ABSTRACTS

DECADE OF THE COOPERATION BETWEEN POLISH, UKRAINIAN AND BELORUSSIAN PHYSIOLOGISTS AND PULMONOLOGISTS (2004 - 2013)

Kowalski J.[1], Gutkowski P.[2], Serebrovskaya T.[3]

[1]Institute of Tuberculosis and Lung Diseases, Warsaw, jh.kowalski@wp.pl;
[2]Military Medical Institute, Warsaw, pgutkowski@wim.mil.pl;
[3]Bogomoletz Institute of Physiology, Kiev, sereb@biph.kiev.ua

The initiative to organize the Polish-Ukrainian Respiratory Working Group has arisen in October 2003 during the official visit of Prof. Janusz Kowalski to the Bogomoletz Institute of Physiology, Kiev, Ukraine. The driving motion of this initiative was the great wish to establish closer collaboration between Polish and Ukrainian researchers and physicians, to inspire the exchange of mutual experiences in research work and clinical practice and finally to help our patients who suffer the same pain and diseases on both sides of Polish-Ukrainian border. This concept has been approved by Prof. Jerzy Kozielski (President of the Polish Respiratory Society, Silesia Medical Academy, Poland), Prof. Platon Kostyuk (Director of the Bogomoletz Institute of Physiology, Ukrainian National Academy of Sciences, Kiev) and National Delegates of the European Respiratory Society Prof. Joanna Chorostowska (National Research Institute of Tuberculosis and Lung Diseases, Warsaw, Poland) and Prof. Yuri Feshchenko (Institute of Phthisiology and Pulmonology AMSU, Kiev, Ukraine). Next year Ukrainian scientists and doctors were invited by the Organizing Committee of 28th Congress of the Polish Respiratory Society to participate in this meeting in Lodz. During the Congress the Polish-Ukrainian Working Group of Clinical and Experimental Pathophysiology of Respiration was organized. Prof. Janusz Kowalski (Institute of Tuberculosis and Lung Diseases in Warsaw) and Prof. Tatiana Serebrovskaya (principal researcher of the Bogomoletz Institute of Physiology in Kiev) have been elected as Coordinators of this group. From 2012 Prof. Piotr Gutkowski headed the Polish section of the working group. During following decade the annual meetings in Kiev (2005), Opole (2006), Donetsk (2007), Katowice (2008), Ternopil (2009), Mikolaiki (2010), Chernivtsi (2011), and Wisla (2012) took place. In 2008 Belorussian colleagues from Grodno and Minsk joined working group. Besides scientific conferences, exchange of therapeutics and students was organized for training courses both in Polish and Ukrainian pulmonological clinics. The fundamental monograph «Lung function in lung diseases» (Eds. J.Kowalski, A. Kozerowski, L.Radwan) written by prominent Polish specialists in physiology and pathophysiology of respiration was translated from Polish to Russian by Dr. Eugenia Kolesnikova. The monograph was published in Poland, transported to Ukraine and distributed among main Ukrainian and Belorussian medical universities and libraries. A number of joint researches were provided, and international scientific papers were published in peer-reviewed journals. Many other initiatives have focused on the exchange of scientific and medical information between the Polish, Ukrainian and Belorussian colleagues to the benefit of the health of our populations. In conclusion, despite many organizational and financial difficulties in cooperation between Polish, Belorussian and Ukrainian universities, this initiative should be considered as significant and fruitful, integrating students, physicians and scientists of Central and Eastern Europe. The history of our Polish-Ukrainian-Belorussian Respiratory Working Group is going on. We ought to write it together.

THE RESPIRING BRAIN – THE REGULATION OF MITOCHONDRIAL FUNCTION AND SIGNALING BY HYPOXIA

Arnold S.

Nijmegen Centre for Mitochondrial Disorders, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, sarnold2012@googlemail.com

Mitochondria play an essential role in the regulation of cellular energy metabolism, intracellular signaling, apoptotic and degenerative processes. Mammalian organs with high energy requirements, such as the brain, essentially depend on oxidative mitochondrial energy metabolism and thereby the availability of oxygen representing the energy substrate for cytochrome c oxidase (COX). COX is the terminal, often rate-limiting and highly regulated enzyme complex of the mitochondrial respiratory chain. We could

show that the catalytic activity of the mammalian enzyme is regulated by the intracellular energy level (ATP/ADP ratio). Binding of ATP to one out of thirteen subunits of COX (COX subunit IV-1) causes an allosteric inhibition of the enzyme at high energy level and thus plays an important role in adjusting energy production to cellular energy requirements. However, in the brain under hypoxic conditions, a second isoform of this subunit, COX IV-2, is induced specifically in astrocytes and causes a change in the kinetic behavior of the enzyme, a suppression of COX sensitivity to the cellular energy level, and an increased mitochondrial peroxide production. In turn, this affects not only astrocytic but also neuronal survival during and after hypoxia and suggests a pivotal role of COX as an oxygen sensor for mitochondrial signaling and brain function. Moreover, this indicates a similar regulatory mechanism for other organs with high energy demand.

