I. L. ARSENTYEVA, E. A. DOTSENKO,
N. L. ARSENTYEVA

SYMPTOMS, DIAGNOSIS, PRINCIPLES OF TREATMENT AND PREVENTION OF BRONCHIAL ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Minsk BSMU 2024

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
КАФЕДРА ПРОПЕДЕВТИКИ ВНУТРЕННИХ БОЛЕЗНЕЙ

И. Л. Арсентьева, Э. А. Доценко, Н. Л. Арсентьева

СИМПТОМАТОЛОГИЯ, ДИАГНОСТИКА, ПРИНЦИПЫ ЛЕЧЕНИЯ И ПРОФИЛАКТИКИ БРОНХИАЛЬНОЙ АСТМЫ И ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНИ ЛЕГКИХ

SYMPTOMS, DIAGNOSIS, PRINCIPLES OF TREATMENT AND PREVENTION OF BRONCHIAL ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Учебно-методическое пособие

Минск БГМУ 2024

УДК [616.248+616.24-036.12]-07-08-084(075.8)
ББК 54.12я73
А85

Рекомендовано Научно-методическим советом университета в качестве учебно-методического пособия 20.12.2023 г., протокол № 12

Р е ц е н з е н т ы: канд. мед. наук, доц., врач-ординатор отделения гастроэнтерологии 6-й городской клинической больницы г. Минска Т. Г. Раевнева; 1-я каф. внутренних болезней Бело-русского государственного медицинского университета

Арсентьева, И. Л.

А85 Симптоматология, диагностика, принципы лечения и профилактики бронхиальной астмы и хронической обструктивной болезни легких = Symptoms, diagnosis, principles of treatment and prevention of bronchial asthma and chronic obstructive pulmonary disease : учебно-методическое пособие / И. Л. Арсентьева, Э. А. Доценко, Н. Л. Арсентьева. – Минск : БГМУ, 2024. – 31 с.

ISBN 978-985-21-1567-4.

Представлены современные принципы клинической диагностики, лечения и профилактики бронхиальная астмы и хронической обструктивной болезни легких.

Предназначено для студентов 3-го курса, обучающихся на английском языке по специальности 1-79 01 01 «Лечебное дело» по учебной дисциплине «Внутренние болезни».

УДК [616.248+616.24-036.12]-07-08-084(075.8)
ББК 54.12я73

ISBN 978-985-21-1567-4

LIST OF ABBREVIATIONS

AB — antibody
AG — antigen
ALV — artificial lung ventilation
ARF — acute respiratory failure
AS — asthmatic status
ASH — anaphylactic shock
BA — bronchial asthma
BHR — bronchial hyperreactivity
COPD — chronic obstructive pulmonary disease
CRF — chronic respiratory failure
FeNO — fraction of nitric oxide in exhaled air
FEV1 — forced expiratory volume in 1 second
FVC — forced vital capacity
GCS — glucocorticosteroids
HRCT — high resonance computer tomography
ICS (IGCS) — inhaled glucocorticosteroids
ICU — Intensive Care Unit
Ig — immunoglobulin
IM — intramuscularly
IV — intravenously
LAAC — long-acting anticholinergics
LABA — long-acting β2-agonist
LHI — lung hyperinflation
LTRA — leukotriene receptor antagonist
NIV — non-invasive pulmonary ventilation
NSAIDs — non-steroidal anti-inflammatory medications
$PaCO_2$ — partial pressure of carbon dioxide in arterial blood
PaO_2 — partial pressure of oxygen in arterial blood
PEF — peak expiratory flow
SAAC — short-acting anticholinergics
SABA — short-acting β2-agonist
SaO_2 — saturation of blood hemoglobin with oxygen
SBP — systolic blood pressure
SC — subcutaneously
SGCS — systemic glucocorticosteroids
TLC — total lung capacity

MOTIVATIONAL CHARACTERISTIC OF THEME

Bronchial asthma and chronic obstructive pulmonary disease, as well as mortality from them, are a very actual and common medical problem. This is due to the high prevalence of these pathologies, high morbidity among people of working age, and a pronounced decrease in the quality of patients' life. Also, often ongoing therapeutic measures are ineffective or partially effective. Diagnostic and therapeutic measures for this pathology are quite expensive. Treatment of patients requires punctuality in organizing the treatment process, strict discipline in the patient's behavior, and tight interaction between the physician and the patient. In persons suffering from obstructive pathology of the bronchopulmonary system, the quality of life is seriously deteriorated because the variety of leisure activities, interpersonal communication and professional opportunities are sharply limited.

Therefore, it is very important to be able to make in time a correct diagnosis, carry out differential diagnosis, adequate treatment and prevention of bronchial asthma and COPD.

BRONCHIAL ASTHMA

Definition. Bronchial asthma is a recurrent disease with reversible airway obstruction, manifested by attacks of dyspnea and developing as a result of allergic or pseudoallergic congenital or acquired hyperreactivity of the bronchi to allergens and nonspecific factors. The clinical manifestations of asthma are attacks of suffocation (attacks of progressive shortness of breath, up to the development of asphyxia).

According to GINA-2020***, BA is a heterogeneous disease characterized by chronic diffuse inflammation of the airways leading to partially or completely reversible bronchospasm and the presence of respiratory symptoms such as wheezing, dyspnea (shortness of breath), chest congestion and cough varying in time and intensity, and occurring together with variable airway obstruction.*** The leading pathophysiological components of BA are hyperreactivity of the bronchial tree and its obstruction due to inflammatory edema of the bronchial walls, bronchospasm (reversible) and hyperproduction of sputum (with the formation of mucous plugs) and, finally, the development of airway remodeling.

Epidemiology. Bronchial asthma is currently a very common disease. About 350 million patients worldwide suffer from BA (according to GINA-2020). At the same time, in such large countries as Russia, the incidence of asthma among adults is 6.9 % (among children and adolescents — about 10 %), the United States — up to 7.9 % of the population.

Etiopathogenesis of BA. Factors influencing the development and manifestations of asthma can be divided into internal (e.g. genetic predisposition to bronchial hyperreactivity and atopy, gender (women over 18 years old are more likely to get sick), obesity) and external: allergens (food products, pollen, house dust mites, pet and cockroach allergens, fungal allergens, medications) and

so-called triggers or nonspecific provocateurs of acute bronchospasm (inections (viruses), occupational factors (e.g. working in conditions of high humidity or cold, frequent temperature changes), air pollutants (e.g. sulfur and nitrogen dioxide, ozone, diesel combustion products), tobacco smoke components (active and passive smoking), physical activity, pungent odors, emotions).

Clinical picture of BA. Main clinical manifestation of bronchial asthma during exacerbations is an attack of suffocation, accompanied by the presence of distantly audible rhonchi (or so-called *wheezing*). Asthma attack can be considered an episode of ARF against the background of BA exacerbation.

Patients may also complain of dyspnea (expiratory or mixed type), heaviness (tightness) in the chest, cough (mostly dry or with a small amount of viscous mucous sputum, usually released at the end of an asthma attack). Sometimes coughing attacks can be the equivalent of asthma attacks (the so-called "cough" variant of BA). In addition, patients may complain of fear of death, anxiety, irritability, and inability to work. With a mild intermittent course of bronchial asthma, these symptoms appear only during infrequent exacerbations, while during the period of remission there may be no complaints at all. As the disease progresses, also during remission, shortness of breath, chest tightness and cough may be constantly observed. With severe asthma, patients complain of frequent and severe attacks of suffocation that occur daily, both day and night.

During ***physical examination*** of patient, one can detect a specific shape of the chest (the so-called emphysematous or barrel chest), which occurs as a result of bronchial obstruction and hyperinflation of the lung alveoli, with progressive destruction of the alveolar walls and with a tendency to form bullae in the lung tissue). During an attack of suffocation the patient takes a forced sitting position with a fixed shoulder girdle (e.g., leaning his hands on the tabletop in front of him), which makes it easier for him to exhale difficultly. The skin is pale, diffuse warm cyanosis develops, and sweating is common. Speech is difficult. The act of breathing involves auxiliary respiratory muscles (wings of the nose, neck muscles and the shoulder girdle). Tachypnea is detected, while the exhalation is lengthened (inhalation / exhalation ratio is at least 1 : 3). Heart rate and blood pressure level also increase. When conducting comparative percussion of the lungs, a bandbox sound is detected, symmetrically. When conducting topographic lung percussion, the following data are revealed: the upper lung borders are shifted upward, the lower ones — downward, there is also a limitation in the mobility of the lower pulmonary edge and an expansion of Krenig's fields. Comparative lung auscultation reveals diffusely weakened vesicular breathing and a variety of dry rales (wheezing sounds) scattered throughout the lung fields and listened both during inhalation and exhalation. In some patients, wheezing can only be detected by auscultation of forced expiration, usually in cases of mild or fading exacerbation. In remission period, complaints and physical changes during examination of the respiratory organs may be completely absent (with a mild course of the disease).

