
# МАТЕРИАЛЫ ПЕРВОГО ЕВРАЗИЙСКОГО РЕСПИРАТОРНОГО КОНГРЕССА

# MATERIALS OF THE FIRST EURASIAN RESPIRATORY SUMMIT

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# CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN REPUBLIC OF MOLDOVA

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Chronic Obstructive Pulmonary Disease (COPD), being a major cause of morbidity and mortality worldwide, is a major problem for public health. It is predicted that its burden will continuously expand over the next years.

In Republic of Moldova there is no official data on prevalence of COPD. We expect high prevalence of COPD in general population, which is determined by underdiagnosis, underestimation of obstructive respiratory diseases, and as a result draws undertreatment. Republic of Moldova is a low-incoming country with very high prevalence of smoking in general population (28% 2012 WHO report). We plan to carry out Burden of Obstructive Lung Diseases (BOLD) Project with primary objectives: to measure the prevalence of COPD and its risk factors in Republic of Moldova in comparison with another countries; to estimate the burden of COPD in terms of its impact on quality of life, activity limitation, respiratory symptoms, and use of health care services and to develop a validated model to project future burden of disease for COPD.

For identification of problems in management of COPD in Moldova we have fulfilled detailed SWOT analysis.

Strengths of our healthcare system are: range of staff expertise, a highly integrated team that is able to adapt itself quickly and efficiently, in-depth knowledge of our patient population, emphasis on a patient centric approach to problem solving approach, dedication and commitment, connections with and active collaboration in the Community and with International Scientific Societies.

Still, the weaknesses we face are: COPD is underdiagnosed, underestimated and undertreated, a lack of awareness of medical community and general population for COPD, lack of interaction with specialists in related fields, evidence based COPD guidelines are available, but not implemented, limited access to COPD education for patients, Care Pathways are fragmented and not integrated, both across organizations and between health care professionals, resulting in fragmented access to services.

Opportunities are: a need of BOLD study to identify the unapproached needs in the chronic respiratory disease management, a need for more evidence-based care of COPD, a need for a better standardization of COPD assessment processes and formats, a need for improved collaboration with primary health care providers, need of more emphasis on prevention in primary care setting.

Threats are: access to medications – financial impacts, potential changes in government and funding models, any changes in government policies, an ageing population with changing patient demographics which will require increased funding to support their care and recruitment, growth and staff retention issues.

# INTERSTITIAL LUNG DISEASES. CLASSIFICATION AND THERAPEUTIC APPROACH

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Interstitial lung diseases (ILDs) encompass a large group of diseases characterized with interstitial inflammatory changes and a fibrosis. The severity of the ILDs mostly depends on the fibroproliferative potential of the pathogenic process in lung interstitium. The typical clinical picture of ILDs encompasses exertion dyspnea and in some ILDs also finger-clubbing and bilateral basal crackles called velcro-rales (typical for idiopathic pulmonary fibrosis- IPF). High resolution computed tomography (HRCT) of lungs is one of the best, if not ultimately the best, method for showing typical changes in ILDs and is very helpful in their diagnosis and differential diagnosis. Moreover an extent of reticulation and honey-combing on HRCT is an important independent predictor of mortality in patients with IPF. Functional investigation shows the severity of the ILDs and enables evaluation of disease progression during follow-up. Bronchoalveolar lavage (BAL) is recommended in most of the patients with ILDs although it has rather differential diagnostic than diagnostic role.

Idiopathic pulmonary fibrosis (IPF), also known as cryptogenic fibrosing alvelitis (CFA), belongs to a group of idiopathic interstitial pneumonias (IIPs) and has the worst prognosis of them all. It is a severe disease with grim prognosis despite the treatment,with a mean survival 3-5 years from a diagnosis. The IPF prevalence is 13-20/100.000 and the incidence 7-11/100.000 and it is estimated that IPF affects to date 5 million people worldwide but may be even more due to undiagnosed cases. Recently a repeated injury of alveolar walls leading to uncontrolled healing is mostly accepted as main pathogenetic mechanism in IPF. The inflammatory reaction is supposed to be secondary, if any. Thus, treatment of IPF should primarily be targeted against excessive fibroproliferation. The first drug for IPF that can slow-down its progression is pirfenidon (Esbriet, InterMune). Pirfenidon is indicated in patients with mild and moderate IPF.

Amongst the ILDs characterized mainly by inflammatory changes and lesser extent of fibroproliferation are most frequently seen nonspecific pneumonia (NSIP) and hypersensitivity pneumonity (HP). NSIP also belongs to the IIPs group, but compared to IPF has different distribution of radiologic changes and more pronounced inflammation. Hypersensitivity pneumonitis belongs to primarily granulomatous ILDs caused by repeated inhalation of organic antigen in genetically predisposed individual. It is oftenly underdiagnosed because the source antigen might not be revealed. Treatment of primarily inflammatory ILDs is based on immunosuppressive drugs, i.e. corticosteroids alone or in combination with immunosuppresants, mainly azathioprine.

