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**XI PULMOLOŠKI DANI**  
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# PREFACE

Dear colleagues

After a long period, we have the opportunity to come together around a common interest, which is improving the treatment of patients with respiratory diseases. Actually we are in XI symposium named "Pneumology days Tešanj 2022". We are very happy that we will have the opportunity to meet our friends from the wider region, exchange experiences and learn a lot. The COVID 19 infection has entertained us all for the past two years. We were faced with great trials, we treated patients with COVID 19, but it often happened that the members of the team treating those patients got sick themselves. It was a situation where we treated both, the patients and us personally. Our motivation for learning while working was even greater. It was a challenging time in which we often witnessed treatment failure, so the learning imperative was even greater. Of course, we all tried to adequately treat the other patients as well. We hope that our theoretical and practical knowledge remained even greater in this challenge. Therefore, we sincerely look forward to these meetings and to learn a lot from each other.

Prof. Dr Besim Prnjavorac  
President of Organizing Committee





# ALPHA-1 ANTITRYPSIN DEFICIENCY (AATD) IN A YOUNG FEMALE PATIENT

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**Introduction:** The alpha-1 antitrypsin deficiency (AATD) is a hereditary autosomal codominant disease. The phenotype Pi ZZ is associated more frequently with pulmonary disease and is responsible for the presence of emphysema early in life, particularly in smokers. Generally, AATD is suspected in young patients with pulmonary emphysema or chronic obstructive pulmonary disease (COPD). Patients often suffer from diagnostic gaps and are misdiagnosed with chronic obstructive pulmonary disease (COPD), asthma, and airway hyper-reactivity (AHR), as AATD may present with nonspecific respiratory symptoms. AATD is most common in white people, and it most frequently affects the lungs and liver. In the lungs, the most common manifestation is early-onset (patients in their 30s and 40s) pan acinar emphysema most pronounced in the lung bases. However, diffuse or upper lobe emphysema can occur, as can bronchiectasis. The most frequently described symptoms include dyspnea, wheezing and cough. Pulmonary function testing shows findings consistent with COPD; however, bronchodilator responsiveness may be seen and may be labelled as asthma.

**Case presentation:** We describe a case of a 40-year-old Caucasian female patient, admitted to hospital because of dyspnea, malaise, cough. Symptoms started one year ago, after mild SARS-COV 2 infection. Chest X-ray during the acute illness described emphysema, with flattened diaphragm, and no signs of consolidation. According to history she was a non-smoker, office worker, with negative family history of

respiratory or liver illness. She never used any regular therapy before, no comorbid diseases and denied frequent respiratory infections during childhood. Chest computer tomography (CT) presented pan acinar emphysema most pronounced in the lung bases. Post bronchodilator spirometry revealed forced expiratory volume in 1<sup>st</sup> second (FEV<sub>1</sub>) 54%, and forced vital capacity (FVC) 84%, with FEV<sub>1</sub>/FVC=0.64. Routine biochemistry laboratory was normal. Gas analyses noted respiratory failure type 1 (partial) with hypoxemia partial oxygen pressure 8.1kPa, hypocapnia because of hyperventilation with partial carbon dioxide pressure 4.1kPa, and oxygen saturation 92%. Echocardiography without any findings of right heart failure, normal systolic pulmonary arterial pressure (sPAP). Abdominal ultrasound without pathological findings, no liver disease detected. According to CT finding the patient was sent to the Institute for clinical immunology and genetic disorders where the serum value of alpha-1 antitrypsin was measured. The value was 0,2 micromoles /L (reference value 5-6 micromole /L). The patient was prescribed inhaled therapy of long acting anticholinergic, short acting beta-2 agonist. She was also suggested therapy with intravenous human alpha 1-proteinase inhibitor (AAT augmentation therapy).

**Conclusion:** It is never too late to suspect AATD, especially in a patient with an unusual medical history. In recent years, evidence is beginning to emerge that there may be value in identifying and treating patients who do not already have deterioration of functional parameters. The Alpha-1 Foundation recommendations for the diagnosis and management of AATD in adult patients indicate that treatment should be provided for patients with FEV<sub>1</sub> between 30 and 65%. It may be useful to evaluate and treat patients based on clinical symptoms, even outside the established parameters, in particular cases.

# INFLAMMATORY MARKERS IN PERIPHERAL BLOOD DURING TREATMENT WITH INHALED CORTICOSTEROIDS IN PATIENTS WITH ASTHMA

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The main attribute of asthma is inflammation, which leads to airway remodeling, bronchial hyper-reactivity and reversible or partly reversible airway obstruction. According to GINA, asthma is a chronic inflammatory disorder of the airways in which many cells play a role, in particular mast cells, eosinophils (Eo), and T lymphocytes. Many cells and mediators take part in creating the asthmatic inflammatory reaction, but eosinophils play a central role.

This study includes 30 patients of the Pulmology and Allergy Clinic, Skopje, with confirmed asthma, treated with ICS. In all of the patients we followed Eo count, ECP and IL-5 in peripheral blood at the beginning of the study, after 2 and 6 months treatment. Following the parameters during treatment with ICS we registered changes in all of the tested parameters.

Our conclusion is that the ICS objectively suppress the inflammatory reaction in asthma and the biologic markers (IL-5, Eo and ECP), which we have followed, can measure the accomplished effect. They could be used in every day practice, not only as diagnostic parameters but also as valid therapeutic guides in the treatment of asthma.

**Key words:** Asthma, Treatment, Eosinophyles, IL-5, ECP

# **CURRENT APPROACH AND CHALLENGES IN THE MANAGEMENT OF PULMONARY EMBOLISM**

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Pulmonary embolism (PE) is the third most frequent cause of cardiovascular death, and a leading preventable cause of mortality in hospitalized patients. The estimated incidence is 60-70/100.000. It is a serious health and socio-economic problem, consuming a great fraction of public resources and represents a great burden of the society.

The symptoms and signs of PE are non-specific, with an inconsistent clinical presentation, varying from asymptomatic to severe acute episodes and lethal outcome, which makes early and accurate diagnosis difficult. Validated clinical probability scores assist the clinician towards accurate diagnosis. In patients with low to moderate probability, D-dimers guide the further diagnostic procedure to objective confirmation with one of the imaging methods. Chest CT-angiography is the golden standard for diagnosis, although the dual phase ventilation/perfusion scan and lung ultrasound have a significant place in the diagnosis and follow up of PE.

The current guidelines of the European Society of Cardiology define the place of the contemporary treatment modalities for treatment of PE, but at the same time, open dilemmas concerning the management of patients with specific health conditions. Recommendations are given for the preferred treatment choices of cancer associated PE, patients with thrombophilia, pregnant and breastfeeding women, patients with chronic conditions and CTPEH. Clear advantage is given to the direct oral anticoagulants in most of the patients when oral treatment is indica-

ted, which opens the opportunity of out-patient treatment of low risk patients, selected by HESTIA criteria. The new categorization of the risk factors for PE determines the recommendations for acute treatment as well as the type and duration of primary and secondary prevention.

PE is a disease with complex presentation and its treatment involves more specialties. The new guidelines encourage formation of multidisciplinary teams on regional and national level for more efficient managing of the patients with acute PE and CTPEH.

# COVID-19 – RISK FACTORS FOR SEVERE DISEASE FORM

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The pathophysiology of COVID-19 is still not fully understood, reliable prognostic factors remain unknown, and several specific therapeutic strategies have been proposed. The project "Survivors of COVID-19: a variety of immune responses to SARS-CoV-2 in correlation with clinical manifestation. Long term follow-up" is carried out in four scientific and research institutions, the host is the Faculty of Medicine in Belgrade, and it is financed by the Fund for Science of the Republic of Serbia. The aim of the project is to analyze the importance of antibodies to SARS-CoV-2, as well as to examine the relationship between the severity and outcome of COVID-19 with clinical, radiological, and biochemical characteristics of patients. Also, the purpose of this research is to examine the long-term consequences of COVID-19, which are still insufficiently known but are significant given the presence of known risk factors for problems that occurred after pneumonia and treatment in intensive care units. The objective of the research is to examine the relationship between the severity of the clinical picture of COVID-19 and the following parameters: clinical indicators of severity of COVID-19, comparing chest radiography or computed tomography (were used as a first-line diagnostic tool), biochemical biomarkers and hemostasis indicators, oxidative and inflammatory status.

Clinical data have indicated that the biochemical status of patients with COVID-19 reflects some deranged indices related to hemoglobin (Hb), such as decreased Hb and increased serum ferritin, erythrocyte sedimentation rate, C-reactive protein, albumin, and lactate dehydrogenase. Long duration of the disease, application of oxygen therapy, im-

plementation of non-invasive mechanical ventilation in patients with COVID-19 affected worse long-term disease outcomes. Pulmonary fibrosis has very rarely occurred as a long-term pulmonary consequence of COVID-19. Comparison of chest radiographs or computed tomography that were used as first line diagnostic tool, have not shown a significant correlation between the severity of clinical picture and the extent of pathological radiology changes.

Oxidative damage and inflammation may be key factors in the pathogenesis of SARS-CoV-2 infection and may trigger a series of events that lead to damage to lipids, proteins and DNA, cellular dysfunction and cell death due to excessive production of reactive oxygen species (ROS), modifications in catecholamine metabolism, increased iron deposition, and increased inflammatory mediators. In addition to lipids, proteins are one of the main targets of ROS, and protein products of advanced oxidation indicate the degree of protein damage by oxidative stress in several pathological conditions.