When **formulating a diagnosis of BA** by physician, the following data must be indicated: etiology (if any), severity (newly diagnosed bronchial asthma or in patients who have already received treatment), level of bronchial asthma control, exacerbation — with indicating its severity (if exacerbation is presented). Physician should also list the concomitant diseases (comorbidities) that may affect the course of bronchial asthma. For example: "Bronchial asthma, allergic form, mild severity, controlled course, moderate exacerbation. CRF of the 2nd stage. Allergic rhinoconjunctivitis, mild course. Sensitization to feline epithelium. Obesity 1st degree".

Recommendations for determining the etiology of asthma, severity and level of control are presented below in the text of this edition.

The etiology of asthma is established in accordance with the International Classification of Diseases, 10th revision (ICD-10), which contains the following codes:

– bronchial asthma (J45);

– bronchial asthma with a predominance of **allergic** component (J45.0);

– **non-allergic** bronchial asthma (J45.1);

– **mixed** bronchial asthma (J45.8);

– Status asthmaticus (J46).

Assessing the severity of BA. To assess the severity of bronchial asthma, the criteria indicated in Table 1 are used.

Table 1

Classification of BA before therapy

Criteria	Intermittent asthma	Mild persistent asthma	Moderate persistent asthma	Severe persistent asthma
Daytime symptoms	Less than once a week	More than once a week, but less than once a day	Daily symptoms; daily use of SABA	Daily symptoms; limitation of physical activity
Nocturnal symptoms	No more than 2 times a month	No more than 2 times a month	Nocturnal symptoms more than 1 time per week	Frequent nocturnal symptoms
Exacerbations	Exacerbations are short	Exacerbations can reduce physical activity and disturb sleep	Exacerbations can lead to limited physical activity and sleep disturbance	Frequent exacerbations
Functional indicators	FEV1 or PEF ≥ 80 % of proper	FEV1 or PEF ≥ 80 % of proper	FEV1 or PEF 60–80 % of proper	FEV1 or PEF ≤ 60 % of proper
Variability of PEF or FEV1	< 20 %	20–30 %	> 30 %	> 30 %

If at least one of the criteria of corresponding group is presented, the patient may be assigned a higher severity level than the level to which the remaining available criteria are met.

Asthma severity is not a fixed characteristic and may change over time. During repeated examinations of patients already receiving treatment, the severity

of asthma is determined in accordance with the presence of relevant symptoms and therapy carried out over the past few months (Table 2).

Table 2

Classification of BA by severity in patients already receiving treatment

Severity	Definition (stage of therapy)	Treatment received
Mild asthma	Asthma well controlled with step 1 and 2 therapy	Low-dose ICS/SABA on demand or low-dose ICS or LTRA
Moderate asthma	Asthma well controlled with step 3 therapy	Low-dose ICS/LABA
Severe asthma	Asthma requiring step 4 and 5 therapy to maintain control, or asthma that remains uncontrolled despite this therapy (step 5)	Medium or high dose ICS/LABA, tiotropium bromide, or fixed combination ICS/LABA/LAAC, targeted therapy and/or SGCS

Assessing the level of BA control is based on the evaluation of patient's symptoms over the past 4 weeks (Table 3).

Table 3

Classification of BA by level of control

Over the past 4 weeks, the patient had:		**Control level**		
		Well controlled	**Partially controlled**	**Uncontrolled**
Daytime symptoms more than twice a week	YES☐ NO☐	None of the above	1–2 of the above	3–4 of the above
Nighttime awakenings due to BA	YES☐ NO☐			
Need for symptomatic medications more than twice a week (excluding pre-exercise bronchodilator use)	YES☐ NO☐			
Any restriction in the patient's activity due to asthma	YES☐ NO☐			

Well-controlled bronchial asthma is a priority in all cases of the disease, regardless of its severity. As a rule, control is achievable, but it can be difficult in cases such as asthma in combination with obesity, asthma in a smoking patient, etc.

Re-evaluation of asthma control is necessary not later than 3 months after the start of therapy. To assess asthma control in adult patients, it is recommended to use the Asthma Control Test (AST) or the Asthma Control Questionnaire (ACQ-5, Appendix 1).

Asthma exacerbations are episodes of sudden, progressive shortness of breath, cough, wheezing, or chest congestion that require a change in usual treatment regimen. Exacerbation of asthma is characterized by a decrease in PEF and FEV1. Exacerbations can develop both in patients with an already established diagnosis of bronchial asthma, and can be the first manifestation of asthma. Exacerbations of bronchial asthma can develop in any patient, regardless of the severity of the disease, but more often occur with difficult-to-control asthma. The duration of an exacerbation of bronchial asthma can vary significantly in different patients and range from 5 to 14 days.

Patients who are at high risk of dying from asthma should seek immediate medical attention in the early stages of an asthma attack. These are patients with risk factors such as:

– A history of life-threatening exacerbation of BA;
– History of episodes of artificial lung ventilation due to BA exacerbation;
– History of pneumothorax or pneumomediastinum;
– Hospitalization for exacerbation of BA during the last year;
– Psychological problems (denial of the disease);
– Socio-economic factors (low income, lack of access to medications);
– Recent dose reduction or complete cessation of glucocorticosteroids;
– Low patient compliance, low adherence to therapy;
– Decreased perception of dyspnea.

Exacerbation of asthma can be caused by various triggers that cause inflammation of the airways or provoke acute bronchospasm. The main triggers include respiratory tract infections (mainly viruses, most often rhinoviruses), allergens, air pollutants, physical activity (in patients with exercise-induced asthma), meteorological factors, certain medications (for example, beta-blockers; use of NSAIDs for aspirin-induced bronchial asthma), emotional reactions, exacerbation of rhinosinusitis, gastroesophageal reflux, pregnancy, insufficient effectiveness of BA therapy, etc.

Risk factors for exacerbations include:

– presence of uncontrolled asthma symptoms;
– IGCS are not prescribed, poor adherence to therapy;
– excessive use of SABA;
– low FEV1, especially < 60 % of predicted;
– significant psychological or socio-economic problems;
– external factors: smoking, allergen exposure;
– concomitant diseases: rhinosinusitis, gastroesophageal reflux disease (GERD), confirmed food allergy, obesity;
– eosinophilia of sputum or blood;
– pregnancy;
– presence of one or more severe exacerbations of asthma over the past 12 months.

Classification of asthma exacerbations according to severity. Regardless of the severity of the course and control of asthma, the patient can experience exacerbations of any severity. The severity of BA exacerbations is determined according to the clinical criteria indicated in Table 4.

In order to classify a patient in a more severe category of exacerbation, it is sufficient to have at least one of the relevant criteria.

Table 4

Determining the severity of asthma exacerbations

Severity	Criteria
Mild or moderate exacerbation of asthma	• worsening of symptoms; • PEF is 50–75 % of the best or calculated result; • increase in the frequency of use of emergency medications ≥ 50 % or their additional use in the form of a nebulizer; • nocturnal awakenings due to the onset of asthma symptoms and requiring the use of emergency medications
Severe exacerbation of BA	• PEF is 33–50 % of the best values; • respiratory rate of 25 per minute or more; • pulse rate is 110 per minute or more; • inability to pronounce a phrase in one exhalation
Life-threatening asthma	• PEF < 33 % of best values; • SaO_2 < 92 %; PaO_2 < 60 mm Hg; normocapnia ($PaCO_2$ 35–45 mm Hg); • identifying signs of "silent" lung; cyanosis; superficial respiratory movements; • bradycardia; hypotension; • stupor / sopor / coma
Asthma closed to fatal	• Hypercapnia ($PaCO_2$ > 45 mm Hg) and/or • Need for mechanical ventilation

ASTHMATIC STATUS

A severe, prolonged attack of bronchial asthma is the so called "Status Asthmaticus". Asthmatic status (AS) is one of the most severe complications of bronchial asthma. Acute progressive airway obstruction occurs with the development of acute hypoxia and hypercapnia with dyscirculatory disorders, a high level of dysmetabolism and, as a consequence, a high risk of developing hypercapnic coma, cerebral edema, dyscirculatory disorders and asystole.

According to the latest international consensus documents (Table 4), AS corresponds to the concepts of "life-threatening asthma" and "near-fatal asthma".

Clinical manifestations of the asthmatic status. In the development of AS, there are 3 conventional stages (initial, decompensation, stage of hypoxic coma).

Stage I. Consciousness is preserved, but the patient is agitated, the skin is pale, moderate cyanosis, tachypnea, respiratory rate > 30 per minute, exhalation is difficult, dry cough (sputum does not come out). Auscultation of lungs reveals weakened vesicular breathing and many dry scattered rales. Heart sounds are muffled, and there is a tendency to increase heart rate and blood pressure. PaO_2 is about 70 mmHg, $PaCO_2$ decreases to 30–35 mmHg due to the development of compensatory respiratory alkalosis.