In ILDs properly and early stated diagnosis enables the patients get appropriate care and treatment which substantially improve their prognosis.

# HIGH ALTITUDE AND RESPIRATORY DISEASE

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Kyrgyz Republic it is mountainous country, located in the Central Asia the population is 5 million. 94% of territory of Kyrgyz republic is occupied by the Tien-Shan and Pamir ranges with the average altitude 2750 m above sea level. This problem, relation with highlanders so is important in the world because over 140 M people lived at altitudes of 2,500 meters and more at the end of the 20th century (WHO, 1996). In Kyrgyzstan, around 200,000 adult population live in highland areas (Mirrakhimov et al., 2002), and total population is 5 million

The main factor of the mountain climate is the oxygen partial pressure in the air. With increasing altitude, we will have a dip of the oxygen partial pressure – exogenous high altitude hypoxia. This is crucial in the mobilization of adaptive physiological responses. Physiological and clinical effects of the mountain climate depend on the altitude of the mountains.

Kyrgyz Republic has the highest death rate from respiratory diseases in Eastern Europe and Central Asia, more than 250 cases per 100 000 population.That is why we have a big scientific interest and following main focus of studies: use of high-altitude climate for the therapeutic and rehabilitation purposes on bronchial asthma and allergic diseases, modifying effects of high-altitude climate on respiratory diseases (COPD, obstructive sleep apnea etc.), sicknesses appearing at high altitudes.

We have a good experience to use the mountain climate for treatment and rehabilitation of asthma patients. Since 1968, Kyrgyzstan has used high altitude climate to treat patients with bronchial asthma. On the Tuya-Ashu pass we have a High altitude hospital (Northern Tien-Shan, 3,200 m above sea level). More than 2,000 patients took the treatment with a positive result. In our research, 84% of asthma patients have a good effect, and 32% of asthma patients have good control during 12 months. During high-altitude rehabilitation significantly reduced the

frequency of daytime and nighttime asthma symptoms, reduced frequency of use of the short action B2-agonists. We observed a reduction of bronchial hyperresponsiveness in patients with asthma in the mountains. An important fact – we found a significant reduction of general and specific JgE in asthma patients after high-altitude rehabilitation. We also had the result, which showed decrease in the number of inflammatory cells in bronchoalveolar lavage fluid, increase synthesis of endogenous cortisol after high altitude rehabilitation. Thus, the effects of high altitude climate therapy associated with increased synthesis of endogenous cortisol and activation of the sympathetic nervous system, which leads to a reduction of inflammation and reduction of bronchial hyperresponsiveness, and provided good control of symptoms.

COPD is another very important problems, especially for highlanders. In Kyrgyzstan, the highest mortality rates from COPD, 95 per 100 000 population (European Lung White Book, 1993). Particularly bad situation for COPD mortality among residents of high mountains, the mortality rate among the highlanders are 2-3 times higher than that among lowlanders. In our country also a high prevalence of COPD among the highlanders than lowlanders. The distribution of patients by age showed an increase in the prevalence of COPD in patients older than 40 years to 25.4%. It is 4 times higher than the official statistics.

Smoking is a major risk factor of COPD among highlanders, we found 60% male smokers. Indoor pollution is a very important reason for the development and progression of COPD among highlanders, especially for women and children. Each highlanders family have large reserves of biomass (dung), which are the main fuel for heating and cooking. Noteworthy is the negative impact of smoke, when many highlanders use open fire for cooking. Also an important risk factor could be the smoke from cooking. We got interesting results, the frequency of respiratory symptoms in 2 times higher in families where they use of biomass than in families where they use of other fuels.

What we can say about the clinical features of COPD in the inhabitants of the mountains. We observed a significant dyspnoea in highlanders with COPD, also in GOLD stages I and II. The quality of life of the mountain people with COPD was

also worse than lowlanders. We also found a significant reduction in physical activity in highlanders with COPD. For 6 minutes, they could go much smaller distance than lowlanders.

Thus, COPD is one of highly prevalent diseases of highlanders which causes high mortality. Major COPD risk factors for highlanders include indoor pollutants and tobacco smoking. COPD in highlanders is severe and progressive.

Prioritized studies in future: to continue the studies of diseases appearing at high altitudes - High-altitude pulmonary hypertension, to research secondary pulmonary hypertension induced by COPD, to research sleep disorders breathing in highlanders.

# DIAGNOSTIC AND TREATMENT APPROACH OF VENOUS TROMBEMBOLIA IN PREGNANCY

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Pulmonary embolism (PE) is a leading cause of death among pregnant women in the developed world.[1] Pregnancy increases the risk of venous thromboembolism (VTE) 4- to 5-fold over that in the nonpregnant state.[2, 3] All 3 elements of Virchow's triad are present during pregnancy and the early postpartum period; they are hypercoagulability, vascular damage, and venous stasis.The 2 manifestations of VTE are deep venous thrombosis (DVT) and pulmonary embolus (PE). Although most reports suggest that VTE can occur at any trimester in pregnancy, some studies suggest that VTE is more common during the first half of pregnancy. Sequelae of DVT and PE include complications such as pulmonary hypertension, post-thrombotic syndrome, and venous insufficiency.