Oxidative damage and the inflammatory process may be key factors in the pathogenesis of SARS-CoV-2 infection and trigger a series of events that lead to lipid, protein, and DNA damage, cellular dysfunction and cell death due to excessive production of reactive oxygen species (ROS), modifications in catecholamine metabolism, increased iron deposition and increase in the level of inflammatory mediators. In pathological conditions, lipid peroxidation products, such as malondialdehyde (MDA) and hydroxynonenal (HNE) exhibit cytotoxic, hepatotoxic, mutagenic, and genotoxic properties, propagating and enhancing oxidative injury and contributing to the aggravation of the disease. They can be used as biomarkers for several diseases, including viral infections. In addition to lipids, proteins are one of the main targets of ROS. Protein advanced oxidation products indicate the degree of protein damage by oxidative stress in several pathological conditions. Prooxidant-antioxidant balance (PAB) reflects the condition dynamic balance

created under conditions of homeostasis between the free radicals that are produced and those that are used (captured) by the components of the antioxidant defense, including non-enzymatic like glutathione (GSH). Phospholipids, such as phosphatidylcholines (PC) and lysophosphatidylcholines (LPC), in addition to their structural functions as the main constituents of cells membrane, act as secondary messengers, triggering inflammatory signaling. Clinical data indicate that the biochemical status of patients with COVID19 reflect some disturbed indices associated with hemoglobin (Hb), such as decreased Hb and increased serum ferritin, speed erythrocyte sedimentation, C-reactive protein, albumin, and lactate dehydrogenase. In addition, some patients with COVID19 show symptoms typical of acquired acute porphyria, such as erythematous rash, extensive urticaria and varicella-like vesicles. Finally, an analysis of the epidemic COVID19 in three Italian regions with different prevalences of beta-thalassemia showed a positive correlation between the distribution of b-thalassemia heterozygotes and population immunity against infections. Recently, an in-silico study indicated the possibility that some of the nonstructural SARS-CoV-2 proteins can bind to hemoglobin (Hb), disrupting the iron-porphyrin bond and separating iron from the 1-beta chain of Hb. This may lead to a lower Hb transfer capacity for oxygen/carbon dioxide, causing symptoms of respiratory distress and generalized inflammation.

It is hypothesized that SARS-CoV-2 can infect host cells through other receptors other than ACE-2, such as the dendritic cell C-type lectin DC-SIGN and DC-SIGNR, glutamyl aminopeptidase (ENPEP), alanyl aminopeptidase (ANPEP) and dipeptidyl peptidase 4 (DPP4) or CD26. In the case of red blood cells, of particular interest is CD147, one of 400 different surface antigens inhabiting the erythrocyte membrane, which has been shown to be able to bind SARS-CoV-2 Spike protein. of ABO blood groups of patients with clinical and biochemical markers will improve the understanding of disease incidence, development, and complications, including the development of fibrosis tissues after



infection. The connection between CD147 and ABO blood groups is not well known. Still, it is known that CD147 is an essential receptor in the process of *Plasmodium erythrocyte invasion falciparum*.

In contrast, the O blood group is the most protected against malaria infection in comparison with A, B or AB types. Therefore, it is possible that SARS-CoV-2 infection of erythrocytes through receptors different from ACE-2 may be associated with ABO blood groups with various levels of sensitivity to infection. In this way, any experimental proof of the above-mentioned hypothesis could obtain completely new insight into the mechanism of SARS-CoV-2 infection, the onset of the disease, and its progression.

By evaluating indicators of erythrocyte hemolysis, the project evaluates the hypothesis that SARS-CoV2 attacks heme, causing early hypoxia that leads to respiratory distress and disturbances in blood coagulation. The results of the project will gain new insights into clinical and molecular features diseases, giving recommendations for future vaccination against COVID-19 and selecting potential convalescent plasma donors.

**Key words:** COVID-19, Risk factor

# CLINICAL AND IMMUNOLOGICAL MONITORING OF THE DELTA AND OMICRON VARIANTS OF THE COVID-19 DISEASE – TWO COMPLETELY DIFFERENT DISEASES

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**Abstract:** Clinical monitoring of the delta and omicron variants of the COVID-19 disease points to completely different diseases. The analysis included 772 hospitalized patients for this disease at the Golnik University Hospital, Golnik, Slovenia; 589 with delta and 174 with omicron variant. COVID-19 is an infectious disease caused by the SARS-CoV-2 virus.<sup>1</sup> At the Golnik Clinic, we hospitalized 838 patients with this disease in the period from August 1<sup>st</sup>, 2021 to and including April 20<sup>th</sup>, 2022. According to the CDC, the delta variant became a VOC (variant of concern) mutation in June 2021<sup>2</sup>, and was present in more than 90% of all virus variants tested until October 2021.<sup>3</sup> The current dominant variant of the SARS-CoV-2 virus is omicron, which was designated as VOC by the CDC on November 26<sup>th</sup>, 2021 and reached more than 98% of all tested virus variants by February 2022.<sup>3</sup> The patient's clinical data in our retrospective analysis from the hospital's digital database were as follows: demographics, vaccination status, associated diseases, history of previous infection with this virus, radiographically confirmed pneumonia, need for oxygen, need for high-flow device (HFO), intensive therapy, complications (bleeding, thrombosis, etc.), need for anti-IL-5 therapy, length of hospitalization, mortality and discharge with need of oxygen. Fischer's test of binomial distribution of data was used for data analysis.

**Results:** In the analysis 772 patients were included, of which 322 were women and 450 were men. 589 patients had the delta variant (of which 40% were women and 60% were men) and 174 patients had the

omicron variant (of which 48% were women and 52% were men). With regard to delta variant vaccinations, there were 403 unvaccinated (67%), 167 incompletely vaccinated (28%) and 28 fully vaccinated (5%) patients. Among the omicron variant, there were 75 unvaccinated (43%), 52 partially vaccinated (30%) and 47 fully vaccinated patients (27%). The duration of hospitalization was an average of 9 days with the delta variant and 8 days with the omicron. Of the 598 patients with the delta variant, 508 had COVID-19 pneumonia or 85%. 466 patients (75%) required oxygen supplementation, of which 86 (14%) required ventilation with a high-flow device (HFO). 29 patients (5%) were discharged with need of oxygen at home. Of the 174 patients with omicron, 86 had pneumonia or 49%. 104 patients (60%) needed oxygen, of which 17 (10%) HFO. 9 patients (5%) were discharged on oxygen. The need for anti-IL-5 therapy (tocilizumab) was mostly with delta patients (105 or 18%), much less than omicron patients (11 or 6%). In patients with the delta variant, 20% needed EIT, but only 7% with omicron variant. Patients had various complications during the course of treatment. The most common were secondary bacterial infections (29% in delta and 25% in omicron), bleeding (more with delta) and pulmonary embolisms (omicron). Other complications were less frequent.

**Conclusion:** The omicron variant of COVID-19 disease in the clinical course is much different from the delta variant. Omicron infection showed less lung damage, less pneumonia and less intensive therapy.

**Key words:** COVID-19; Omicron variant; Delta variant;

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# CENTRAL AND EASTERN EUROPE GUIDELINES FOR TREATMENT OF COPD

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**Introduction:** The Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy report provides guidance on effective management of chronic obstructive pulmonary disease (COPD) according to local healthcare systems. However, COPD is a heterogenous disease and certain aspects, including prevalence, disease-time course and phenotype distribution, can differ between countries. Moreover, features of clinical practice and healthcare systems for patients with COPD can vary widely, even in geographically close and economically similar countries.

**Areas covered:** Based on an initial workshop of respiratory physicians from eleven countries across Central and Eastern Europe (CEE) in December 2018 and subsequent discussions, this article offers region-specific insights from clinical practice and healthcare systems in CEE. Taking recommendations from the GOLD 2022 report into account, we suggest approaches to adapt these into national clinical guidelines for COPD management in CEE.

**Expert opinion:** Several factors should be considered when optimizing management of COPD in CEE compared with other regions, including differences in smoking status, vaccination uptake, prevalence of tuberculosis and nontuberculous mycobacteria, and variations in healthcare systems. We provide guidance and algorithms for pharmacologic and non-pharmacologic management of COPD for the following scenarios: initial and follow-up treatment, treatment of patients with frequent exacerbations, and withdrawal of inhaled corticosteroids where appropriate.

**Key words:** Central and Eastern Europe; Chronic obstructive pulmonary disease; Algorithms; Clinical guidelines; Exacerbations; Inhaled corticosteroids; Non-pharmacologic management; Pharmacologic management.

# DIFFERENTIAL DIAGNOSIS OF COVID-19 PNEUMONIA - A RADIOLOGICAL CHALLENGE

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The radiological finding of COVID-19 in the lungs has some similarities with pneumonias caused by other viruses, including influenza viruses, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, and others. Viruses within the same species (SARS and MERS) have a very similar radiological finding because they belong to the same coronaviridae family, so they need to be excluded through clinical manifestations and laboratory detection of pathogens. The radiological findings seen in COVID-19 pneumonia can be seen in other viral pneumonias as well as in numerous other diseases. Peripherally localized ground glass opacities may be present in mycoplasma pneumonia, acute interstitial pneumonia, non-specific interstitial pneumonia (NSIP) and other diseases such as connective tissue diseases and drug toxicity. Central or diffuse ground glass and "crazy paving" are present on CT findings indeterminate for COVID-19 and it is difficult to distinguish them from other diseases analyzing only the CT features (other viral pneumonias, ARDS, Acute hypersensitivity pneumonitis, Pneumocystis jiroveci pneumonia, Sarcoidosis, pulmonary hemorrhage, alveolar proteinosis). Peripherally localized consolidations with marginal ground glass opacities do not differ in appearance from the findings in Cryptogenic Organizing Pneumonia (COP), Eosinophilic Pneumonia, Vasculitis, Invasive Aspergillosis. Organizing pneumonia in COVID-19 has the same characteristics as OP in any other disease. Nodules with a halo sign, except for COVID-19, are a common finding in numerous other diseases: Infectious diseases (septic

emboli, tuberculosis, viral pneumonia, invasive aspergillosis); Non-infectious diseases (vasculitis, sarcoidosis, metastases).

The wide spectrum of manifestations of COVID-19 pneumonia represents a great challenge for the radiologist, considering that many other diseases can have the same or similar radiological findings.