Stage II. Development of stupor. Cyanosis increases, the jugular veins swell. Paradoxical pulse appears (characterized by a decrease in SBP of more than 15 mm Hg per minute during inhalation of each respiratory cycle). Tachycardia. Respiration rate up to 40 or more per minute. When listening of lungs, a typical auscultative sign appears — the so-called "silent" lung is identified (areas of

the lung fields over which respiratory sounds are not detected due to complete obstruction of the bronchi of various calibers). The blood pH shifts towards acidosis. PaO_2 decreases to 60 mm Hg and below, $PaCO_2$ rises to 50–60 mm Hg.

Stage III. Development of coma (hypoxic, dysmetabolic, dyscirculatory). Diffuse gray cyanosis. Sweating. Respiratory rate 60 or more per minute, suoperficiial, auscultative sign — diffuse "silent lung". Heart rate up to 140 or more per minute, heart sounds are muffled, sometimes arrhythmia; pulse on the radial arteries is threadlike; blood pressure drops sharply to the point of collapse. Alkalosis. PaO_2 is below 50 mmHg, $PaCO_2$ increases to 70–80 mm Hg and higher.

DIAGNOSIS OF BRONCHIAL ASTHMA

The diagnosis of bronchial asthma is recommended to be established on the basis of complaints, medical history (Anamnesis data), results of a physical examination and data from functional examination methods (spirography, pneumotachometry, bronchodilation test), specific allergological examination and exclusion of the presence of other diseases.

When taking an anamnesis of a patient with bronchial asthma, it is necessary to find out the probable causes of the onset and resolution of symptoms, their duration, and the presence of allergic reactions in the patient and his blood relatives. When discussing the entire set of symptoms, special attention should be paid to those that have bothered the patient over the past 3–4 months, and it is also necessary to take into consideration the patient's response to therapy aimed at controlling the disease.

Laboratory examination plan**:** *general blood test* to assess eosinophilic inflammation; *levels of general and specific immunoglobulins E* in the blood of immunoglobulins E in the blood, including when performing skin tests is not possible; *general sputum analysis* to assess eosinophilic inflammation (the frequency of the study in dynamics is determined individually for all of these tests).

Instrumental examination plan. All patients with suspected asthma are recommended to use *spirometry* as an initial study to identify and assess the severity of airway obstruction, then in dynamics with an interval of 3 months. Normal results of spirometry (or peakflowmetry) in mild cases of the disease does not exclude the diagnosis of asthma.

In addition, all patients with bronchial asthma are recommended to undergo a *bronchodilation test* to determine the degree of ***reversibility*** of ***obstruction*** using SABA (medications for the treatment of obstructive respiratory disease). A bronchodilator test is considered positive if, after inhalation of a bronchodilator, the increase in FEV1 is at least 12 %, and the absolute increase is 200 ml or more.

In case of normal spirometry and with negative bronchodilation test, it is recommended to use a test to detect bronchial hyperreactivity (BHR) using *bronchoconstrictor test* to confirm the diagnosis of BA. Detection of BHR is based on measuring the FEV1 response to inhalation of increasing concentrations of Methacholine. Response is calculated as the concentration (or dose) of the provoking agent causing a 20 % decrease in FEV1.

Patients with suspected the so-called “exercise-induced asthma” (non-allergic form of BA), a bronchoconstrictor test with physical activity is recommended for revealing bronchospasm caused by cooling and drying of the respiratory mucosa during exercises. A positive response to exercise (FEV1 decrease of more than 10 %) is a specific indicator of Exercise-Induced Asthma. This test is more specific, but less sensitive than Methacholine test, for diagnosing asthma.

Monitoring the study of peak expiratory flow (peak flowmetry is an estimation of unprovoked respiratory volumes using a peakflowmeter). In patients with clinical symptoms of asthma who do not have the opportunity to perform spirometry or additional diagnostic tests, it is recommended to use multiple measurements of PEF measurements over at least 2 weeks to confirm diurnal airflow variability. In patients with typical respiratory symptoms, detection of increased mean daily PEF variability (> 10 % in adults) confirms the diagnosis of asthma. PEF monitoring has a high degree of sensitivity and specificity but less than spirometry. Results of PEF monitoring should be interpreted in the context of the clinical situation, since PEF variability may be increased in diseases that are most often differentially diagnosed as asthma.

As additional markers of eosinophilic inflammation (Table 5), if necessary, it is recommended to study the fraction of nitric oxide in exhaled air (FeNO). FeNO level is elevated in eosinophilic bronchitis, the presence of atopy and allergic rhinitis, and reduced in smokers, during bronchospasm, and in the early phase of an allergic reaction. FeNO is associated with a good short-term response to ICS. Normal FeNO values, especially during the absence of symptoms, do not exclude the diagnosis of BA.

Table 5

Methods for assessing airway inflammation

Test	Norm	Validity	
		Sensitivity	Specificity
Methacholine PC20 (provocative concentration of methacholine, causing a 20 % drop in FEV1)	> 8 mg/mL	High	Moderate
Physical activity	Fall in FEV1 > 10 % of baseline	Moderate	High
FeNO	< 25 ppb	High	Medium
Sputum eosinophils	< 2 %	High	Moderate
PEF variability (% of maximum)	< 8 (with double measurement during the day) < 20 (with more than 4 measurements during the day)	Low	Medium

Differential diagnosis of bronchial asthma in adults. Spectrum of diseases and conditions for which differential diagnosis is necessary depends on the presence or absence of bronchial obstruction in the patient, defined as FEV1/FVC < 0.7 (prior to the use of a bronchodilator). Patients with asthma may also have other diseases that cause bronchial obstruction, which complicates the interpretation of study results. Combination of asthma and chronic obstructive pulmonary disease (COPD) is considered especially common.

For the purpose of differential diagnosis of asthma, patients with bronchial obstruction and possible asthma are recommended to undergo a bronchodilation test and/or trial therapy. Patients at high risk of developing asthma, it is recommended to start trial treatment for certain period immediately. If the bronchodilation test is positive (this means that the bronchial obstruction is reversible) and a positive effect is achieved with the treatment test, after that the patient should be treated as a patient with BA. If bronchial obstruction is not reversible and there is no positive response to a trial course of therapy, additional examination should be continued to clarify the diagnosis.

In patients with normal spirometry, to confirm the diagnosis of asthma, it is recommended to repeat the examination during the period of symptoms, or, if the patient's condition allows, after stopping the use of bronchodilators.

In patients with clinical symptoms of asthma and normal spirometry, additional testing for BHR and/or airway inflammation is recommended. These tests (Table 5) are quite sensitive, so the results obtained during them within the normal range can serve as confirmation of the absence of BA.

PRINCIPLES OF TREATMENT OF BRONCHIAL ASTHMA

Initiation of asthma therapy should begin with the exclusion of exposure to a causally significant factor. Unfortunately, this is not possible in all cases. Diet control is also necessary, especially in patients with allergic or mixed BA. Asthma medication therapy is carried out using *basic therapy* aimed to *preventing asthma attacks* (treatment of stable asthma) and *emergency treatment*, the purpose of which is *to treat an asthma attack* (treatment of exacerbation of BA).

Basic therapy. Modern goals of BA therapy: achieving and maintaining control of asthma symptoms over a long period of time; minimizing the risk of future exacerbations of asthma, fixed airway obstruction and unwanted side effects of therapy. It is recommended that every patient with asthma be assessed for symptom control, risk of exacerbations, irreversible airway obstruction, and drug side effects. Basic therapy medications include:

1) anti-inflammatory medications: Sodium Cromoglycate (e.g. Intal), ICS (IGCS) — inhaled glucocorticosteroids = Fluticasone propionate, Beclomethasone dipropionate, etc., SGCS — systemic glucocorticosteroids = Methylprednisolone (e.g. Medrol);

2) long-acting bronchodilators: β2-agonists = LABA (Salmeterol, Formoterol, Vilanterol (ultralong-acting β2-agonist)), anticholinergics = LAAC (Umeclidinium bromide, Tiotropium bromide (e.g. Spiriva) and their combinations (Vilanterol + Umeclidinium bromide (e.g. Anoro Ellipta); Theophylline (e.g. Theotard);

3) anti-leukotriene medications: these exist in two forms: drugs that inhibit leukotriene formation (e.g. Zileuton), and leukotriene receptor antagonists = LTRA (Montelukast, Zafirlukast).

Principles of ***Basic therapy*** are based on Step therapy. When treating bronchial asthma, it is recommended to use a stepwise approach, adjusting

the amount of therapy depending on the level of control and the presence of risk factors for exacerbations of bronchial asthma. Each stage includes treatment options that can serve as an alternative when choosing maintenance therapy for bronchial asthma (Table 6).