The fact that PE remains such a threat is a clear indication of the difficulty in diagnosing it.

The signs and symptoms of VTE are nonspecific and common in pregnancy. Diagnosis of VTE by physical examination is frequently inaccurate, even though one study found that 80% of pregnant women with DVT experience pain and swelling of the lower extremity.

Clinical signs and symptoms of PE are rarely encountered together; the classic symptoms are as follows[4] :Dyspnea - 82%, Abrupt onset of chest pain - 49%, Cough - 20% The most common presenting signs of PE are as follows:Tachypnea, Crackles,Tachycardia. Patients with massive PE may present with the following:syncope,hypotension,pulseless cardiac electrical activity,death.

The coexistence of pregnancy makes the workup and management of PE even more problematic, for many reasons. First, there are 2 patients at risk rather than 1. Second, overdiagnosis results in unnecessary, dangerous treatments that jeopardize

both patients and makes the pregnancy and delivery far more complicated. Third, the usual imaging modalities, which we use without a second thought in nonpregnant patients, suddenly become more complicated in pregnant patients.

The authors point out the differences which exist in diagnostic approach between non pregnant and pregnant subjects. Will we trust d- dimer as biomarkers in diagnosis of VTE in pregnant subjects?

Which are the diagnostic steps in diagnosis of PE in pregnant women? The decision to use imaging modalities that produce radiation exposure in pregnant patients is difficult because of concerns with teratogenicity. Radiation exposure of 1 Gy at any stage of pregnancy is regarded as the level above which the risk for induction of congenital abnormalities is possible. The authors present the imaging tools commonly used in PE diagnosis.

Which are the major benefits of one imaging procedure to another one? Which is the accuracy and outcome of these diagnostic imaging procedures?

With heparin treatment which are alternative approaches? During low molecular heparin treatment should we measure the the factor Xa? How long we have to continue the anticoagulant treatment and when we have to switch from heparin in vitamin K antagonists? Could we prevent venous trombembolia in pregnancy and how?

The authors try to give answer all this questions which we are faced in practice.

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# APPROACH TO COPD AND CHRONIC RESPIRATOY DISEASES IN MACEDONIA- CAN WE DO MORE FOR OUR PATIENTS?

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Chronic obstructive pulmonary disease is a global health problem, affecting 15-20 % of the population of the developing countries and representing a huge economic burden because of its large direct and indirect costs. Even though traditionally referred to as “a disease of the elderly”, more than 60% of the affected population is between 45 and 65 years old, in the peak of their professional and physical activity, affecing not only the patients, but also their families, employers and the society in general. The importance of the problem increases in the developing countries, such as Macedonia, because of the high incidence of active and passive smoking, the high percentage of indoor pollution due to usage of organic heating materials in the rural regions and the high and uncontrolled atmospheric pollution in the industrialized regions. The centuries long tradition of growing, processing and consummation of tobacco involves whole families and takes part in the GDP of the country. The high prevalence of smoking and the lack of resources for epidemiologic surveys complicates gathering the necessary data to create a comprehensive picture of the problem of COPD in the country. Part of the efforts to surpass the problem of detection and standardization of the treatment of COPD in Macedonia is implementing the international guidelines in the several editions of the National guidelines for COPD, revised in 2012 and the creation of a network of fourteen regional Centres for asthma and COPD with educated personal and available basic spirometry for accurate diagnosis.

COPD is a highly invalidating disease which can not be cured, but treatments are available for improving quality of life of the patients, their physical, social and professional rehabilitation and for reducing the rate of exacerbations and dynamics of loss of lung function, consequently reducing mortality. New treatments which target airways and systemic inflammation in COPD are already introduced in Europe , but unfortunately not available in the developing countries due to high cost,

leaving the treatment choices to the LABA, LAMA or ICS/LABA combination therapy, and /or methilxantines as the most affordable.

The natural history of COPD is associated with vast co-morbidities and progressive, irreversible loss of lung capacity, but prevention is possible and recommended. Joint efforts of health professionals, national governments, employers, unions, mass media, patients and the general population as well as positive legal regulations are necessary in the global fight for reducing the prevalence of this global health and socio-economic problem.

# USAGE OF B- BLOCKERS IN COMBINATION WITH CORONARY HEART DISEASE AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Among all drugs, β- blockers (β- AP), which proved a positive impact on cardiovascular system occupy a leading position.

New direction of development pharmaceutics is create drugs, directly regulated the synthesis of endothelial NO. The first in this class should be considered a new original preparation nebivolol- β1- blocker of the third generation (company "Berlin-Chemie, Menarini Group", Germany).

The aim of the work was to evaluate the efficacy on patients with chronic obstructive pulmonary disease and coronary heart disease during treatment by new β- blocker. There examined in 62 patients (male 58, female 4) leading pathology which was CHD, of whom 36 had comorbidities of COPD. Their average age was the average age of 62,5±1,7.