**Key words:** Pneumonia, COVID, Chest x-ray, CT scan



# LUNG CANCER AND COVID-19

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Patients with lung cancer are especially vulnerable to COVID-19 (25% - 36% mortality rate). The reasons for this are: Tumor cells are more sensitive to viral replication due to lack in innate antiviral immunity, ACE2 receptor (main places of entry and replication of SARS-COV2) expression is elevated in tumor, including tumor-adjacent lung tissue in patients with lung cancer, as well as in lung tissue of smokers, the ability to create an antiviral immune response is reduced. All together leads to the development of a harder clinical disease of COVID-19.

Patients with cancer are at a heightened risk for developing serious complications from COVID-19 due to: advanced age, increased risk of relative immunosuppression from the underlying malignancy and anti-cancer treatments. In the same time it's patients with additional comorbidities, including a history of smoking and preexisting lung disease.

When we talking about the prognosis of patients with lung cancer and COVID-19, a systematic review and meta-analysis of cancer patients affected by a novel coronavirus by Venkatesulu BP et al. from 2020 include 26 clinical trials and involving 23,736 cancer patients, resulted with much more all-cause mortality rates, ICU admission rates, intubation rates and more severe disease between cancer patients and non-cancer patients. In the same meta-analysis among cancer subtypes, the mortality was highest in hematological malignancies (OR 2.43) followed by lung cancer (OR 1.8).

Guiding Principles of lung cancer management recommended by ESMO (European Society for Medical Oncology) during the COVID-19 pandemic are designed across three levels of priorities: high priority, medium priority and low priority both in terms of diagnosis and treat-

ment. The primary aim of diagnosis in a patient with suspected lung cancer is to obtain tissue specimens for histologic diagnosis, using the least invasive method, but the risk of spreading SARS-CoV-2 infection needs to be considered. Prioritizing treatment options for lung cancer during the COVID-19 pandemic by IASLC (International Association for Study Lung Cancer) go further and define the possible initial delay of treatment for every clinical scenario that is, the stage of the disease. Initial delay for treatment lung cancer is possible from less than 2 weeks till more than 8 weeks, but in the case of stage IV NSCLC and extensive disease of SCLC it should be less than 2 weeks. Active cancer treatments do not worsen COVID-19 outcomes in patients with lung cancer and COVID-19.

When we talking about the COVID-19 vaccine, two dose mRNA vaccines are highly effective (~90%) in patients with cancer, though patients with cancer have lower titers than health controls. Chemotherapy treatment was associated with lower rates of seropositivity when compared to biological and immunotherapy treatments (73% vs. 90%,  $p=0.02$ ). The ideal timing for vaccination is still to be defined, although a recent study showed that most of the initial non-responders had blood collected for immune analysis 7–14 days after their most recent treatment with cytotoxic agents. That is time when a nadir in blood counts and the peak of myelosuppression from traditional chemotherapy agents is observed. While the duration of COVID-19 vaccine protection among patients with cancer generally, and lung cancer in particular, is unknown, but vaccines are effective and safe.

**Key words:** Lung cancer, COVID 19, Vaccine, Management

# CHOOSING BIOLOGICAL THERAPY IN SEVERE ASTHMA

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Biological therapy is reserved for severe asthma, and belongs to step 5 treatment according to the current GINA recommendations. It is mainly given to patients with high type 2 inflammation and/or eosinophilic inflammation. This type of asthma most often begins in childhood, however, it can also occur in adults, as eosinophilic asthma, which is less often associated with aeroallergy. Following exposure to allergens, pollutants, viruses, or bacteria, airway epithelial cells release alarmins (ie, epithelial cytokines) such as interleukin-25, interleukin-33, and thymic stromal lymphopoietin (TSLP). In allergen-sensitized patients, myeloid dendritic cells present inhaled allergens, together with costimulatory molecules, to tissue-resident memory CD4<sup>+</sup> type 2 Th2 lymphocytes, expressing antigen-specific T-cell receptors (TCRs) and initiating responses in an allergen-specific manner. In adult eosinophilic asthma, epithelial cell-released alarmins and eicosanoids (ie, cysteinyl leukotrienes C4 and D4 and prostaglandin D2) activate innate lymphoid type 2 cells (ILC2), which lack antigen-specific TCR receptors but express receptors for these alarmins and leukotrienes. Both Th2 cells and ILC2 produce large amounts of type 2 cytokines, IL-4, IL-5, and IL-13. It is important to say that IL-4 plays a key role in the differentiation of naïve CD4<sup>+</sup> T cells into Th2 cells. However, IL-5 promotes the proliferation and differentiation of bone marrow progenitor eosinophils, which prolongs the survival of Eo and activates eosinophils, which release cysteinyl leukotrienes and toxic granules, causing tissue damage, which leads to worsening of chronic airway inflammation, but also acute exacerbation of asthma. Furthermore, IL-13 induces the expression of the enzyme inducible nitric oxide synthase (iNOS) in epithelial cells, leading to an increase in fractional exhaled nitric oxide (FeNO). It also causes mucosal hypersecretion and stimula-

tes the contraction of airway smooth muscle cells, causing bronchoconstriction. By targeting the Fc fragment of IgE, Omalizumab inhibits the binding of IgE to receptors on mast cells and basophils. Mepolizumab and reslizumab target the interleukin-5 ligand, and benralizumab binds to the interleukin-5 receptor. This leads to both a reduction in the number and function of Eo. Dupilumab inhibits both IL-4 and IL-13 signaling by binding to IL-4R $\alpha$ , which they share. The epithelial cytokines thymic stromal lymphopoietin (TSLP), IL-25, and IL-33 are released by airway epithelial cells in response to allergens, air pollutants, and viruses, enhancing inflammation. Tezepelumab inhibits TSLP, IL-25 and IL-33.

Before starting biological therapy, the number of exacerbations in the past year, status in relation to oral glucocorticoid use, biomarkers (number of blood eosinophils, Fe and serum total and allergen-specific IgE), FEV1, FeNO, asthma control and quality of life. Criteria such as frequency of dosing, route of administration (subcutaneous or intravenous), whether administration of the drug requires supervision by healthcare personnel, age at onset of asthma, biomarkers, coexisting conditions (eg, atopic dermatitis and nasal polyposis), insurance, cost, and the patient's preferences are taken into account when choosing the available therapy. Biomarkers and coexisting conditions should be integrated with the clinical phenotype when making decisions regarding the choice of initial biologic therapy. Treatment of uncontrolled severe asthma involves several steps: first, confirming the diagnosis by differentiating difficult-to-treat asthma from severe asthma; second, determining the phenotype of severe asthma by integrating clinical characteristics, biomarkers, and coexisting conditions to select the appropriate initial biologic therapy; and finally, monitoring the therapeutic response and side effects to decide whether the biologic should be continued or discontinued (and changed, if feasible). An increasing number of eosinophils in the blood indicates an improvement in the response to treatment with a biological drug.

**Key words:** Severe asthma, Treatment, Biologic therapy, GINA recommendations

# INFLAMMATION AND PROTEOLYSIS IN PATHOGENESIS OF COVID 19 INFECTION (Proceedings-Editorial)

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According to generally adopted opinion the main feature in pathogenesis of COVID 19 is inflammation<sup>1</sup>. On the start of disease upper part of respiratory tract are involved in inflammation. In next phases of the disease the main place of inflammation is in down part of respiratory system. Inflammation caused by SARS CoV-2 go not as usual viral infection. As a first pneumonia in COVID 19 is not typical interstitial (viral) pneumonia. White blood cells count is showing no leukopenia with increased percentage of lymphocyte, as is usual in viral infection. In COVID 19 inappropriate neutrophil/lymphocyte with lack of lymphocytes<sup>2</sup> was seen.

**Local (alveolar) inflammation.** In COVID 19 inflammation is type I, with vasodilatation, exudation, recruitment of immunological cells in inflamed tissue. According to early research, papers from April and May 2020, the local inflammatory milieu is the most important for development of tissue damage. Predominant exudation, but also significant proteolytic activity of "inducible proteases" destroy the wall of alveoli. It seems that these proteolytic enzymes cause the hardest problem in the local inflammatory response. With very high level of exudation the alveoli become fulfill of fluid, and there are no possibilities for air to exchange in the alveoli<sup>4,5</sup>.

**General inflammatory syndrome during COVID-19 infection.** Cytokine storm occurs mostly in 5<sup>th</sup> – to 7<sup>th</sup> day, in early phase of diseases. But cytokine storm can be seen just in the late phase of diseases, two

– three weeks after beginning of the disease. In our own experience we have seen increase of cytokines during all phases of the disease<sup>6</sup>. We had the opportunity to see the most pronounced cytokine storms in the third and fourth week of the disease. The level of all proinflammatory cytokines increase. The concentration of IL-6 significantly increases within a few hours. In our own material the level of IL-6 has been increased up to a maximum of 2600 pg/L (reference value of the manufacturer 2-7 pg/l).

IL-1 increase so during COVID 19 infection. It is known as "acute phase response" parameter. The "variability" of increase of IL-1 is significantly narrower range (according to method Becton Dickinson normal value is as much as 4.85-5.25 pg/ml)

TNF- $\alpha$  – has the great variability in response. IL-8 with chemotactic action predominantly is involved with this function in pathogenesis of COVID 19.

TGF- $\beta$  – up to date there are a few papers addressed to this cytokine in pathogenesis of COVID-19. It is known as „anti-inflammatory“ cytokine, but that not so precise in description of their action. TGF- $\beta$  change behavior of inflammation toward to subacute and chronic phase. Granulomatous and mesenchymal tissue formation is stimulated by TGF- $\beta$ . A lot of scars can be seen thereafter. Tissue „remodeling“ is in widespread use in literature for determination of this process<sup>7,8</sup>.

In recent literature can be seen that around 85 % of COVID 19 infection was related to lung tissue. But rest of 15 % can cause very heavy clinical cases, including skeletal muscles inflammation (general myositis), neuritis, encephalitis, vasculitis and so on. Inappropriate coagulation status with inflammation of wall vessels, or without, cause the “infarctions” of any organ in the body. That's include cerebral stroke, lung emboli, embolization of arteries of both extremities and so on<sup>9,10</sup>. Amputation of limbs can be seen very often during or after COVID 19 infection.