Table 6

Step therapy of BA

<table>
<tr><th>Stage 1</th><th>Stage 2</th><th>Stage 3</th><th>Stage 4</th><th>Stage 5</th></tr>
<tr><td>Preferred therapy:
low dose ICS-SABA as needed</td><td>Preferred therapy: daily:
low-dose ICS or low-dose ICS-SABA as needed

Additional variants of therapy:
LTRA or
low dose of Theophyllinum</td><td>Preferred therapy:
low dose ICS/LABA

Additional variants of therapy:
middle-dose ICS or
low dose ICS + Tiotropium bromide or
low dose ICS + LTRA or
low dose ICS + Theophyllinum with slow releasing</td><td>Preferred therapy:
middle-dose ICS/LABA or fixed combination of low (middle) dose ICS/LABA/LAAC

Additional variants of therapy:
ICS/LABA + Tiotropium bromide or
high dose ICS + LTRA or
high dose ICS + Theophyllinum with slow releasing</td><td>Preferred therapy:
high-dose ICS/LABA or fixed combination of high-dose ICS/LABA/LAAC

Tiotropium bromide + ICS/LABA

Phenotype estimation and additional therapy: (Omalizumab, Mepolizumab, etc.
A less desirable treatment option is the lowest possible dose of systemic corticosteroids)</td></tr>
<tr><td colspan="2">Preferred therapy for BA attack treatment:
low-dose ICS-SABA</td><td colspan="3">Preferred therapy for BA attack treatment:
low-dose ICS-LABA</td></tr>
<tr><td colspan="5">Another therapy as needed: SABA</td></tr>
<tr><td colspan="5">Increase therapy until control improves ⇒</td></tr>
<tr><td colspan="5">⇐ Reduce therapy to the minimum that maintains control</td></tr>
</table>

The initial choice of treatment stage depends on the severity of asthma clinical manifestations. Increase in the volume of therapy (transition to next step up) is indicated in the absence of control and/or the presence of risk factors for exacerbations. Reduction in the volume of therapy is indicated when stable control is achieved and maintained for ≥ 3 months and there are no risk factors, in order to establish the minimum volume of therapy and the lowest doses of medications sufficient to maintain control.

When deciding which medication should be decreased first and at what rate, it is recommended to take into consideration the severity of asthma, the side effects of treatment, the duration of the current dose, the benefit achieved and patient preference. ICS dose reduction should be slow due to the possibility of exacerbation. With sufficient control, it is possible to reduce the dose by about 25–50 % every three months.

Treatment of asthma exacerbations. The goal of treating asthma exacerbations is to eliminate bronchial obstruction and hypoxemia as quickly as possible and prevent further relapses.

Principles of asthma exacerbations treatment (therapy of attacks):

1. Using of bronchodilators (short-acting beta-2 agonists (SABA, including Salbutamol, Berotek (Phenoterol)); or short-acting anticholinergics (SAAC), also named as cholinolytics (Ipratropium bromide (Atrovent); or a combination of both (Berodual). Usual therapy includes two inhalations in a row (maximum of 8 inhalations per day, to avoid side effects).

2. For severe attacks of bronchial asthma (no effect from 2 inhalations of SABA/SAAC) additionally Prednisolone 60–90 mg IV, 2.4 % Aminophylline solution IV (5–10 ml IV dropwisely with isotonic Sodium chloride solution).

Treatment of Asthmatic Status:

– oxygen therapy through a mask or nasal catheter;

– use of bronchodilators (short-acting beta-2-agonists (SABA), 1–2 ml of 0,1 % Fenoterol solution or 2–4 ml of short-acting anticholinergics (SAAC), or their combination (Ipratropium bromide + Fenoterol = Berodual), *via a nebulizer*. If there is insufficient effectiveness, it can be repeated up to 3 times during the first hour of use, and then, as necessary, 1 time every 4 hours, with dosage control;

– simultaneously with bronchodilators, the use of Prednisolone up to 2 mg/kg/day IV is indicated; it is possible to use the so called Pulse-therapy (500–1000 mg of Methylprednisolone IV during 35–45 minutes once a day for 3 days);

– if there is no effect of treatment, a 2.4 % solution of Aminophylline with isotonic Sodium chloride solution up to 4–5 mg/kg is prescribed intravenously using an infusion pump;

– if the patient is unable to create a sufficient peak flow during exhalation, the use of a 0.18 % Epinephrine solution, at a dose of 0.01 ml/kg (up to 0.5–1 ml) is indicated;

– with progressive impairment of pulmonary ventilation (PEF less than 60 %, SaO_2 less than 90 %, pH more than 7.3 and an increase in $PaCO_2$ to 70 mm Hg, as well as pronounced changes in vital signs), the patient must be hospitalized into the intensive care unit for tracheal intubation and artificial lung ventilation;

– in the presence of mental agitation, the use of Droperidol 1 ml (2.5 mg) IV slowly with 20 ml of a 5 % Glucose solution is indicated;

– it is also important to adjust the pH of the blood (if necessary);

– it is necessary to use expectorants (Ambroxol IV slowly, 2 ml);

– after removing the patient from Status Asthmaticus, maintenance therapy with glucocorticosteroids up to 32–48 mg of Methylprednisolone = Medrol per day is indicated, as well as prolonged methylxanthines (Theotard at a dose of 200–500 mg depending on the results of peak flowmetry); as well as LABA/LAAC and expectorants (Ambroxol) over a long course and with long-term oxygen therapy.

Indications for hospitalization in adult patients with bronchial asthma:

1. Severe attack of bronchial asthma or Satus Asthmaticus.
2. Suspicion of the development of complications.
3. Lack of a rapid response to bronchodilation therapy.
4. Further deterioration of the patient's condition due to the treatment started.
5. Long-term use or recently discontinued use of SGCS.
6. Decreased perception of dyspnea.

PRINCIPLES OF ASTHMA PROPHYLAXIS

All patients with asthma are advised to control environmental factors that act as asthma triggers. A significant proportion of patients, have the idea that asthma can be triggered by numerous environmental, dietary and other factors, the elimination of which can improve the course of the disease and reduce the amount of medication therapy. Asthma exacerbations can be caused by many factors, sometimes called triggers; these include allergens, viral infections, pollutants and medications.

Currently, there are only a small number of measures that can be recommended for the prevention of asthma, since the development of this disease involves complex and not fully understood mechanisms. In order to prevent the development of asthma, asthma symptoms or exacerbation of asthma, all patients with asthma are recommended to stop smoking, eliminate causative allergens, and reduce body weight in case of obesity. Reducing a patient's exposure to certain categories of factors/triggers may improve asthma control and reduce the need for medications.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Chronic obstructive pulmonary disease (COPD), according to GOLD-2020, is a ***disease characterized by persistent airflow limitation that is usually progressive and results from a chronic inflammatory response of the airways and lung tissue due to the inhalation of harmful particles or gases.*** Exacerbations and comorbidities (concomitant diseases) are an integral part of the disease and make a significant contribution to the clinical picture and prognosis of COPD.

Epidemiology. According to WHO, today COPD is the 3rd leading cause of death in the world, about 2,8 million people die from COPD every year, accounting for 4.8 % of all causes of death. The main cause of death in patients with COPD is progression of the underlying disease.

Etiology and risk factors of COPD. Both endogenous and environmental factors play a role in the development of COPD. Smoking is considered the main cause of COPD. Occupational hazards, passive smoking and air pollution may also play an etiological role. Workplace air pollution from biological, mineral dusts, gases and smoke (as measured by patients' self-assessment of their workplace) was associated with a higher prevalence of COPD. *Endogenous risk factors* include genetic, epigenetic, and other patient characteristics, such as a history of bronchial

hyperreactivity and bronchial asthma (BA), as well as a history of severe respiratory infections. At the same time, bronchial hyperreactivity is a risk factor for the development of COPD even in the absence of BA; there is evidence that the symptoms of chronic bronchitis may increase the risk of developing COPD. Development of COPD is associated with multiple gene polymorphisms, but only some of these associations have been shown in independent population samples. Also, congenital alpha-1 antitrypsin deficiency is an autosomal recessive hereditary disease that predisposes to the development of COPD, but is detected in less than 1 % of cases.

Pathogenesis of COPD. COPD is accompanied by irreversible or poorly reversible airway obstruction associated with chronic progressive inflammation of the bronchial tree, predominantly of a bacterial nature, edema of the bronchial wall, hyperproduction of sputum and bronchospasm. All this leads to bronchial obstruction and, as a consequence, to the progressive development of emphysema, as well as fibrosis of the airways and progressive respiratory failure. Emphysema develops as a result of gradual destruction of the alveolar walls caused by increased pressure within the alveoli (formation of the so called air traps and lung hyperinflation (LHI) due to progressive airway obstruction). Expiratory airflow limitation is the main pathophysiological disorder in COPD. But lung hyperinflation also plays a significant role in the pathogenesis of COPD. LHI is based on an air trap that develops due to incomplete emptying of the alveoli during exhalation due to loss of elastic traction of the lungs (static LHI) or due to insufficient exhalation duration under conditions of severe limitation of expiratory airflow (dynamic LHI). The consequence of LHI is an increase in lung volumes (functional residual capacity (FRC), residual volume (RV), total lung capacity (TLC)) and a decrease in inspiratory lung capacity (ILC). Increase in dynamic LGI occurs during physical activity, since during exercise the respiratory rate increases, which mean that the expiratory time is shortened, and an even larger part of the air volume is retained inside of alveoli.