The results of study of the dynamics of SBP and DBP in the transition to a standing position (Table 1) evidence testified about absence of orthostatic hypotension in all control periods.

Table 1. Changes in blood pressure before and after treatment with nebivelol

| indexes | Baseline | After 2 weeks | After 4 weeks |
|---|---|---|---|
| Middle SBP, mm Hg. | | | |
| Sitting | 165,26 ± 4,52 | 146,8 ± 4,7 | 139,9 ± 3,86 |
| Standing | 165,5 ± 5,01 | 147,05 ± 4,3 | 138,3 ± 4,3 |
| Middle DBP , mm Hg | | | |
| Sitting | 97,5 ± 3,08 | 88,5 ± 2,7 | 85,4 ± 2,9 |
| Standing | 101,2 ± 2,9 | 89,7 ± 2,8 | 83,5 ± 2,3 |

The monotherapy with nebivelol allowed to normalize blood pressure in 37 (62,7 %) patients. During hypertension, 1st degree nebivelol dose of 5 mg/day was sufficient to control hypertension in 13 of 15 patients, in 2 patients normalization of blood

pressure was achieved while taking the drug at a dose of 10 mg/day. During hypertension 2nd degree while taking nebivelol 5 mg/day normalization of blood pressure was achieved in 11 (25 %) patients, 10 mg/day - even in 13 (29,5%). Adding to 5 mg nebivelol 25 mg/day hydrochlorothiazide allowed to normalize the blood pressure in 13 (29,5%) patients

Table 2. Change indicators externally breathing before and after nebivelol

| Indexes | initially | After 2 weeks | After 2 months |
|---|---|---|---|
| FVC , % | 2,82 ± 0,15 | 2,84 ± 0,16 | 2,81 ± 0,15 |
| FEV1 , % | 1,97 ± 0,15 | 2,05 ± 0,11 | 1,94 ± 0,14 |
| Tiffenau index , % | 70,8 ± 2,1 | 71,1 ± 1,3 | 70,7 ± 1,5 |
| MEF 25–75% | 1,49 ± 0,19 | 1,58 ± 0,17 | 1,55 ± 0,17 |
| MEC 25% | 3,63 ± 0,35 | 3,81 ± 0,34 | 3,38 ± 0,41 |
| MEC 50% | 1,89 ± 0,80 | 1,80 ± 0,18 | 1,9 ± 0,21 |
| MEC 75% | 0,59 ± 0,07 | 0,58 ± 0,07 | 0,53 ± 0,06 |

It was determined the following parameters of external respiration: the forced life capacity (FVC), the volume expiratory volume in 1 second (FEV); Tiffenau index, mean expiratory flow (MEF 25-75 %); maximum expiratory flow at 25, 50 and 75 % vital capacity (MEC 25 %, MEC 50 %, MEC 75 %).

In 16 patients with concomitant chronic obstructive pulmonary disease (cough for the past 3 years at least 3 months of the year, emphysema) traces dynamics of symptoms and indices of external respiration (Table 2) within 8 weeks of therapy. In neither case intensityof auscultatory signs of bronchial obstruction, cough or shortness of breath were not marked. After 2 and 8 weeks of treatment, lung function remained stable.

Side effect of the nebivelol during treatment was observed only 1(1,69 %) patients as of short temporary vertigo, which recovered spontenously and did not require discontinuation of therapy. Nebivelol does not causes of increase orthostatic hypotension, disorders of lipid and carbohydrate metabolism, has no effect on respiratory function on patients with chronic obstructive pulmonary disease.

# EVOLUTION OF TOBACCO CONTROL - ROMANIAN PRACTICE

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The Romanian Society of Pneumology with 800 members is the only professional association with a section of tabacology. We are organizing in this context many types of actions and we are very active in this field .We arrived to have our update conferences every 2 years and we are present as partners in common actions with the Cardiology and Internal Medicine Societies. In the same time we create a partnership with Romanian NGO ( Romtens, Aer Pur); we are included as partners in the "Romanian Network for Smoking Prevention". Another modality to develop our self was to develop the partnership with international organizations as ENSP, ERS, SPLF.

We initiate studies of prevalence to specific and important samples of risk groups of populations: to teachers, children's, students, doctors, lung physicians, etc. We are describing in our presentation the evolution of prevalence in the last 10 years.

We studied the prevalence of COPD patients and the connections with smoking. In this manner we defined our next steps on tobacco control. We developed programs on education in schools, universities

Another modality to develop our self was to educate our doctors and to initiate them in quitting smoking with some e learning activities funded by programs of the EU for lung physicians. We are present with round table and workshops in the regular congress of Internal Medicine and Cardiology Associations in the last 5 years.

The prevalence in Romanian after the last study GATS is 27% .In the same time we have a weak law ,not well implemented .That's why we observed some evolutions in the prevalence of teenagers who are not under control. We are reacting and as members of the "Romanian Forum of Prevention" we are sustaining the new directives of EU and this was a permanent fight with authorities who do not understand the benefits of tobacco control in Romania. Even so we made progress in

organizing this battle, in evaluating correct our honest partners and our hidden enemies.