**Proteolysis in COVID 19.** Not only inflammation, just local proteolysis was accused for destruction of alveolar walls and vera high level of destruction of alveolocapillary membrane. That's is the main reason why the use of respirator was not successful in most cases of COVID 19. Proteolysis is responsible for decreased number of lymphocytes in COVID 19.

**Conclusion.** Inflammation and proteolysis are the main feature in COVID 19 infection, the last one for destruction of alveolo-capillary membrane, and former for performing general inflammatory status, mostly by type I inflammation with predominant exudation in swelling of all tissue.

**Key words:** Inflammation, COVID 19, Proteolysis, Cytokines

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# PULMONARY MANIFESTATIONS OF SYSTEMIC AUTOIMMUNE DISEASES

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Systemic autoimmune disease (SAD) are a heterogeneous group of immune-mediated inflammatory disorders in which the body's function to distinguish its own from other people's antigens has failed. The body consequently reacts to its own antigens and causes multisystem inflammation of the organism. The most common SADs in which pulmonary complications occur are: systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, Sjögren's syndrome, polymyositis/dermatomyositis and mixed connective tissue disease. It is hard to determine the exact prevalence of pulmonary manifestations in SAD because they are often asymptomatic and the proof of their existence is found on autopsy or accidentally during performing regular diagnostic procedures. The most common symptoms are cough, dyspnoea on exertion, chest pain and fever, but they can vary and depend on which is the predominant pathophysiological mechanism and which part of the respiratory system is predominantly affected. Although pulmonary complications occur predominantly in developed stages of SAD, sometimes the first manifestation can be from the respiratory tract. Clinical manifestations of SADs include: interstitial lung disease, pleuritis, pleural effusion, pulmonary hypertension, bronchiolitis and pneumonia. At the appearance of the first symptoms or signs of the disease, routine laboratory findings and a chest X-ray are taken. Although most of the changes can already be seen on X-ray, high-resolution computed tomography has been proven superior then the X-ray for further classification of changes of the lungs. Pulmonary function tests should be performed to demonstrate functional lung changes. If that is not enough for establishing the diagnosis, bronchoscopy with bronchoalveolar lavage

is indicated as the next step, and the lung biopsy is the final choice. General treatment measures include smoking cessation, administration of flu and pneumococcal vaccinations, maintenance of bronchopulmonary hygiene and pulmonary rehabilitation. In case of reduced saturation, the use of oxygen is indicated. Drug treatment includes anti-inflammatory and immunomodulatory drugs such as nonsteroidal antirheumatic drugs, corticosteroids, drugs that modify the course of the disease and immunosuppressants. Recently, biological therapy has become more represented. It is very important to diagnose the disease in its early onset in order to start adequate therapy in time and prevent irreversible changes of the respiratory system.

**Key words:** Autoimmune diseases, Pulmonary manifestations, Diagnosis, Treatment

## WHAT IS NEW IN ANAPHYLAXIS

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Anaphylaxis is a serious and rapid systemic hypersensitivity reaction that can cause death. (1). The most severe forms of anaphylaxis can be manifested by collapse or sudden severe respiratory distress, without obvious symptoms and signs of skin and another organic system involvement.

The most severe anaphylaxis occurs in patients with clonal mast cell disease (indolent mastocytosis or clonal mast cell activation syndrome (MCAS)) or familial alpha-tryptasemia. Clonal mast cell disease is detected by determining the mutation of the KIT gene. This requires bone marrow biopsy or overly sensitive quantitative PCR, which can detect mutation in a blood sample. Family alpha-tryptasemia is measured by the digital droplet PCR method.

The presence of the p.D816V mutation in the KIT gene is a predictive factor of severe anaphylaxis after a sting Hymenoptera, regardless of the basal level of tryptase (BT) (2). About 30% of patients with very severe anaphylaxis had this mutation and almost none with mild disease. Most patients (~75%) with a KIT mutation had BT values below the upper limit of BT in the normal population (<11.4 µg/L). In patients with a cKIT mutation, immunotherapy with insect venom is less successful, as allergy returns after insect sting when immunotherapy is stopped in most patients.

Most patients with elevated BT do not have mastocytosis, but hereditary alpha tryptasemia (HAT) (3). HAT doubles the risk of severe anaphylaxis. About 0.3% of anaphylaxis results in death. Most often, the first anaphylaxis in life is fatal. Risk factors for fatal outcome are associated diseases (asthma, cardiovascular diseases, mast cell disea-

se), antihypertensives (ACE inhibitors, beta-adrenergic receptor blockers), age (children, teenagers, elderly), anaphylaxis after intravenous drugs, improper action or unrecognized anaphylactic reaction. In Slovenia, the KIT p.D816V mutation was demonstrated in the last three patients known, that have died during anaphylaxis.

In 2020, the World Allergy Organization (WAO) prepared updated guidelines for anaphylaxis. The purpose of the revised definition is primarily to emphasize that all anaphylactic reactions must be treated with intramuscular adrenaline.

**Key words:** Anaphylaxis, Hypersensitivity, Treatment

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# OPTIMAL TREATMENT OF COPD IN PATIENTS WITH HEART DISEASE

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Chronic obstructive pulmonary disease (COPD) is common but preventable disease, which is characterized by permanent respiratory symptoms and restriction of air flow, which are usually caused by airways and / or alveoli abnormalities, caused by significant exposure to harmful particles or gases, and under the influence of host factors, including abnormalities in lung development. COPD is currently the 3rd leading cause of death in the world!

Acute or chronic heart failure, ischemic heart disease and atrial fibrillation in COPD should be treated like those without COPD!!! However, most studies come from clinical studies, where COPD or heart disease was actually the only disease! That's why is necessary ALWAYS to carefully consider the existence of comorbidities and treat both conditions AT THE SAME TIME!!!

A reduced risk of mortality in patients with COPD and heart disease is evident if the following drugs are used correctly: LAMA, combination of ICS / LABA, angiotensin receptor blockers,  $\beta$  blockers, aldosterone antagonists, statins.

LABA and LAMA cause excessive sympathetic activation by activating sympathetic  $\beta$ 2 adrenergic receptors, i.e. suppressing parasympathetic muscarinic-3 receptors, which can contribute to the risk of cardiovascular diseases.

Also, LABA and LAMA in COPD increase the level of inflammatory cytokines, which may also have significance in worsening existing

cardiovascular risks. Careful monitoring of medication dosage and duration of treatment is necessary, as well as very close and coordinated cooperation between pulmonologists and cardiologists when choosing therapy.

**Key Words:** COPD, Treatment, Heart disease, Comorbidity

# EFFECTS OF NEOADJUVANT THERAPY AFTER THE INITIAL ASSESSMENT OF OPERABILITY IN PATIENTS WITH BORDERLINE OPERABLE AND INOPERABLE STAGE IIIA NON-SMALL CELL LUNG CANCER

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**Introduction:** Lung cancer is a neoplasm with the highest mortality rate in the world. The role of neoadjuvant therapy in patients with initially assessed borderline operable or inoperable lung cancer is to improve survival by downstaging the tumor and allowing surgical resection, as well as the potential treatment of micrometastatic disease.

**Aim:** Establishing the justification and efficacy of neoadjuvant therapy after the initial assessment of operability in patients with borderline operable and inoperable histopathologically verified stage IIIA non-small cell lung cancer.

**Patients and methods:** The retrospective study included 65 patients with initially assessed stage IIIA lung cancer, who underwent neoadjuvant therapy. After the cycles of neoadjuvant therapy, 19 patients who achieved the regression of the tumor underwent surgery. We analyzed the histological type of the tumor, extent, and prevalence of surgical resection, the status of regional lymph nodes, and the achieved R status.

**Results:** Of the total number of patients who underwent neoadjuvant therapy, after reevaluation of the disease, 19 patients (19/65, 29.23% of cases) achieved a clinical response, i.e. tumor downstaging. Of 19 patients who underwent surgery, 16 patients underwent surgical resection, while three patients underwent surgical exploration. The largest number of patients had N0 and N1 status (six patients each). R0 status was

achieved in 14 patients (14/16, 87.5% of cases), while R1 in the remaining two. One patient had a fatal outcome.

**Conclusion:** Neoadjuvant therapy plays an important role in the treatment of initially assessed borderline operable or inoperable lung cancers. By downstaging the tumor, it allows surgical resection and potential treatment of micrometastatic disease.

**Key words;** Non small lung Cancer, Therapy, Surgery, Micrometastatic disease



# GIGANT SOLITARY TUMOR

(Case report)

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A 40-year-old female patient was admitted to the Clinic for Thoracic Surgery, the Clinical Center University of Sarajevo for surgical treatment of a radiologically verified tumor of the left hemithorax. Complete pulmonary diagnostics was performed at the General Hospital Tešanj. During the hospitalization, an urgent contrast-enhanced chest CT scan was performed, which demonstrated an extensive soft tissue mass, leading to a marked right-sided cardiomedial shift. The patient was preoperatively examined by an internal medicine specialist, pulmonologist, and endocrinologist. Later, she was referred to a CT-guided puncture, as indicated by a multidisciplinary team. Taking into consideration the patient's general condition, she was surgically treated as a vital indication. The tumor was removed *in toto* and the postoperative course was uneventful. A definitive histopathological examination demonstrated a solitary fibrous tumor.

**Key words:** Fibrous tumor, Surgery, CT scan, Treatment

## CASE REPORT: UNIORT VATS

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A 49-year-old female patient was admitted to the Clinic for Thoracic Surgery, the Clinical Center University of Sarajevo for surgical treatment of a radiologically verified tumor of the left lower lobe. After a contrast-enhanced chest CT scan, a left lower lobectomy was performed, using a less invasive operative approach - *Uniport video-assisted thoracoscopic surgery* (Uniport VATS). The operation was performed through a 5 cm skin incision in the middle axillary line through which a fiberoptic camera and two working instruments were introduced into the pleural cavity. The entire operation (incision, dissection, disposal of vascular elements and bronchus, extraction of lobes using an endo-bag, lymphadenectomy, control of aero- and hemostasis, placement of a chest tube, suturing of the incision) lasted for approximately four hours. The advantage of the Uniport VATS technique compared to previous approaches in lung resections stands in favor of a minimally invasive approach, with less postoperative pain and earlier postoperative recovery.