Gas exchange disorders. COPD is characterized by the progressive development of hypoxemia and hypercapnia. The main pathogenetic mechanism of hypoxemia is a violation of the ventilation-perfusion ratio: AV / Q balance (AV — alveolar ventilation, Q — cardiac output). Oxidative stress, i.e. the release of an increased amount of free radicals into the airways, has a powerful damaging effect on all structural lungs components and leads to irreversible changes in the lung parenchyma, respiratory tract, and pulmonary vessels.

Microscopically, COPD is characterized by an increase in the number of neutrophils, macrophages, and T-lymphocytes (especially CD8+) in various parts of the airways and lungs. An increased number of inflammatory cells in patients with COPD are found in both the proximal and distal airways.

Clinical picture of COPD. The main complaints of COPD are dyspnea (shortness of breath) on physical exertion, decreased exercise tolerance, and chronic cough with sputum (with an exacerbation of COPD, the sputum usually turns yellow, green, or brownish due to the presence of pus in the sputum).

Severity of dyspnea is recommended to be assessed using the modified mMRC scale (Appendix 2, 4). For a comprehensive assessment of COPD symptoms, it is recommended to use the CAT scale. The CAT scale better reflects the impact of COPD on daily life and the well-being of patients and closely correlates with health status (Appendix 3, 4).

The goals of ***physical examination*** for all patients with COPD are the following: to identify signs of bronchial obstruction, emphysema, respiratory failure, assess the function of respiratory muscles, and rule out comorbidities.

During a physical examination of the patient, a typical change in the shape of the chest can be detected (the so-called emphysematous or barrel-shaped chest appears due to bronchial obstruction and lung hyperinflation). During an exacerbation, body temperature rises due to activation of a pulmonary infection. The skin of patients is often pale grayish; due to the development of diffuse warm cyanosis; speech may be difficult. Accessory respiratory muscles (the wings of the nose, neck muscles and muscles of the upper shoulder girdle) can participate in the act of breathing. Tachypnea is detected, and exhalation is prolonged. The heart rate also increases; an increase of blood pressure is also observed. When performing comparative percussion of the lungs, a bandbox sound is detected on both sides. When performing topographic percussion of the lungs, a displacement of the upper borders of the lungs upward, lower borders downward, limitation of mobility of the lower ling border, and expansion of Krenig's fields are revealed. Comparative auscultation of the lungs reveals diffusely weakened vesicular breathing and a large number of dry whistling sounds of different timbres (both on inhalation and exhalation). During the period of remission, the above-described complaints and pathological signs detected during physical examination are usually present, but with less intensity and body temperature is normal.

Complications of COPD. Pulmonary hypertension in COPD can develop due to hypoxia-induced spasm of small pulmonary arteries, which ultimately leads to structural changes: intimal hyperplasia and subsequent hypertrophy / hyperplasia of the smooth muscle layer. In this case, in parallel, inflammation occurs in the vessels, similar to the inflammatory reaction in the respiratory tract, and endothelial dysfunction. Progressive pulmonary hypertension can lead to right ventricular hypertrophy and ultimately to right ventricular failure (Cor Pulmonale).

A characteristic feature of COPD is the presence of systemic effects, the main of which are cachexia, skeletal muscle dysfunction, osteoporosis, cardiovascular disorders, anemia, depression, etc. The mechanisms underlying these systemic manifestations are very diverse and have not yet been sufficiently studied. It is known that hypoxemia, smoking, sedentary lifestyle, and systemic inflammation occupy an important place among them.

When a physician formulates diagnosis of COPD, the following data must be indicated: type of disease; stage of disease (severity depends on the level of bronchial obstruction (GOLD I-IV)); disease group (determined by the intensity of symptoms and frequency of exacerbations, Table 8); presence/absence of exacerbation (if there is an exacerbation, it is also necessary to indicate its severity —

severity of clinical symptoms (Table 9, Appendix 2, 3); finally, it is also necessary to list complications and concomitant diseases that may affect the course of COPD. For example: "COPD, bronchitis type, moderate severity (GOLD II), group B, exacerbation of moderate severity. CRF of the 2nd stage. Obesity of the 2nd degree (BMI is 36 kg/m^2)".

Types of COPD are possibly to find in the International Classification of Diseases, 10th Revision (ICD-10) which provides the following coding features for COPD:

• J44. 8 — Other specified chronic obstructive pulmonary disease. Bronchitis type, emphysematous type, mixed type.

Assessing the severity and stage of COPD. Previously, the classification of COPD was based on indicators of the functional state of the lungs, based on post-bronchodilation values of forced expiratory volume in 1 second (FEV1), and distinguished 4 stages of the disease (Table 7).

Table 7

Spirometric (functional) classification of COPD

GOLD stage of COPD	Severity	FEV1 / FVC	FEV1, % predicted
I	Mild	< 0.7 (70 %)	FEV1 ≥ 80 %
II	Moderate	< 0.7 (70 %)	50 % ≤ FEV1 < 80 %
III	Severe	< 0.7 (70 %)	30 % ≤ FEV1 < 50 %
IV	Very severe	< 0.7 (70 %)	FEV1 < 30 % or < 50 % +combined with chronic respiratory failure

COPD group assessment. The GOLD document (Global Initiative for Chronic Obstructive Lung Disease, revised 2011) proposed a new classification based on an integrated assessment of the severity of COPD (Table 8). This takes into consideration not only the degree of bronchial obstruction based on the results of a study of unprovoked respiratory volumes and flows (spirometric test), but also clinical data about the patient — the number of COPD exacerbations in 1 year and the severity of clinical manifestations according to the mMRC scale (modified Medical Research Council Dyspnea Scale) and the CAT test (COPD Assessment Test, Appendix 2, 3, 4).

Table 8

COPD groups classification

Group of patients	Characteristic	Spirometry classification	Number of exacerbations in 1 year	mMRC scale	CAT test
A	Low risk of exacerbations Symptoms are not significant	GOLD 1–2	≤ 1	0–1	< 10
B	Low risk of exacerbations Significant symptoms	GOLD 1–2	≤ 1	≥ 2	≥ 10
C	High risk of exacerbations Symptoms are not significant	GOLD 3–4	≥ 2	0–1	< 10
D	High risk of exacerbations Significant symptoms	GOLD 3–4	≥ 2	≥ 2	≥ 10

When assessing risk, it is recommended to select the highest degree based on GOLD airflow limitation or history of exacerbations. It also important that if a patient had at least one exacerbation leading to hospitalization during the previous year (i.e., *a severe exacerbation*), they should be classified as high-risk.

Assessment of COPD exacerbations. Exacerbation of COPD is an acute event characterized by a worsening of respiratory symptoms beyond their normal daily fluctuations (Appendix 2, 3, 4) and leads to a change in the therapy regimen used.

Exacerbation of COPD leads to a long-term period (up to several weeks) of deterioration in respiratory function and gas exchange. Moreover, exacerbations of COPD lead to decompensation of concomitant chronic diseases. One of the most well-known classifications of the severity of COPD exacerbation is presented in Table 9.

Table 9

Classification of the severity of COPD exacerbations

Severity	Level of medical care
Mild	Patient needs an increase in the volume of therapy, which can be carried out by the patient on their own
Moderate	Patient needs to increase the volume of therapy (prescription of antibiotics and/or systemic glucocorticosteroids), which requires consultation with a physician
Severe	Patient/physician notes a clear and/or rapid worsening of the patient's condition. Patient is required to be hospitalized

It has been noted that exacerbations of COPD most often develop in the autumn and winter months. The most common causes of COPD exacerbations are bacterial (Haemophilus influenzae, Streptococcus pneumoniae and Moraxella catarrhalis, Enterobacteria and Pseudomonas aeruginosa) and viral (Rhinoviruseres) respiratory infections and air pollutants, but the causes of approximately 20–30 % of exacerbations cases cannot be determined. Conditions that may resemble and/or cause COPD exacerbations include pneumonia, pulmonary embolism, congestive heart failure, pneumothorax and pleural effusion. These conditions should be differentiated from exacerbations and, if present, appropriate treatment should be carried out.

DIAGNOSIS OF COPD

The diagnosis of COPD is recommended to be established the basis of patient’s complaints, medical history, results of a physical examination and data from functional examination methods and after excluding other diseases.

When taking an anamnesis it is recommended to assess smoking status and determine the smoking index. It is also recommended to assess the frequency of previous exacerbations of COPD. Exacerbations of COPD are considered frequent if they occur 2 or more times a year. In patients with COPD, screening for comorbidities is recommended because COPD is often associated with cardiovascular diseases, skeletal muscle dysfunction, osteoporosis, lung cancer, and depression.