# ACUTE EXACERBATIONS OF THE CHRONIC OBSTRUCTIVE PULMONARY DISEASE: HOW CAN WE PREVENT THE EXACERBATIONS OF THE SEVERE DISEASE?

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Exacerbation of chronic obstructive pulmonary disease (COPD) are associated with accelerated loss of lung function and death. Among factors which associated with lung eased for COPD exacerbation severity of airway obstruction chronic bronchial mucous hypersecreation with elected cough and sputum antibiotic or systemic corticosteroid use in the past year bacterial colouration and comorbid conditions are considerable frequent exacerbation of the disease are associated with more rapid decline in pulmonary function and this type decline is associated with increased rise of mortality.

The importance of treatment options for reducing of exacerbation of COPD is clear and since recent years several studies suggests the presentable effect of different treatment options.

Increased oxidative stress and inflammation has a role in the pathogenesis of chronic obstructive pulmonary disease (COPD).

Drugs with antioxidant and anti-inflammatory properties ,such as N-acetyl cysteine, might provide an useful therapeutic approach for COPD. The findings show that in patient with moderate to save 600mg daily can prevent exacerbations especially in disease of moderate severity .

The effect of non-invasive positive pressure ventilation (NPPV) use in patients following a hospitalization for acute exacerbations of COPD (AE COPD) with acute hypercapnic respiratory failure an element-free survival after an index admission.

Patient who used NPPV following an admission for (AE COPD) with hypercapnic respiratory failure had low readmission rates and improved ebmt-free survival after 180 days from an index admission compared to patients who did not use NPPV post discharge.

A combination of inhaled corticosteroid and a long –acting beta 2 agonist (ICS/CABA) is used frequent to treat COPD patient.previous exacerbation is a strong predictor of ICS/LA BA prescribing only in patient eith severe COPD.

Because of the low emphasis on previous exacerbation when precribing for COPD patients with mild to moderate disease, the actual prescribing rate agreed more closely with the GOLD svidelines from 2007 then with those published in 2011.

The effect of anti-inflammatory drugs in COPD patient is ongoing up,however roflumilast as phosphodiesterase-4 (PD4) inhibitor shown significantly effect to exacerbations rate in patients with COPD with history of chronic bronchitis and frequent exacerbation on in medical history in the management of COPD patients one of active direction is prevention of exacerbation of severe disease and the macrolides , especially azythromycin has been shown markedly effect of the exacerbation frequency in patient with moderate-to-severe and severe disease.

# SLEEP APNEA EPIDEMICS, SYMTOMS AND DIAGNOSIS :

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Obstructive sleep apnea (OSA)—also referred to as obstructive sleep apnea-hypopnea—is a sleep disorder that involves cessation or significant decrease in airflow in the presence of breathing effort. The prevalence of OSA is 2-4%. There is a male dominance. It is the most common type of sleep-disordered breathing and is characterized by recurrent episodes of upper airway collapse during sleep. These episodes are associated with recurrent oxyhemoglobin desaturations and arousals from sleep.

**Signs and symptoms**

Symptoms of OSA begin insidiously and are often present for years before the patient is referred for evaluation.

Nocturnal symptoms may include the following:

- Snoring, habitual, and bothersome to others
- Witnessed apneas
- Gasping and choking sensations that arouse the patient from sleep, though in a very low proportion relative to the number of apneas they experience
- Nocturia
- Insomnia; restless sleep, with patients often experiencing frequent arousals and tossing or turning during the night

Daytime symptoms may include the following:

- Nonrestorative sleep (ie, “waking up as tired as when they went to bed”)
- Morning headache, dry or sore throat
- Excessive daytime sleepiness that usually begins during quiet activities (eg, reading, watching television); as the severity worsens, patients begin to feel sleepy during activities that generally require alertness (eg, school, work, driving)

- Daytime fatigue/tiredness
- Cognitive deficits; memory and intellectual impairment (short-term memory, concentration)
- Decreased vigilance
- Morning confusion
- Personality and mood changes, including depression and anxiety
- Sexual dysfunction, including impotence and decreased libido
- Gastroesophageal reflux
- Hypertension, Arytmia

**Diagnosis**

In general, the physical examination is normal in patients with OSA, aside from the presence of obesity (body mass index: >30 kg/m$^2$), an enlarged neck circumference (men: >43 cm [17 in]; women: >37 cm [15 in]), and hypertension.

Evaluate the upper airway in all patients, particularly in nonobese adults with symptoms consistent with OSA.

Examination findings may include the following:

- Abnormal (increased) Mallampati score: Identifies risk for difficult tracheal intubation
- Narrowing of the lateral airway walls: Independent predictor of the presence of obstructive sleep apnea in men but not women
- Enlarged (ie, "kissing") tonsils (3+ to 4+)
- Retrognathia or micrognathia
- Large degree of overjet
- High-arched hard palate
- Systemic arterial hypertension: Present in about 50% of obstructive sleep apnea cases
- Congestive heart failure
- Pulmonary hypertension
- Stroke
- Metabolic syndrome
- Type 2 diabetes mellitus

*Testing*

An overnight sleep study, or polysomnography, is required to diagnose OSA.