**Keywords:** Uniport VATS, Lung tumor, CT scan

# NEWS IN THE DIAGNOSIS AND TREATMENT OF LUNG CANCER

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Lung cancer is the most commonly diagnosed cancer worldwide and the leading cause of cancer mortality. In 2022, an estimated 236,740 new cases (117,910 in males and 118,830 in females) of lung and bronchial cancer will be diagnosed, and 130,180 deaths (68,820 in males and 61,360 in females) are estimated to occur because of the disease. Only 21.7% of all patients with lung cancer are alive 5 years or more after diagnosis.

Much progress has been made recently for lung cancer, such as screening; minimally invasive techniques for diagnosis and treatment; advances in radiation therapy (RT), including stereotactic ablative radiotherapy (SABR); new targeted therapies; and new immunotherapies. These new treatments are reflected in the improved survival rates for patients with NSCLC. Patients with metastatic lung cancer who are eligible for targeted therapies or immunotherapies are now surviving longer; 5-year survival rates range from 15% to 50%, depending on the biomarker. Several biomarkers have emerged as predictive and prognostic markers for NSCLC. A predictive biomarker is indicative of therapeutic efficacy, because there is an interaction between the biomarker and therapy on patient outcome. A prognostic biomarker is indicative of patient survival independent of the treatment received, because the biomarker is an indicator of the innate tumor behavior.

Predictive molecular biomarkers include ALK rearrangements, BRAF p.V600E point mutations, EGFR mutations, ERBB2 (also known as HER2) mutations, Kirsten RA<sub>t</sub> Sarcoma virus (KRAS) mutations, mesenchymal-epithelial transition factor exon 14 (METex14) skipping mutations, neurotrophic tyrosine receptor kinase 1/2/3

(NTRK1/2/3) gene fusions, rearranged during transfection (RET) rearrangements, and ROS proto-oncogene 1 (ROS1) gene rearrangements; PD-L1 expression is the predictive immune biomarker.

In the treatment of metastatic disease, it is crucial before starting treatment, determine the exact histological subtype and molecular profile. Patients with positive genetic changes in the tumor such as EGFR, ALK, ROS1 is currently treated with targeted therapy.

Immunotherapy has found its place in the treatment of all malignant tumors, including lung cancer. Patients with high expression of PDL1 >50% receive Pembrolizumab as monotherapy in the first line of treatment, while patients with expression <1% as well as patients with PDL1 expression 1-49% receive combined chemotherapy with immunotherapy. Results were followed in five-year survival. Patients treated with immunotherapy, mono or combined, had significantly longer five-year survival.

**Key words:** NSLC, Lung cancer, Diagnosis, Treatment

# RIGID BRONCHOSCOPY-A 21st CENTURY TOOL?

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Rigid bronchoscopy is a technique that directly visualizes the trachea and proximal bronchi. It is most commonly used to manage patients who have obstruction of either their trachea or a proximal bronchus, since the rigid bronchoscope's large lumen facilitates suctioning and the removal of debris, or for interventional procedures such as insertion of airway stents, thus making it an optimal and invaluable tool for diagnosis and especially treatment (combined with laser, argon plasma coagulation or cryotechniques) of central airway stenosis in 21st century. The knowledge of rigid bronchoscopy, based on proper, structured educational programme is mandatory for every interventional pulmonologist.

**Key words;** Rigid bronchoscopy, Interventional procedure

# EMERGENCY TRACHEOBRONCHOSCOPY IN CHILDREN

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In our study we analyzed of the cases urgent bronchoscopies of children up to 14 years of age, from January 1954 to December 2021. To determine the clinical characteristics and outcomes urgent bronchoscopies of children due to foreign body aspiration. Each patient was analyzed for age, sex, nature and location of the foreign body, results of bronchoscopic removal, complications of bronchoscopy and presence of foreign body in the airways. Eight hundred and eighty-nine children underwent urgent bronchoscopy on suspicion of a foreign body in the lower respiratory tract over a period of 67 years. Most cases (66.7%) occurred within the first three years of the evaluation period. In all periods there were 10.6% of the cases children under one year old. Recently, there has been a rapid decrease in the number of positive cases under the age of one. From evaluation period children 62.5% were boys, age ranging from eight months to fourteen years. In the observed period in most cases foreign bodies are organic in nature, pumpkin seeds are predominantly represented. The predominant location of foreign bodies were the right bronchus 51%. In the last observed period, the location of foreign bodies in several places has increased significantly compared to the period before 2004. The number of urgent bronchoscopies per year, and the percentage of positive findings has been reduced recently, and the type of the locations of foreign bodies does not different from Europe.

**Key words:** Urgent bronchoscopy, Children, Foreign body, Removal

# UNIportal VATS Lobectomy, From Introduction to Standard

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Video assisted thoracoscopic approach means operative surgical technique on lungs, pleura, mediastinum and other intrathoracic organs through the one or more holes of 3-5 cm using optic instruments. Indications for VATS are diagnostic or therapeutic like biopsy of tumors on lungs, pleura, or lymphatic tissue of mediastinum, than excisions or extirpations of benign and malignant tumors, and also small or anatomic-oncological resections of malignancy, and also benign illness like TBC cavitations.

VATS gives to us same oncological results like open thoracic surgery and it's cheaper for healthcare system of country.

In UCC Tuzla VATS is in program from earlier 2000'. First VATS tymectomy performed on 2015. First VATS lobectomy performed 2019.

In period from January 2019. to September 2022. we performed 101 lobectomies (UVATS 46, open 55).

In pathological diagnoses there was planocellular carcinoma, adenocarcinoma, carcinoid tumor and bronchiectasies.

In the future, for better results, we need reform of healthcare system, educations of young surgeons, better equipment and training in simulation centers, dry and wet labs.

**Key words:** VATS, Lobectomy, Lung surgery.

# ANALYSIS OF RISK FACTORS FOR BACTERIAL SUPERINFECTION IN PATIENTS WITH COPD

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**Introduction:** Chronic bronchitis is defined as a condition of repeated episodes of coughing cumulatively for three months in the last two years. Bronchiectasis is a state of chronic inflammation of the bronchi with lumen expansions, which allows retention of secretions and mucus. Patients with bronchiectasis and chronic obstructive pulmonary disease are often colonized with pathogenic microorganisms that pose a risk for the development of infection.

**Aim:** Microbiological analysis of sputum in patients suffering from chronic bronchitis with and without bronchiectasis who were hospitalized at the Pulmonology Department of General Hospital Tešanj in the period from 01.09.2021. to 31.08.2022.

**Methods:** In addition to regular laboratory, radiological and clinical examinations, a sputum sample was taken from hospitalized patients and sent for microbiological analysis. The data were statistically processed.

**Results:** The total number of patients analyzed was 99, of which 71 (71.72%) were diagnosed with chronic bronchitis, 5 (5.05%) were diagnosed with bronchiectasis, and 23 (23.23%) were diagnosed with chronic bronchitis and bronchiectasis together ( $\chi^2=70,55$ ;  $p<0.001$ ). Out of the total number of patients, there were 38 (38.38%) female and 61 (61.62%) male ( $\chi^2=24,52$ ;  $p<0.001$ ). Analyzing age characteristics, it was found that the average age was 70.2 years (SD= $\pm 9.76$ ), ranging from 43 to 86 years. Out of the total number of patients with chronic



bronchitis (71), 48 of them (67.61%) had saprophytic flora. The most frequently isolated bacterium is *Pseudomonas aeruginosa* in 7 (9.86%) patients. The following bacteria in order of frequency were *Enterobacter* spp. isolated in 4 cases (5.63%), *Moraxella catarrhalis* in 3 cases (4.23%), *Proteus mirabilis* isolated in 2 cases (2.82%), *Citrobacter freundii* isolated in 1 case (1, 40%) while *Candida* spp was isolated in 6 (8.45%) patients. In patients suffering from chronic bronchitis with bronchiectasis, the most frequently isolated bacteria was *Pseudomonas aeruginosa*, present in 3 (10.71%) patients. The next most frequent bacteria were *Acinetobacter* spp. in 2 (7.14%), *Streptococcus pneumoniae* isolated in 2 (7.14%), *Klebsiella oxytoca* isolated in 1 (3.57%) and *Serratia marcescens* isolated in 1 (3.57%) patient. *Candida* spp was isolated in 4 (14.29%) patients. However, the largest number of patients, 15 of them (53.58%) had saprophytic flora. Statistically, pathological bacteria are isolated more often from patients who have described bronchiectasis with chronic bronchitis compared with those who only suffer from chronic bronchitis ( $\chi^2=19,07$ ;  $p<0.001$ ).

**Conclusion:** Most of those hospitalized were patients suffering from chronic bronchitis. Most of the patients had saprophytic flora, while in patients whose sputum bacteria were isolated, *Pseudomonas aeruginosa* was the most common. Patients who already have bronchiectasis are more susceptible to pathogenic bacteria than patients who do not have bronchiectasis.