Laboratory examination plan: *complete blood count* (CBC) is recommended for all patients with COPD to screen for common pathologies; *laboratory testing of sputum* is also recommended (general analysis, sputum culture for flora and its sensitivity to antibiotics).

Instrumental examination plan: all patients with suspected COPD are recommended to have functional testing (spirometry and pneumotachometry) to identify and assess the severity of airway obstruction; *the criterion "FEV1/FVC < 0.7" confirms expiratory airflow limitation*.

If signs of bronchial obstruction are detected (FEV1 FVC < 0.7), a *bronchodilation test* is recommended to determine the degree of obstruction reversibility after using of bronchodilator medications. As bronchial obstruction progresses, there is a further decrease in expiratory flow, an increase in air traps and LHI, which leads to a decrease in FVC.

To exclude mixed obstructive-restrictive disorders in patients with decreased FVC, it is recommended to determine TLC using *body plethysmography*. To assess the severity of emphysema, it is recommended to use TLC determination and an assessment of the diffusion capacity of the lungs.

All patients with COPD are recommended to use *pulse oximetry* to assess hemoglobin oxygen saturation (SaO_2). Hypoxemia is an important issue in patients with COPD, determining exercise intolerance and disease prognosis. If patient with COPD has erythrocytosis, hypoxemia should also be suspected.

Study of the *acid-base composition and blood gas composition* is recommended for patients with COPD and SaO_2 <= 92 %.

To determine exercise tolerance in patients with COPD, *exercise testing, such as a 6-minute walk test* or, in some cases, *bicycle ergometry*, is recommended.

Radiological methods. *Anterior chest x-ray* is recommended in all patients with suspected COPD to rule out other respiratory diseases. Chest x-ray is not sensitive enough to detect mild to moderate emphysema. Chest HRCT is recommended only in patients with COPD and severe emphysema to determine the feasibility of surgical lung lung volume reduction.

It is recommended to determine the *level of α1-antitrypsin* in the blood of patients with COPD younger than 45 years of age, patients with rapid progression of COPD, or in the presence of emphysema, mainly in the basal parts of the lungs.

In case of increased daytime sleepiness, *nighttime pulse oximetry* is recommended for the initial screening diagnosis of sleep breathing disorders, followed by diagnosis using *polysomnography*.

The main prognostic factors in a patient with COPD are the degree of bronchial obstruction (FEV1), the severity of dyspnea, the distance traveled by the patient during the 6-minute walk test and body mass index.

Differential diagnosis of COPD. At certain stages of COPD development, especially at the first meeting with the patient, it becomes necessary to differentiate COPD from a number of diseases with similar symptoms — BA, chronic (non-obstructive) bronchitis, lower respiratory tract infections (including pneumonia), also from lung cancer, interstitial lung diseases and cardiovascular diseases.

When differentially diagnosing bronchial asthma and COPD, it is recommended to take into consideration a history of smoking and allergy, clinical picture and comorbidities, and family history.

The main distinguishing features of asthma and COPD are the following: risk factors for the development of asthma include allergens, loaded heredity, onset at a young age (common) and conversely, risk factors for COPD include smoking and air pollutants, onset typically occurs in adulthood; clinical manifestations of asthma are attacks of dyspnea and suffocation, however, with COPD, dyspnea is constant and gradually progressive; airway obstruction is reversible in asthma (spontaneously or with treatment) and irreversible in COPD.

COPD TREATMENT

COPD therapy includes non-pharmacological and pharmacological approaches.

1. *Non-pharmacological options* include smoking cessation, pulmonary rehabilitation, oxygen therapy, respiratory support, and surgery.

2. *Pharmacological treatments* include bronchodilators, combinations of ICS and long-acting bronchodilators, phosphodiesterase-4 inhibitors, theophylline, and influenza and pneumococcal vaccinations.

When prescribing pharmacotherapy, it is recommended to achieve control of symptoms and reduce future risks, such as exacerbation of COPD and mortality. The decision to continue or discontinue treatment is recommended to be made on the basis of reducing future risks (exacerbations).

All patients with COPD are recommended to implement non-pharmacological measures, prescribe a short-acting bronchodilator (medication for the treatment of obstructive respiratory disease) for use as needed, and treat concomitant diseases.

Principles of treatment for stable COPD (no exacerbation) are presented in Table 10.

For all patients with COPD, LABA is recommended, or combination of LAAC/LABA or one of these medications by monotherapy. If the patient has severe symptoms (mMRC ≥ 2 or CAT ≥ 10), the combination of LAAC/LABA is recommended immediately after the diagnosis of COPD is established.

Most patients with COPD experience rather severe symptoms, such as intense shortness of breath and decreased exercise tolerance. Administration of the combination of LAAC/LABA allows, due to maximal bronchodilation, to relieve shortness of breath, increase exercise tolerance and improve the quality of patient's life. Initiation of monotherapy with a single long-acting bronchodilator (LAAC or LABA) is recommended for patients with mild symptoms (mMRC < 2 or CAT < 10) and if there is a contraindication to one of the components of the medication combination. The advantage of LAAC is a more if symptoms persist (shortness of breath and reduced exercise tolerance) during monotherapy with LABA alone, it is recommended to intensify bronchodilator therapy — switch to a combination of LAAC/LABA. In case of repeated exacerbations (2 or more

moderate exacerbations within 1 year or at least 1 severe exacerbation requiring hospitalization) in patients receiving mono-component bronchodilation, it is recommended to increase the volume of therapy to a double combination of LAAC/LABA or IGCS/LABA. The choice of IGCS /LABA is preferable in case of peripheral blood eosinophilia of 100 cells in 1 ?l, as well as in the presence of a history of bronchial asthma. It is recommended to switch the patient to triple therapy (LAAC/LABA/IGCS) if the combination of LABA/IGCS or LAAC/LABA combination is insufficiently effective (taking into consideration the level of eosinophylia) and /or history of BA.

Table 10

Pharmacological classes of medications used in the treatment of COPD

Pharmacological class	Decoding abbreviations	Medications
SABA	Short-acting β2-agonists	Salbutamol, Fenoterol
LABA	Long-acting β2-agonists	Indacaterol, Formoterol
SAAC	Short-acting anticholinergics	Ipratropium bromide
LAAC	Long-acting anticholinergics	Aclidinium bromide, Glycopyrronium bromide, Tiotropium bromide
IGCS	Inhaled glucocorticosteroids	Budesonide, Fluticasone
Fixed combinations LAAC/LABA	Long-acting anticholinergics / long-acting β2-agonists	Glycopyrronium bromide + Indacaterol, Tiotropium bromide + Olodaterol, Vilanterol + Umeclidinium bromide, Aclidinium bromide + Formoterol
Fixed combinations of IGCS/LABA	Inhaled glucocorticosteroids / long-acting β2-agonists	Beclomethasone + Formoterol, Budesonide + Formoterol, Salmeterol + Fluticasone, Vilanterol + Fluticasone furoate
Fixed combinations of LABA/LAAC/GCS	Long-acting anticholinergics / long-acting β2-agonists / glucocorticosteroids	Vilanterol + Umeclidinium bromide + Fluticasone furoate
PDI	Phosphodiesterase-4 inhibitors	Roflumilast
SGCS	Systemic glucocorticosteroids	Methylprednisolone, Dexamethasone
Others	–	Theophylline, antibiotics, expectorants

For patients with COPD who also have upper lobes emphysema and poor exercise tolerance, lung volume reduction surgery is recommended. Lung reduction surgery is performed by removing part of the lung to reduce hyperinflation and allow the breathing muscles to function more efficiently. Currently, less invasive methods can also be used to reduce lung volume — occlusion of segmental bronchi using valves, special glue, etc. Lung transplantation (in the absence of alternative treatment options) can improve the quality of life and functional pulmonary parameters in patients with COPD.

One of the most severe complications of COPD, developing in the late (terminal) stages, is chronic respiratory failure (CRF), requiring the use of long-term oxygen therapy. Indications for long-term oxygen therapy: PaO_2 less than 55 mm Hg, SaO_2 less than 88 %), cor pulmonale, edema, polycythemia (Ht > 55 %).

Treatment of exacerbations of COPD and their management. Patients with exacerbation of COPD are recommended to be hospitalized in the presence of the following indications*:* significant increase in severity and/or appearance of new clinical symptoms (dyspnea at rest, unstable hemodynamics, deterioration of mental state, cyanosis, peripheral edema, signs of fatigue of the respiratory muscles), a drop in SaO_2 < 90 % (or 4 % or more from the initial level); inability to stop exacerbation with initial therapy. As a mandatory diagnostic minimum upon admission to a hospital, it is recommended to perform a detailed clinical blood test, examination of C-reactive protein in blood serum, pulse oximetry, chest X-ray, and electrocardiography.