Routine laboratory tests, however, are usually not helpful in OSA unless a specific indication is present. Pulmonary function tests are not indicated to make a diagnosis of, or treatment plan for, OSA alone. The standard indications for such testing apply to all patients, with or without OSA.

Obtain a thyrotropin test on any patient with possible OSA who has other signs or symptoms of hypothyroidism, particularly in elderly individuals.

*AASM standards and guidelines for diagnostic polysomnography*

The American Academy of Sleep Medicine guidelines for the indications and performance of polysomnography include the following

- Sleep stages are recorded via an electroencephalogram, electro-oculogram, and chin electromyogram
- Heart rhythm is monitored with a single-lead electrocardiogram
- Leg movements are recorded via an anterior tibialis electromyogram
- Breathing is monitored, including airflow at the nose and mouth (using both a thermal sensor and a nasal pressure transducer), effort (using inductance plethysmography), and oxygen saturation

The breathing pattern is analyzed for the presence of apneas and hypopneas (as per definitions standardized by the American Academy of Sleep Medicine)

# SMOKING CESSATION METHODS

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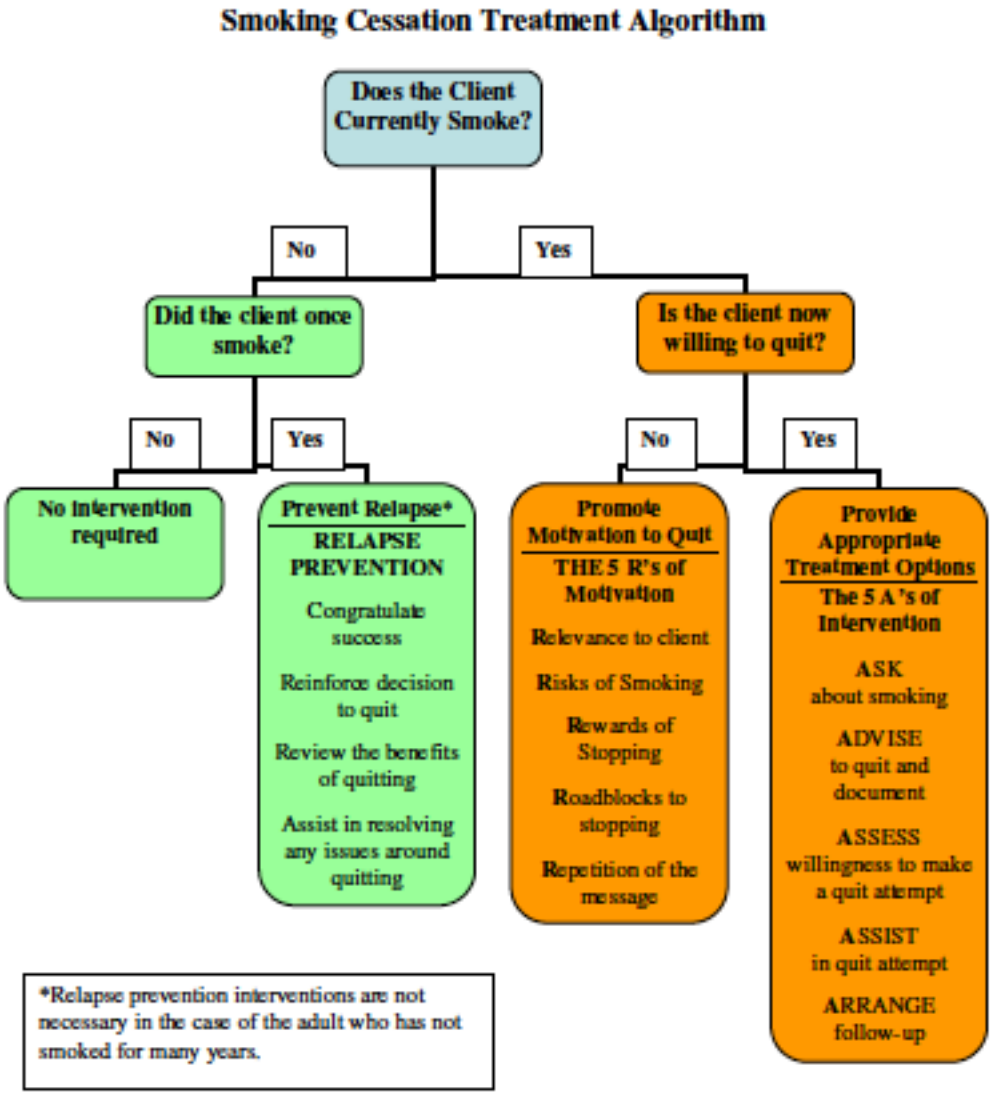
The benefits of quitting smoking are well established. Successfully quitting smoking can result in an increase in life expectancy of up to 10 years, if it occurs early . There is also substantial evidence that advice from health professionals including doctors, nurses, pharmacists, psychologists, dentists, social workers and smoking cessation specialists helps smokers to quit. While spending more time (longer than 10 minutes) advising smokers to quit yields higher abstinence rates than minimal advice,offering brief advice (as little as 3 minutes) has been shown to have clear providing brief advice to most smokers is more effective and efficient than spending a longer time with a few patients.