**Key words:** Sputum, Chronic bronchitis, Bronchiectasis, Microbiology,

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# PATIENT WITH HYPERSENSITIVITY PNEUMONITIS (EXTRINSIC ALLERGIC ALVEOLITIS) (Case Report)

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**Introduction:** Extrinsic allergic alveolitis (EAA) or hypersensitivity pneumonitis is an immune-mediated disease, an inflammatory reaction of the alveoli that occurs after previous sensitization and repeated inhalation of dust of organic origin.<sup>1</sup> Dust contains microorganisms such as bacteria and fungi, animal or plant products, and chemical agents that act as antigens. Inhaled agents trigger type III and IV hypersensitivity reactions.<sup>2</sup> An acute isolated attack is characterized by elevated body temperature, fever, cough and shortness of breath, headache, and occurs 4 to 6 hours after exposure to the allergen. A subacute condition occurs after one to two months of exposure to an inhaled allergen, characterized by shortness of breath, dry cough.<sup>3</sup> Lung images are characterized by fine alveolar spots that are especially visible in the middle and lower lung fields.<sup>4</sup> The chronic phase occurs after long-term exposure to the agent, which develops into pulmonary fibrosis.

**Case report:** A 52-year-old woman was referred by her family doctor to our institution because of a cough that has lasted for 15 days, shortness of breath, fever, and malaise. The patient works on an agricultural farm. On admission, the patient was dyspneic, with diffuse crackles on auscultation over the lungs. Slightly elevated inflammatory parameters, leukocytosis are verified in the laboratory. Arterial blood gas analysis shows a low partial pressure of oxygen. On the chest x ray of the lung, band-like patchy infiltrates can be seen bilaterally basally

and paracardially. On the performed CT, the signs of increased density of the lung parenchyma with mild pulmonary mosaic perfusion through the middle and lower lung fields are dominant, which speak in favor of allergic alveolitis. With this knowledge, laboratory tests are performed in the form of total IgE and specific IgE to inhalant agents birch pollen, alder pollen, oak pollen, olive pollen, wild wormwood pollen, buckthorn pollen, which are positive. The patient was treated with corticosteroid therapy and antibiotics, and her health, laboratory and radiographic parameters improved.

**Discussion:** Hypersensitivity pneumonitis is a syndrome caused by inhalation of specific antigens at the workplace or environmental exposure in sensitized individuals. Episodes of fever with shortness of breath, dry cough and malaise followed by exposure to the environment are typical for extrinsic allergic alveolitis.<sup>2</sup> The clinical condition of our patient, as well as the immunological and CT findings of the thoracic organs are in favor of extrinsic allergic alveolitis. The presence of specific IgE to birch, alder, oak, olive, wild wormwood and buckthorn pollen confirms the diagnosis of hypersensitivity pneumonitis.

**Conclusion:** Based on the clinical picture of the patient and the performed CT, laboratory analysis, the diagnosis of extrinsic allergic alveolitis was confirmed.

**Key words:** Hypersensitivity Pnuemonitis, Extrinsic Allergic Alveolitis, IgE-Mediated Hypersensitivity

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# CASE REPORT: PATIENT WITH PULMONARY AND INTESTINAL TUBERCULOSIS

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**Introduction:** Tuberculosis of the gastrointestinal tract (GIT) is currently a rare disease with a share of 11% of total extrapulmonary tuberculosis.<sup>1,2</sup> Intestinal tuberculosis can occur after ingestion of bacilli from sputum, by blood spread or *per continuitatem* from neighboring organs. It is characterized by transverse ulcers, fibrosis, thickening and strictures of the intestine, as well as lymphadenopathy and thickening of the omentum.<sup>3</sup> The predilection site of tuberculosis in the GIT is the terminal ileum and the ileo-cecal region and ascending colon.<sup>2</sup>

**Case Report:** A 53-year-old man was referred from the Zenica Cantonal Hospital to our institution for active lung miliary tuberculosis. At the admission, patient stated that he has lost 30 kg in the past year and had difficulty breathing and coughing in the last couple of months. Slightly elevated non-specific parameters of inflammation, hypoalbuminemia and medium-severe secondary anemia were verified in the laboratory. On the chest X-ray, bilateral hazy-speckled changes were observed, with hyperinflation of the parenchyma on the left, which were confirmed on CT scan as numerous cavitations and pulmonary micronodules. With that knowledge, diagnosis of miliary tuberculosis was confirmed. Due to abundant diarrheal stools for the past three months, extensive microbiological examinations of the stool were performed, which failed to isolate the causative agent. Abdominal ultrasound showed thickening of the colon, which is described on the abdominal CT scan as a diffuse thickening of the entire colon, with a predominance of the caecum, colon, and wall of the terminal ileum. A stool sample was

taken, where the sample was re-examined and many mycobacteria were found. Currently, the patient is being treated with antituberculosis therapy (PFD) with improvement in health and laboratory parameters.

**Discussion:** The caecum and terminal ileum are the predominant sites of GIT tuberculosis. With the advancement of effective ATD therapy, extrapulmonary tuberculosis is quite rare.<sup>4</sup> Mucous ulcerations that are found circumferentially, together with the deformity of the intestinal wall, can indicate intestinal tuberculosis as it was in our patient. Clinical signs of intestinal tuberculosis include abdominal pain, weight loss, elevated body temperature, night sweats and changes in stool.<sup>5</sup> Our patient had some of the above symptoms.

**Conclusion:** In patients with severe weight loss and diarrheal stools, it's necessary to think about the spread of the pulmonary tuberculosis center to the GIT. Intestinal tuberculosis can mimic colon malignancy due to the similarity of the symptoms they cause.

**Key words:** Tuberculosis, Intestinal tuberculosis, Miliary tuberculosis

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# INTRAPARTAL WORSENING OF CONSCIOUSNESS IN A PREGNANT WOMAN WITH BRONCHIAL ASTHMA AGGRAVATED BY A PREVIOUS COVID 19 INFECTION: IS THERE ANY CONNECTIONS BETWEEN?

(Case report)

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**Introduction:** Physiological changes in pregnancy, such as a decrease in pulmonary residual functional volume and edema of the respiratory tract's mucous membrane, as well as immune changes, can increase susceptibility to SARS-CoV-2 infection and lead to more serious consequences [1]. Pregnant women with SARS-CoV-2 infection were more likely to have preeclampsia, preterm birth, increased perinatal mortality, neonates with low birth weight, low Apgar score, fetal distress and stillbirth [1]. Optimal delivery mode for infected pregnant women needs to be based on obstetric indications and COVID-19 severity<sup>1</sup>.

**Aim:** The aim of this paper is to present the case of a patient whose state of consciousness worsened during childbirth, who has exacerbation of bronchial asthma caused by a COVID 19 infection.

**Case report:** The patient was admitted to the maternity ward due to irregular contractions, 6 days after the due date of delivery. In her personal anamnesis, she states that she has been treated for bronchial asthma for a long time, she uses an inhaled preparation of a combination of bronchodilators (formoterol fumarate dihydrate) and corticosteroids (beclomethasone dipropionate). Ten days ago, there was a worsening of bronchial asthma in the form of difficulty breathing and coughing, when

it was established that she was positive for the SARS-CoV-2 virus. The pulmonologist prescribed oxygenotherapy, intravenous corticosteroid therapy (hydrocortisone), inhaled bronchodilators and corticosteroids, antibiotics (azithromycin). After the prescribed therapy, the disease was brought under control, and SARS-CoV-2 became negative.

Obstetric findings at admission; cervix shortened, length 0.5 cm, medioponed, soft, dilatation 3 cm, amniotic membranes exists, fetal head is on -1 height, sutura sagitalis in the first oblique diameter, small fontanelle at 14h, large fontanelle at 20h, contractions irregular, CTG record reactive.

A general examination shows that the patient is conscious, communicative, eucardic, mildly dyspnoic, with discrete wheezing audible on auscultation. Given the favorable obstetric findings, it was decided to start a vaginal delivery.

Two hours after admission, the midwife called the obstetrician for an examination because she noticed that the patient's state of consciousness had worsened. The patient is conspicuously sleepy, wakes up with difficulty when called and motor stimulation maintains alertness and keeps her eyes open, breathes rapidly and shallowly, does not answer questions or answers intermittently. Internist, pulmonologist and anesthesiologist are consulted. Laboratory tests are performed (blood count, acid-base status, electrolytes, ECG). In the acid-base status, respiratory alkalosis is verified, on the ECG recording mild tachycardia (100/min). The CTG record indicates fetal tachycardia (180/min). Consultants prescribe therapy according to the protocol for asthma exacerbation and recommend an accelerated completion of childbirth due to the condition of the mother, without going into obstetric indications.

Considering the mother's vital threat due to worsening of bronchial asthma and worsening of consciousness, threatening asphyxia of the fetus and the impossibility of quickly ending the initiated vaginal delivery (initial dilatation, irregular contractions), it is indicated to end the



delivery by caesarean section under spinal anesthesia. A live male birth weight of 3000, length 53 cm, Apgar score in the 1st minute is 8 in the 5th minute is 9. After the birth, the intensified therapy of exacerbated asthma continues and the mother's condition improves, she becomes awake, conscious, eupnoic and eucardic with an occasional dry cough.

The postoperative recovery is progressing smoothly, with occasional attacks of difficulty breathing in the mother, but with an adequate response to the prescribed therapy. Mother and baby are discharged to home recovery on the 3rd postoperative day with recommendations for therapy.

**Discussion:** We presented a case of sudden exacerbation of bronchial asthma during childbirth. The previous deterioration was verified 10 days ago, when the infection with SARS-CoV-2 was verified, but thanks to the prescribed therapy, there is a recovery and a negativisation to the infection. During childbirth, the state of consciousness worsens again and breathing becomes difficult. The question arises whether asthma exacerbation or recent SARS-CoV-2 infection is the cause of cerebral hypoperfusion and deterioration of consciousness.

In their cohort study, Grgić et al analyzed the perinatal outcome in patients who were SARS-CoV-2 positive during childbirth with and without symptoms. They came to the conclusion that symptomatic pregnant women with SARS-CoV-2 infection at the delivery show more frequently altered laboratory parameters compared with asymptomatic ones; also, they have a slightly higher but non-significant rate of preterm delivery and of cesarean section, as well as lower neonatal birth weight and Apgar score compared with asymptomatic women<sup>1</sup>.