Bronchodilators are a key element in the treatment of COPD exacerbations. All patients with exacerbation of COPD are recommended to be prescribed inhaled bronchodilators — SABA (Salbutamol, Fenoterol) or SAAC (Ipratropium bromide). Beta-agonists (selective beta2-adrenergic agonists) have a faster onset of action, while anticholinergics are highly safe and well tolerated. Increasing the dose of SABA and SAAC, especially when administered via a nebulizer, may further relieve dyspnea during an exacerbation of COPD. Side effects are usually dose-dependent.

Systemic corticosteroids shorten the time before remission onset, improve pulmonary function (FEV1) and reduce hypoxemia, and can also reduce the risk of early relapse and treatment failure, and shorten the length of hospital stay. Short-term treatment with systemic or inhaled corticosteroids is recommended for all patients with exacerbation of COPD requiring hospitalization. A safer alternative to systemic corticosteroids for exacerbation of COPD are inhaled corticosteroids, especially when administered via a nebulizer. Patients with exacerbation of COPD and blood eosinophilia > 2 % have a better response to systemic corticosteroids.

Antibiotic therapy is recommended for patients with exacerbation of COPD — with increased dyspnea, an increase in the volume and degree of purulence of sputum (in the presence of at least two of the three listed signs). The most common microorganisms are Haemopylus influenza / Moraxella catarrhalis / Streptococcus pneumoniae / Chlamydia pneumoniae / Mycoplasma pneumoniae. The use of Amoxicillin, macrolides (Azithromycin, Clarithromycin), and third-generation cephalosporins (Cefixime, etc.) is usually considered effective. For mild to moderate COPD: Amoxicillin+Clavulanic Acid, fluoroquinolones (Levofloxacin, Moxifloxacin). Severe COPD: Ciprofloxacin and other medications with antipseudomonal activity.

Non-invasive pulmonary ventilation (NIV) provides safe and effective relaxation of the respiratory muscles, restoration of gas exchange and reduction of dyspnea in a patient with ARF. In patients with COPD, as well as with the development of ARF , NIV is recommended in the presence of the following symptoms: severe dyspnea at rest; respiratory rate > 24 per 1 min, participation of auxiliary respiratory muscles in breathing; signs of impaired gas exchange ($PaCO_2$ > 45 mm Hg, pH < 7.35, PaO2/FiO_2 < 200 mm Hg).

Artificial lung ventilation (ALV) is recommended for patients with COPD + ARF whose condition does not improve with medication therapy and NIV. Indications for mechanical ventilation should take into consideration not only the lack of effect of conservative methods of therapy and the severity of changes in respiratory function, but also the tempo of their development and the potential reversibility of the process that caused ARF. *Absolute indications for ALV:* respiratory arrest; severe disturbances of consciousness (stupor, coma); unstable hemodynamics (systolic blood pressure < 70 mm Hg, heart rate < 50/min or > 160/min); tiredness of the respiratory muscles. *Relative indications for ALV:* respiratory rate > 35/min; arterial blood pH < 7.25; PaO_2 < 45 mm Hg, despite oxygen therapy.

COPD PROPHYLAXIS

Identification, reduction and control of risk factors such as smoking, occupational exposure and indoor pollution are recommended as measures to prevent COPD.

Annual influenza vaccination is recommended for all patients with COPD to reduce the risk of exacerbations. Influenza vaccination for people over 65 years of age significantly reduces the risk of pneumonia, hospitalization, and death. Vaccination against pneumococcal disease is also recommended for COPD patients.

TASKS FOR INDEPENDENT WORK OF STUDENTS

1. Possible causes of allergic BA exacerbations are:

a) food products;
b) medications;
c) pollen allergens;
d) warm weather.

2. BA attack is characterized by the following:

a) suffocation;
b) frequent urination;
c) cough;
d) body temperature increase.

3. Auscultatory signs of the 2nd stage of Asthmatic Status are:

a) bronchial breathing;
b) weakened vesicular breathing;
c) “a silent lung” symptom;
d) rough breathing.

4. Auscultatory signs of the 1st stage of Asthmatic Status are:

a) bronchial breathing;
b) weakened vesicular breathing;
c) saccadic (intermittent) breathing;
d) dry rales (rhonchi).

5. Complaints of patients with COPD are:

a) skin itching; b) cough; c) sputum; d) dyspnea.

Answers: 1 – a, b, c; **2** – a, c; **3** – b, c; **4** – b, d; **5** – b, c, d.

LITERATURE

Basic

1. *Global* Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2020. Mode of access: www.ginasthma.org. Date of access: 15.08.2024.

2. *Global* Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. 2020. Mode of access: https://goldcopd.org. Date of access: 15.08.2024.

3. *Пронько, Т. П.* Пропедевтика внутренних болезней = Propedeutics of Internal Diseases : учеб. пособие / Т. П. Пронько. Минск : Адукацыя і выхаванне, 2020. 472 с.

4. *Bickley, L. S.* Bates' guide to physical examination and history taking / L. S. Bickley ; guest ed. R. M. Hoffmann. 12th ed. Philadelphia (etc.) : Wolters Kluwer, 2017. 1034 p.

5. *Nemtsov, L. M.* Special Propedeutics of Internal Diseases : Lecture course / L. M. Nemtsov. Витебск : ВГМУ, 2016. 319 с.

Additional

6. *Kovalyova, O. M.* Propedeutics of internal medicine. Part 2. Syndromes and diseases: textbook for English learning students of higher medical schools / O. M. Kovalyova. 3rd ed. Vinnytsia : Nova Knyha, 2017. 264 p.

7. *Diagnosis* and Management of Difficult-to-treat and Severe Asthma in adolescent and adult patients // A GINA pocket guide for health professionals. 2019. Vol. 2.0. Mode of access: www.ginasthma.org. Date of access: 15.08.2024.

8. *World* Health Organization. Evidence-informed policy-making. 2016. Mode of access: http://www.who.int/evidence. Date of access: 15.08.2024.

9. *Efficacy* and safety of once-daily single-inhaler triple therapy (FF/UMEC/VI) versus FF/VI in patients with inadequately controlled asthma (CAPTAIN): a double-blind, randomised, phase 3A trial / L. A. Lee [et al.] // Lancet. 2021. Vol. 9, Is. 1. P. 69–84.

10. *Wise, R.* Treatment of Acute COPD Exacerbation. Last full review / revision. Jun 2020 / R. Wise. Mode of access: https://www.merckmanuals.com professional/pulmonary-disorders / chronicobstructive-pulmonary-disease-and-related-disorders/treatment-of-acute-copd-exacerbation. Date of access: 15.08.2024.

11. *Diagnosing* COPD in primary care: what has real life practice got to do with guidelines? / G. Ragaisiene [et al.] // Multidiscip. Respir. Med. 2019. Vol. 14, N 28.

12. *Time* to revise COPD Treatment Algorithm / K. Matsunaga [et al.] // Int. J. Chron. Obstruct. Pulmon. 2019. Vol. 14. P. 2229–2234.

13. *Standardization* of Spirometry 2019 Update / B. L. Graham [et al.] // An Official American Thoracic Society and European Respiratory Society.

14. *COPD* management by Swedish general practitioners — baseline results of the PRIMAIR study / H. Sandelowsky [et al.] // Scand. J. Prim. Health Care. 2018. Vol. 36 (1). P. 5–13.

Appendix 1

ASTHMA CONTROL QUESTIONNAIRE

Please answer Questions 1–5.

Circle the number of the response that best describes how you have been during the past week.

1. On average, during the past week, how often were you woken by your asthma during the night?
   - 0 Never
   - 1 Hardly ever
   - 2 A few times
   - 3 Several times
   - 4 Many times
   - 5 A great many times
   - 6 Unable to sleep because of asthma

2. On average, during the past week, how bad were your asthma symptoms when you woke up in the morning?
   - 0 No symptoms
   - 1 Very mild symptoms
   - 2 Mild symptoms
   - 3 Moderate symptoms
   - 4 Quite severe symptoms
   - 5 Severe symptoms
   - 6 Very severe symptoms

3. In general, during the past week, how limited were you in your activities because of your asthma?
   - 0 Not limited at all
   - 1 Very slightly limited
   - 2 Slightly limited
   - 3 Moderately limited
   - 4 Very limited
   - 5 Extremely limited
   - 6 Totally limited

4. In general, during the past week, how much shortness of breath did you experience because of your asthma?
   - 0 None
   - 1 A very little
   - 2 A little
   - 3 A moderate amount
   - 4 Quite a lot
   - 5 A great deal
   - 6 A very great deal

5. In general, during the past week, how much of the time did you wheeze?
   - 0 Not at all
   - 1 Hardly any of the time
   - 2 A little of the time
   - 3 A moderate amount of the time
   - 4 A lot of the time
   - 5 Most of the time
   - 6 All the time

Interpretation of ACQ-5 results. The ACQ-5 score ranges from 0 (good control) to 6 (extremely poor control). Each question is scored on a scale from 0 to 6, then a total score is calculated, which is the average of all questions. With well-controlled asthma, the total score ranges from 0–0.75; with partially controlled from 0.75–1.5; with insufficiently controlled > 1.5 total score.