Smoking cessation is both cost and clinically effective compared with other medical and disease preventive measures, such as the treatment of COPD and shows that the cost per life year saved by smoking cessation interventions makes it one of the most cost-effective healthcare.

Advice based help and pharmacotherapy can both increase the rate of success of quit attempts, and when they are used the benefits are should be offered cessation treatment, either counselling (individual or group) or medication ( NRT, Bupropion, Varenicline), or both, which is individualised and customised to their own personal situation and experience. (Zwar N, Richmond R, Borland R, Peters M, Litt J, Bell J, Caldwell B, Ferretter I. Supporting smoking cessation: a guide for health professionals. Melbourne: The Royal Australian College of General Practitioners, 2011.)


Smoking Cessation Treatment Algorithm
Does the Client Currently Smoke?
No
Yes
Did the client once smoke?
Is the client now willing to quit?
No
Yes
No
Yes
No intervention required
Prevent Relapse*
RELAPSE PREVENTION
Congratulate success
Reinforce decision to quit
Review the benefits of quitting
Assist in resolving any issues around quitting
Promote Motivation to Quit
THE 5 R's of Motivation
Relevance to client
Risks of Smoking
Rewards of Stopping
Roadblocks to stopping
Repetition of the message
Provide Appropriate Treatment Options
The 5 A's of Intervention
ASK about smoking
ADVISE to quit and document
ASSESS willingness to make a quit attempt
ASSIST in quit attempt
ARRANGE follow-up
*Relapse prevention interventions are not necessary in the case of the adult who has not smoked for many years.

# IMPORTANCE OF MORFOFUNCTIONAL AND IMMUNOLOGICAL EXAMINATIONS IN THE TREATMENT OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASES

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The purpose of the present research was the study of cellular structure and cytokine's spectrum in peripheral blood, bronchoalveolar liquid (BAL) and induced sputum (IS) and possibility of application of these inflammatory biomarkers for optimization diagnosis of chronic obstructive pulmonary diseases (COPD) with irreversible bronchial obstruction, as well as for evaluation of influence of long-acting $\beta_2$-agonist salmeterol (Serevent) and fixed combination salmetorol/fluticasone propionate (Seretid) with non-steroid anti-inflammatory drug fenspirid (Erespal) in COPD of the 2-3 stages. 20 patients with severe BA and 90 patients with COPD 2-3 stages were examined. The patients were divided in to 4 groups: the study group (22 patients) with COPD of 2 stage received Serevent+Erespal, the comparative group (23 patients) received only Serevent, the study group (23 patients) with 3-stage of COPD received Seretid+Erespal, the comparative group-only Seretid.

Basic parameters of external breath, clinical, X-ray tomography immunological, bacteriological, cytological researches were investigated in all patients. Also were counted a numbers of eozinofils, neutrofils, alveolar macrofags and lymphocyte, by the method of IFA was determined the content of proinflammatory (IL-8, IL-6) and anti-inflammatory (IL-4) cytokines in BAL liquid and induced sputum. Researches have shown that ventilational disturbances aren't basic methods in providing differential diagnosis between obstructive diseases. On the contrary such univasive methods as determination of the contents of eosinophil's and neutrophils, pro- and anti-inflammatory cytokines in induced sputum can help to differentiate severe BA and 2-3 stages COPD with irreversible bronchial obstruction. Regular combined brochnodilatation and glucocorticoid therapy leads to minimization of respiratory symptoms, parameters of bronchial patency;

simultaneously there is a decrease in the maintenance of proinflammatory cytokines in BAL liquid and IS.proinflammatory cytokines in BAL liquid and IS.

# OPTIMIZING ANTIBACTERIAL THERAPY IN PATIENTS WITH BRONCHIECTASIS

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Objective of research: to study the composition of sputum specimens and identification of sensitivity to antibiotics in patients with bronchiectasis. Subjects: 35 patients with bronchiectasis at the age of 13 to 72 years. Collection of anamnestic data revealed the frequency of exacerbations of disease in average of 2 times per year in 5 patients, 3-4 in 15 patients. The remaining patients had persistent signs of active inflammation during the year. Antibiotic therapy has been empirically conducted in 96,8% cases, in 38,4% of them no substantial positive results were reported.

Results: The morning portion of sputum has been tested. inoculation was carried out on various media. Test results revealed Staphylococcus aureus in 11 cases, Streptococcus pneumonia in 6, Pseudomonas aureginosae 5, Diplococcus pneumonia in 2, Enterobacter in 3, Ech. Coli in 1 case. In 18 cases, the sputum test detected Candida albicans, with high titer in 11 of them. In all cases, sputum inoculation was done to determine the sensitivity to antibiotics. Subsequent prescription of antibiotics within the complex treatment of patients was based on study results.