**Conclusion:** Aggravation of asthma during pregnancy and childbirth can sometimes be pronounced and endanger the condition of the mother and the fetus, as shown in our case. The dilemma remains whether the exacerbation of asthma or the recent COVID 19 infection caused the deterioration of consciousness and pathological sleepiness in the

mother. A quick and team approach in coordination with a midwife, pulmonologist, internist, anesthesiologist and obstetrician results in a good and successful perinatal outcome for mother and fetus.

**Key words:** Pregnancy, Delivery, Asthma bronchiale, COVID 19

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# PHARMACOLOGICAL TREATMENT OF TUBERCULOSIS IN PREGNANCY AND PUERPERIUM

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**Introduction.** The exact incidence of tuberculosis in pregnancy is not available in many countries<sup>1,2,3,4</sup>. Obstetric complications that have been reported in these women include a higher rate of spontaneous abortion, suboptimal weight gain in pregnancy, preterm birth, low birth weight and increased neonatal morbidity and mortality<sup>1,2,3,4</sup>.

**Aim.** A review of the literature was compiled from searches of the Medline database and PubMed. Search terms included: *Pregnancy, Puerperium and Tuberculosis*.

**Treatment of tuberculosis in pregnancy.** The combination of drugs in pregnancy is isoniazid, rifampicin and pyrazinamide. Ethambutol is used in the treatment of tuberculosis in pregnancy only if it is absolutely necessary as the fourth drug in the combination of antituberculosis drugs<sup>4</sup>. The use of these first-line antituberculous drugs in pregnancy are considered safe for the mother and the baby by the World Health Organization<sup>1,2,3,4</sup>.

Antituberculosis drugs are well tolerated during pregnancy, with the exception of streptomycin, which is contraindicated because it is ototoxic and nephrotoxic for the fetus<sup>4</sup>. During childbirth, a mother taking antituberculosis drugs is advised to give vitamin K to the newborn because of the risk of postnatal hemorrhage<sup>4</sup>.

## **Tuberculosis and the newborn**

Congenital tuberculosis may be as a result of haematogenous spread through the umbilical vein to the foetal liver or by ingestion and aspiration of infected amniotic fluid. As much as half of the neonates delivered with congenital tuberculosis may eventually die<sup>1,2,3,4</sup>.

### **Treatment of tuberculosis in puerperium**

The decision to breastfeed is made as a team in consultation with a neonatologist, obstetrician and clinical pharmacologist. During breastfeeding, all drugs for the treatment of tuberculosis can be used, it is not necessary to interrupt the administration of the drug, and it is not necessary to separate the mother and the child<sup>4</sup>. If the mother is infectious during childbirth, the child should be given prophylactic isoniazid for 3 months. BCG vaccination is postponed until the end of isoniazid prophylaxis<sup>4</sup>.

### **Conclusion**

Treatment of tuberculosis during pregnancy and breastfeeding is necessary and safe. The only contraindicated antituberculosis drug is streptomycin because of its ototoxicity and nephrotoxicity.

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# CORONAVIRUS DISEASE AND CORONARY FLOW RESERVE ASSESSED BY TRANSTHORACIC ECHOCARDIOGRAPHY - IS THERE A LINK?

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**Background:** Coronary flow reserve (CFR) ratio is ratio of hyperaemic coronary blood flow during maximum vasodilation in relation to resting coronary blood flow (measure of augmentation of flow by exercise, stress or microcirculatory vasodilation).

**Objective:** To indicate the possible influence of coronavirus disease 2019 (COVID-19) on CFR values in patients without verified coronary artery disease (CAD).

**Methods:** The paper presents an analysis of the available literature from reference databases covering the mentioned topic.

**Results:** Normal value of CFR is greater than 2. The most commonly used vasodilators are dipyridamole (0.84 mg/kg/6 min) and adenosine (140 mcg/kg/min). CFR presents additional test to stress echocardiography. Clinical presentation of patient should be noted prior the test. A 24 hours abstinence from caffeine, tobacco, food containing significant amount of methylxanthines (coffee, tea, chocolate, cola and banana) and anti-ischaemic agents, antihypertensive medication and diuretics should be done. Interobserver and intraobserver variability of CFR measurements are in the range of 5 %.

Heart with preserved CFR can be referred to as a “warm heart,” opposed to the “cold heart” with reduced CFR. The left anterior descending (LAD) coronary artery has been the most commonly investigated, followed by the posterior descending artery (PDA). Technical feasibility to investigate LAD is high with more than 90% (nearly 100 %

with the use of intravenous contrast agents). The feasibility of CFR assessment in PDA is in the range between 54 and 86%.

Age has a decreased effect on values of hyperemic CFR, and this is also applicable for female gender. There is evidence that there are ethnic differences that can affect the structure of the myocardium, as well as the anatomical variations of the coronary circulation. In addition it can be found in literature that modifiable (or conditionally preventable) risk factors have negative effect on CFR values (obesity, smoking, hyperlipidemia, elevated values of low-density lipoproteins (LDL), arterial hypertension, diabetes mellitus, obstructive sleep apnea) in a healthy population. CFR decreases with increase of body mass index (BMI). COVID-19 has been characterized by microvascular dysfunction. There is evidence that the severity of COVID-19 significantly affects the CFR values, and that the sequelae characterized by long-COVID-19 can also be explained by the CFR values. Also, CFR values significantly correlate with high-sensitivity cardiac troponin and brain natriuretic peptide values, as well as interleukin-6 and C-reactive protein values, thus indicating the role of inflammation in endothelial dysfunction, which is a characteristic of COVID-19.

**Conclusion:** Echo-based CFR is a non-radioactive, cost-efficient and feasible technique with incremental prognostic information. It is a marker of early stages of coronary atherosclerosis, and also measure of coronary microvascular dysfunction and as such it can be part of the mosaic in the stratification of patients in regards to cardiovascular risk. Also, CFR could be part of the decision regarding patient's therapeutic modality, and the use of agents with nitroxide-mediated vasodilating properties should be therapy of choice.

**Key words:** Coronavirus disease, Coronary flow, Reserve endothelial dysfunction.

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Articles of nurses - radovi sestara

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# ANALIZA VREMENA NEGATIVIZACIJE BK POZITIVNIH PACIJENATA PRIJE I POSLIJE PANDEMIJE COVID-19

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**Uvod:** Tuberkuloza je zarazna bolest uzrokovana bacilom *Mycobacterium tuberculosis*, koji prvenstveno zahvata pluća. Infekcija se uglavnom prenosi kapljičnim putem. Kod plućnog TBC-a proširenost bolesti može varirati, ali bez učinkovite terapija bolest vrlo brzo napreduje.

**Cilj rada:** Praćeno je vrijeme negativizacije pacijenata u periodu prije i poslije Covid-a, oslanjajući se na historije bolničkih pacijenata koji su liječeni na pulmološkom odjelu OBT.

**Rezultati:** U periodu od 01.01.2017. do 30.09.2017. godine, prije Covid-a ispitan je 21 pacijent. Prema starosnoj dobi bila su 2 pacijenta do 20 godina, od 20-40 godina bilo je 7 pacijenata, od 40-60 godina bilo je 7 pacijenata, 60-80 godina bilo je 5 pacijenata. U toku prvog mjeseca liječenja, 13 pacijenata se negativiziralo, za 2 mjeseca je 5 pacijenata negativizirano i za 3 mjeseca su 2 pacijenta negativizirana. 4. mjesec liječenja svi pacijenti su negativizirani. Od 01.01.2022. do 30.09.2022. godine u POST-COVID periodu ispitan je 21 pacijent. Prema starosnoj dobi do 20 godina nije bilo pacijenata, od 20-40 godina je bilo 7 pacijenata, od 40-60 godina je bilo 5 pacijenata i od 60-80 godina je bilo 9 pacijenata. U toku prvog mjeseca liječenja 10 pacijenata se negativiziralo, za 2 mjeseca su 4 pacijenta negativizirana, za 3 mjeseca 2 pacijenta, za 4 mjeseca nije negativiziran niti jedan pacijent, za 5 mjeseci - 2 pacijenta. 6. mjesec liječenja svi pacijenti su negativizirani.

**Zaključak:** Analizirajući podatke do kojih smo došli, da se zaključiti da pacijenti koji su liječeni od tuberkuloze prije Covid-a dosta brže uspjeli negativizirati u odnosu na POST-COVID period.

**Ključne riječi:** Tuberkuloza, Negativizacija, COVID 19

# ANALYSIS OF TIMES FOR NEGATIVIZATION OF BK POSITIVE PATIENTS BEFORE AND AFTER COVID-19

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**Introduction:** Tuberculosis is contagious disease that is caused by bacillus *Mycobacterium tuberculosis*, which primarily affects the lungs. Infection is mainly transmitted by droplets. Talking about pulmonary TBC, the extent of the disease can vary, but without effective medicines disease is progressing very quickly.

**Work goal:** The time of negativisation of patients has been followed in period before and after COVID, leaning on patients' documents histories that have been treated on pulmonologists department.

**Results:** In period 1.1.2017.-30.9.2017., before COVID, 21 patients have been tested. According to age, there have been 2 patients up to 20 years, 7 patients that were 20-40 years old, 7 patients that were 40-60 years old, and 5 patients that were 60-80 years old. During the first month of treatment, 13 patients has been negativized, in 2 months 5 patients got negativized and in 3 months 2 patients has been negativized. In 4th month of treatment all of the patients have been negativized. Since 1.1.2022. to 30.9.2022. in POST-COVID period, 21 patients have been tested. According to age, there were no patients up to 20 years old, 7 patients that were 20-40 years old, 5 patients that were 40-60 years old, and 9 patients that were 60-80 years old. In period of first month of treatment, 10 patients were negativized, in 2 months 4 patients were negativized, in 3 months 2 patients were negativized, and in 4 months none of the patients were negativized, in 5 months, 2 patients were negativized, and in the 6th month of treatment, 2 patients were negativized.

**Conclusion:** According to data we got, it can be concluded that patients that have been treated from tuberculosis before COVID, managed to become negative faster in comparison with post-COVID period.

