during epidemic outbreaks of influenza, vaccination is necessary (Evidence level A). It has been shown that the influenza vaccine reduces the severity of the course and mortality of patients with exacerbation of COPD by 50%. In addition, there is a decrease in the frequency and severity of exacerbations of the disease against the background of influenza infection, a lower need for hospitalization, which indicates the importance of vaccinating patients with COPD. The pneumococcal vaccine can be used to

prevent exacerbations of COPD, although data on its benefit are still lacking (Evidence level B). A special place in the prevention of COPD is occupied by smoking cessation and the prevention of infectious diseases of the respiratory tract, hypothermia. The role of anti-smoking programs is also important. At the same time, many studies have shown that advertising increases not only the spread of smoking, but also those brands of cigarettes, which are aggressively advertised. In the development of tobacco dependence itself, both psychological and pharmacological components can be distinguished[8,13]. It is known that tobacco nicotine is a narcotic substance that is easily addictive or addictive with withdrawal symptoms. In this situation, smoking cessation and the fight against subsequent abstinence become very difficult tasks for the smoker, many of them require special medical care. According to the Research Institute of Pulmonology, FMBA, the treatment of tobacco dependence should be based on the principles of interpersonal contact between the doctor and the patient. A significant role is given to the use of nicotine -containing drugs: nicotine chewing gum, nicotine inhaler.

Forecast. The prognosis for recovery is poor. The disease is characterized by a steadily progressive course, leading to the development of early disability and a decrease in life expectancy. Complications of COPD are acute or chronic respiratory failure, secondary polycythemia, chronic cor pulmonale, congestive heart failure, pneumonia, spontaneous pneumothorax, pneumomediastinum . To assess the prognosis, the following parameters play a decisive role: the possibility of eliminating provoking factors, the patient's adherence to treatment, socio-economic conditions. Unfavorable prognostic signs are severe comorbidities in COPD, the development of heart and respiratory failure, and the elderly age of patients.

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