Conclusion: Analysis of clinical and radiographic changes after treatment showed that adequately conducted antibacterial therapy allows cutting off the symptoms quickly, as well as reducing the frequency of exacerbations and improving quality of life of patients.

# DIFFERENTIAL DIAGNOSTIC VALUE OF IMMUNOLOGICAL PARAMETERS IN SMALL AIRWAY DISEASE IN CHILDREN

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**Purpose :** To determine the differential diagnostic role of humoral immunity in small airways diseases in children

**Materials and methods :** The humoral immunity were determined in 79 patients with chronic bronchiolitis obliterans ( COB) and 100 patients with bronchial asthma (BA ) . Studied the concentration of immunoglobulins (Ig) A, M, G, E , and circulating immune complexes (CIC ) . Studies conducted in the acute phase of diseases.

**Results:** The leading clinical symptom in both nosological forms was bronchial obstruction manifested by shortness of breath , spastic cough , wheezing remote . Signs of intoxication ( high fever, malaise , loss of appetite ) occurred in 12% of cases of BA, 47% of children with COB . Humoral immunity in BA: IgA 142,6 ± 9,3; IgM 139,4 ± 7,3; Ig G 1437,6 ± 34,5; Ig E 342,2 ± 20,6; CIC 75,0 ± 3 , 1. COB indicators were as follows: IgA273 , 4 ± 10,6; IgM 218,6 ± 4,5; Ig G 1206,7 ± 29,2; Ig E100 , 9 ± 4,7; CIC 101,9 ± 3,9 .

**Conclusion :** High numbers of Ig E indicate on the role of atopic mechanisms in the pathogenesis of BA. The downward trend of Ig G and high level of CIC are the indicators of infectious inflammatory in COB.

# THE STATE OF NON-SPECIFIC RESISTANCE FACTORS IN SMALL AIRWAYS DISEASES OF BRONCHIAL TUBES IN CHILDREN

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Objective: To study the dependence of the state of phagocytic activity of granulocytes on the stage of the pathological process in asthma (BA) , chronic bronchiolitis obliterans(BO) and bronchopulmonary dysplasia (BPD).

Materials and Methods: 112 children with BA and 139 patients with BO and 103 with BPD were observed in age from 1 year to 15 years. Studies were conducted in the period of exacerbation and remission. In all patients the study was carried out phagocytic activity of neutrophils through the spontaneous and stimulated nitroblue tetrazolium reduction test (NBT)

Results of the study: In all cases aggravation observed increase of phagocytic activity of neutrophils in the spontaneous (BA-10, 1±0,37, BO-8, 04±0,26, BPD-10.0±1,12) and a stimulated (BA-31, 6±0,57; BO-30, 3±1,0; BPD -30,9±0,43) test. In the case of BO phagocytic activity of neutrophils was slightly reduced in comparison with BA and BPD. In remission indicators of these continue to grow (BA-11, 26±1,3, BO-9.97±0,25; BPD-10.1±1,1) and (BA-37, 5±1,5; BO-39±0,9, BPD-40, 0±0,5) in all groups

Conclusion. Thus, the phagocytic activity of granulocytes not suffer in BA, BO and BPD. However, indicators of NST are on the lower limit of normal at BO. Probably slight inhibition of phagocytosis is associated with the presence of viral infection.

# RADIATION INDUCED ALVEOLITIS

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After bombing of targets in the Persian Gulf and the Balkans with missiles with depleted uranium, exposed zone included the local, as well as thousands of miles distant areas. Due to exposure to low-slow- repeated doses of radiation, concomitant Petkau effect can be expected in the numerous populations in the wide geographic area due to the nuclear disasters and after the use of depleted uranium missiles (1986- Chernobyl, 1991, 1995, 1999, 2003-2011 Gulf Wars and Balkan's bombing campaigns, 2011-Fukushima).

BAL samples were analyzed in this study of all the patients originated from geographically close territories of Former Yugoslavia that were repetitively stroked by DU armaments. All of them underwent flexible bronchoscopy for clinical symptoms and radiological changes consistent with persistent pulmonary infiltrates, as well.

Ten-year (December 1992 - December 2002) evaluation of 225 pediatric bronchoalveolar lavage (BAL) differential cell counts showed appearance of the cells corresponding to cytological entity - lupus erythematosus cell (LEC) in 47 specimens of which not a single case was associated with coexistent autoimmune disease. Differential cell counts were compared and statistical significance of differences for estimated cell population percentages calculated in groups of LEC positive (LEC+) and LEC negative (LEC-) BAL specimens. Significant increase of percentages of neutrophils and eosinophils and decreased percentages of macrophages were found in the group of LEC+ in comparison with LEC- BAL specimens ($p < 0.05$, $p < 0.001$, $p < 0.001$, respectively). Statistically significant negative correlation was found between BAL eosinophils and alveolar macrophages in LEC+ BAL specimens. LEC- BAL specimens showed statistically significant negative correlations between neutrophils and lymphocytes.