Appendix 2

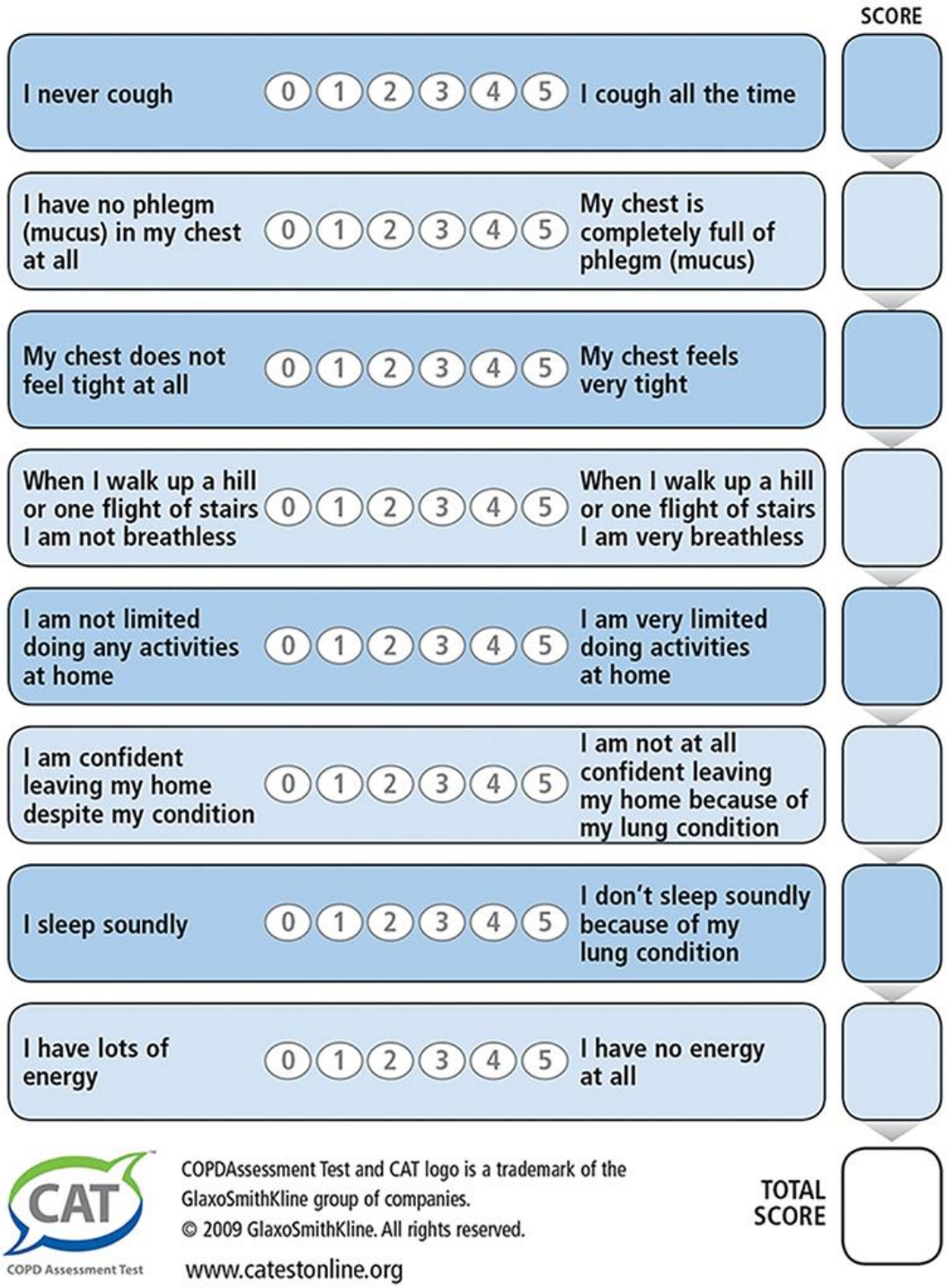
mMRC scale (modified Medical Research Council Dyspnea Scale)

Modified MRC Dyspnea Scale

Used with Permission from 2020, Global Initiative for Chronic Obstructive Lung Disease (GOLD), available from www.goldcopd.org

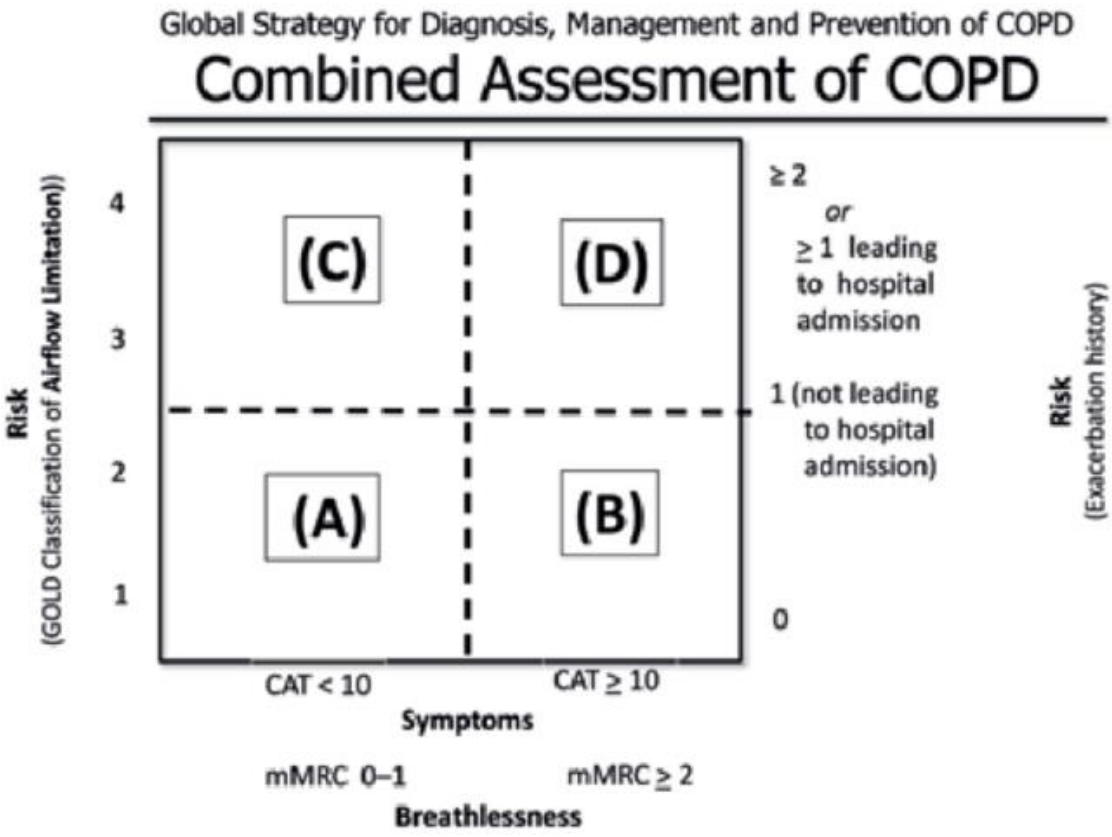
MRC Grade	Description	MRC Severity Grouping
1	Breathless with strenuous exercise	MILD
2	Short of breath when hurrying on the level or walking up a slight hill	MODERATE
3	Walks slower than people of the same age on the level or stops for breath while walking at own pace on the level	
4	Stops for breath after walking 100 m	SEVERE
5	Too breathless to leave the house or breathless when dressing	

CAT (COPD Assessment Test)



Appendix 4

SCALE FOR COPD ASSESSMENT



CONTENT

Учебное издание

Арсентьева Ирина Леонидовна
Доценко Эдуард Анатольевич
Арсентьева Наталья Леонидовна

СИМПТОМАТОЛОГИЯ, ДИАГНОСТИКА, ПРИНЦИПЫ ЛЕЧЕНИЯ И ПРОФИЛАКТИКИ БРОНХИАЛЬНОЙ АСТМЫ И ХРОНИЧЕСКОЙ ОБСТРУКТИВНОЙ БОЛЕЗНИ ЛЕГКИХ

SYMPTOMS, DIAGNOSIS, PRINCIPLES OF TREATMENT AND PREVENTION OF BRONCHIAL ASTHMA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Учебно-методическое пособие

На английском языке

Ответственный за выпуск Э. А. Доценко
Компьютерная вёрстка Н. М. Федорцовой

Подписано в печать 21.05.24. Формат 60×84/16. Бумага писчая «Xerox Марафон Бизнес».
Ризография. Гарнитура «Times».
Усл. печ. л. 1,86. Уч.-изд. л. 1,7. Тираж 90 экз. Заказ 311.

Издатель и полиграфическое исполнение: учреждение образования
«Белорусский государственный медицинский университет».
Свидетельство о государственной регистрации издателя, изготовителя,
распространителя печатных изданий № 1/187 от 24.11.2023.
Ул. Ленинградская, 6, 220006, Минск.