**Key Words:** Tuberculosis, Negativization, BK, COVID 19.

# APLIKACIJA I PRAĆENJE INHALACIJSKE TERAPIJE

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**Uvod:** Bronhijalna astma i hronična opstruktivna bolest pluća (HOPB) (hronični bronhitis i emfizem pluća) su oboljenja disajnih puteva i zbog toga tzv. inhalacioni put (udisanjem) primjene lijekova ima prednost nad ostalim (tablete, sirup ili injekcije). Pravilna upotreba „pumpica“ ima veoma veliki značaj u liječenju. Ako se pravilno koristi, udisanjem se unose lijekovi u obliku aerosola na mjesto gdje će djelovati, a to su mali disajni putevi (10–17 generacije bronha, a kod dobre upotrebe i dalje).

**Cilj rada:** Praćenje i obuka pacijenata za korištenje dezopstuktivne inhalacione terapije na Odjelu Pulmologije Opće bolnice Tešanj u periodu od 1.1.2022. do 31.10.2022. godine.

**Metode:** Po već pripremljenom obrascu za praćenje obuke inhalacijske terapije praćena je dužina trajanja obuke, obučenosť za korištenje inhalatorne terapije i tip inhalatorne terapije koja se koristi. Podaci su statistički obrađeni.

**Rezultati:** U periodu od 1.1.2022. do 31.10.2022. godine obrađeno je 100 istorija bolesti pacijenata koji su ležali na Odjelu Pulmologije Opće bolnice Tešanj. Od toga 26 pacijenata je imalo dijagnozu HOPB. Od 26 pacijenata njih 11 (42,3%) je po prijemu bilo obučeno za korištenje inhalatorne terapije, dok ostali 15 (57,7%) pacijenata na prijemu bio neobučeni. Kod pacijenata koji su bili neobučeni, obuka za pravilno korištenje inhalatorne terapije je trajala u prosjeku 3-7 dana (prosječno 4,47 dana). Pet pacijenata, koji su koristili inhalatornu terapiju više od dvije godine su, bili neobučeni na prijemu. Pacijenti su najsporije obučavani za inhalere pod pritiskom, a donekle i na inhalere s kapsulom. Za ostale vrste inhalera obučenosť bila individualna.

**Zaključak:** Najveći broj hospitaliziranih pacijenata koji su primljeni sa dijagnozom HOPB je bio neobučeni za korištenje inhalacijske terapije. Dužina obuke je bila individualna za svakog pacijenta, a u prosjeku je trajala od 3-7 dana. Pacijenti su se najteže obučavani za inhalere pod pritiskom, a donekle i sa kapsulom za inhaler.

**Ključne riječi:** Inhalacijska terapija, Inhaleri, COPD

# APPLICATION AND MONITORING OF INHALATORY THERAPY

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**Introduction:** Bronchial Asthma and Chronic Obstructive Pulmonary Disease (COPD) (chronic bronchitis and pulmonary emphysem) are diseases of the airways which is why inhalatory application of drugs has the advantage over other ways of drug administration (tablets, syrups, and injections). Proper use of inhalers play a big role in curing the disease. If used properly medication is inhaled in a form of aerosol right to the place of action, which are small airways (10th to 17th generation of bronchs, and with a good application even further).

**Aim:** Monitoring and education patients for use disruptive inhalatory therapy at the Department of Pulmology in General Hospital Tešanj in the period from 01.01.2022. to 31.10.2022.

**Methods:** By already prepared form for monitoring education of inhalatory therapy we followed the length of education, level of education for inhalatory therapy and type of inhalatory therapy. The data was statistically processed.

**Results:** In the period from 1.1.2022. to 31.10.2022. 100 patient histories from the Department of Pulmology in General Hospital Tešanj were processed. Out of all the processed patient data, 26 of the patients had COPD. Out of those 26 patients, 11 of them (42.3%) had prior knowledge for the use of inhalatory therapy, while the remaining 15 patients (57.7%) were uneducated. In the case of uneducated patients, the education for use of inhalatory therapy lasted approximately 3-7 days (4.47 days). 5 patients who had used inhalatory therapy for more than 2 years were uneducated on admission. Patients took the most time to get educated on the use of hard capsule inhalers (Seebri, Spyro, Brequal), while education for other types of inhalers varied from patient to patient.

**Conclusion:** Most hospitalized patients with diagnosis of COPD were not educated for use of inhalatory therapy. The length of education was individual for every patient, but approximately lasted 3-7 days. Patients took the most time to get educated on the use of hard capsule inhalers.

**Key Words:** Inhalation, Therapy, COPD

# HIDRACIJA KOD COVID POZITIVNIH PACIJENATA

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**Uvod:** COVID 19 je virusna infekcija uzrokovana koronavirusom SARS-CoV-2. Prvi put se pojavila krajem 2019. god. Zbog brzog širenja ove bolesti Svjetska zdravstvena organizacija (WHO) je proglasila pandemiju, što znači da je bolest prisutna u cijelom svijetu. Uzročnik bolesti primarno se širi najčešće kapljičnim putem, uglavnom u bliskom kontaktu.

Rizik za prijenos bolesti najveći je u prva tri dana od pojave simptoma. Glavni simptomi su temperatura, kašalj, gubitak čula okusa i mirisa, bolovi u mišićima, kratak dah i gubitak apetita.

**Cilj rada:** Praćenje COVID 29 pozitivnih pacijenata tokom liječenja sa glavnim osvrtom na status ukupne tjelesne vode, tj. hidraciju.

**Metode:** Kod pacijenata su tokom bolničkog liječenja praćeni parametri bilansa vode, sa posebnim osvrtom na stanje dehidracije. Pored vizuelnog pregleda (jezik,koža), hidracija pacijenta se pratila putem laboratorijskih nalaza (K,Na). Tokom cijelog liječenja evidentiran je peroralni unos i date infuzije.

**Rezultati:** Analizirani su podaci COVID pozitivnih pacijenata u periodu od 1.1.2021. do 1.4.2021. god. Najšešća dehidracija je zabilježena kod osoba starije životne dobi, a nešto češće je zabilježena kod muškaraca dobi 60-69 god.

**Zaključak:** Adekvatna hidracija pacijenata je značajno uticala na pozitivan ishod bolesti, te ju je potrebno pratiti istovremeno sa saturacijom hemoglobina kisikom.

**Ključne riječi:** Saturacija kisikom, Hidracija, COVID 19

# HYDRATION IN COVID 19 POSITIVE PATIENTS

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**Introduction:** COVID 19 is a viral infection caused by SARS-CoV-2 coronavirus. It appeared for the first time at the end of 2019. Due to the rapid spread of this disease, the World Health Organization (WHO) declared it a pandemic, which means that the disease is present all over the world. The causative agent of the disease is primarily spread by droplets, mostly through close contact. The risk of disease transmission is highest in the first three days after the onset of symptoms. The main symptoms are fever, cough, loss of sense of taste and smell, muscle pain, shortness of breath and loss of appetite.

**Aim:** Monitoring of COVID 19 positive patients during treatment with the main focus on the status of total body water, i.e. hydration.

**Methods:** During hospital treatment, water balance parameters were monitored in patients, with special reference to the state of dehydration. In addition to the visual examination (tongue, skin), the patient's hydration was monitored through laboratory findings (potassium, sodium). During the entire treatment, oral intake and given infusions were recorded.

**Results:** The data of COVID- 19 positive patients in the period from 1.1.2021 to 1.4.2021 were analyzed. The most common dehydration is recorded in elderly people, and it is slightly more often recorded in men aged 60-69 years.

**Conclusion:** Adequate hydration of patients had a significant impact on the positive outcome of the disease, and it should be monitored simultaneously with oxygen saturation of hemoglobin.

**Keywords:** Oxygen saturation, Hydration, COVID 19

# SATURACIJA KISIKOM KOD COVID POZITIVNIH PACIJENATA

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**Cilj rada:** Praćenje zdravstvenog stanja COVID pozitivnih pacijenata sa glavnim osvrtom na saturaciju hemoglobina kisikom.

**Metode:** Saturacija hemoglobina kisikom pacijenata praćena putem puloximetra, često i plinskim analizama krvi, ABS nalazom.

**Rezultati:** Analizirajući podatke COVID pozitivnih pacijenata, prilikom prijema najniža izmjerena saturacija je 61,0 % dok je najviša – 97,8 %. Najviša izmjerena saturacija tokom hospitalizacije je 95,8%, dok je najniža – 28,0 %. Saturacija kisikom je praćena istovremeno s drugim parametrima važnim za pacijente, tj. donošenje odluka o liječenju.

**Zaključak:** Prema stanju COVID pozitivni pacijenti zahtijevali su permanentno praćenje i blagovremeno reagovanje. Pored održavanja zadovoljavajuće saturacije O<sub>2</sub>, drugi bitan faktor je dobra hidracija koja uveliko pomaže da se tegobe ublaže i da se ostvari brži oporavak.

# OXYGEN SATURATION LEVELS OF COVID POSITIVE PATIENTS

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**The aim of the study:** Monitoring of COVID positive patients' condition with special focus on the saturation of haemoglobin by oxygen.

**Methods:** Saturation of patients was monitored using pulse oximeter, and with blood gas analyses (ABS) if it is necessaire.

**Results:** The analysis the data of all COVID positive patients revealed that the lowest measured saturation on admission was 61.0 %, while the highest was 97.8 %. The highest measured saturation during the hospital stay was 95.8%, while the lowest was 28.0. Measurement of saturation was done everyday for prepare the date for appropriate decision making treatment of COVID patients.

**Conclusion:** Depending on their state, COVID patients required continuous monitoring of their oxygen saturation levels, hydration, change of patient position (patients lying flat on their back as little as possible lead to good results in their recovery). Apart from maintaining a satisfactory level of O<sub>2</sub> saturation. The second important factor is good hydration which is very helpful in mitigating discomfort and achieving a faster recovery.

**Key words:** COVID 19, Oxygen saturation, Diagnosis, Treatment.



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