METHODS OF THE BREATHING RESTORATION AFTER THE RESPIRATORY ARREST UNDER DEEP HYPOTHERMIA IN RATS

Arokina N.K.

I.P. Pavlov Institute of Physiology. RAS, St. Petersburg, Russia, arokina@mail.ru

The purpose of this study is to compare the effects of injections of Na_2EDTA and polyglucinum on the breathing and cardiovascular system in the terminal stage of deep hypothermia and the breathing arrest. The experiments were performed on white male Wistar rats, which were cooled in water (9-10°C) up to respiratory arrest (rectal temperature is 15-16ºC, the brain temperature is 16.5-18ºC). After removal from the water, the first group of rats was injected intravenously by Na_2EDTA, the second group - by polyglucinum, and the third group – by the two drugs. After removal from the water, control animals (without pharmacological support) have not breathing restored. It is shown that the breathing is recovered in rats with Na_2EDTA injection. Respiratory rate in these rats increased to higher values (25-30 cycles/min) compared to rats who received polyglucinum (5-12 cycles/min) only. The polyglucinum introduction led to high blood pressure maintenance (60-80 mm Hg) which was observed in experiments both with polyglucinum introduction and additional introduction of Na_2EDTA. It is concluded that the main factor that contributes to the restoration of respiration after the cold paralysis is the concentration of calcium ions reduction in the blood by intravenous injection of Na_2EDTA. It is shown that the combined use of Na_2EDTA and polyglucinum provides faster recovery after respiratory arrest and the maintenance of high blood pressure under deep hypothermia.

AGE-RELATED CHARACTERISTICS OF MICROCIRCULATION AT BREATHING WITH POSITIVE EXPIRATORY PRESSURE

Asanov E.O., Dyba I.A.

State Institute of Gerontology of NAMS of Ukraine named after Academician D.F.Chebotarev, Kiev, 04114; eoasanov@ukr.net

The term Positive End Expiratory Pressure (PEEP) is widely used in clinical medicine and refers to breathing with the positive pressure at the end of expiration. Effect of PEEP on the microcirculatory part of the vascular system in aged people is still poorly investigated. Meanwhile, the microcirculatory system plays an important role in the mechanisms of adequate oxygen supply to the organs and tissues of the body and hypoxic tissue disorders compensation. *Material and methods*: A study was conducted on 16 aged (60-74 years old) and 12 young people (20-35 years old). The state of skin microcirculation was estimated by volume speed of blood flow at the inner side of forearm. Test with reactive hyperemia (by the method of O. V. Korkushko et al., 2002) was used to evaluate functional state of endothelium at the microcirculatory system level. Reactive hyperemia was caused by cross-clamping of the shoulder vessels for 3 min with help of a sphygmomanometer cuff with a pressure which exceeds systolic BP of a patient at 50 mmHg. The level of maximum volume speed of blood flow and time of blood stream renewal to normal were estimated. This test characterizes the ability of endothelium to synthesize endothelial factors of relaxation and reveals functional state of endothelium. Investigation was performed at the initial state (without resistance to exhale) and after 15 min of PEEP breathing with different settings of resistance for the exhale: 5 mm H2O, 10 mm H2O, 15 mm H2O. PEEP breathing was achieved with help of breathing device “Threshold PEP” (Germany). *Results:* Investigation showed that skin micro-

circulation in young people does not change with PEEP breathing neither at 5 mm H_2O or 10 mm H_2O nor at 15 mm H_2O. Microcirculation in aged people does not also change with PEEP breathing at 5 mm H_2O, but at 10 and 15 mm H_2O a decrease in the volume speed of skin blood flow in the forearm was shown. Breathing with resistance to exhale causes a decrease in cardiac troop landing of aged people. So, the decrease of the skin microcirculation as a result of breathing with resistance to exhale can be considered as compensation reaction of the circulatory system and particularly of the microcirculation which was caused by rearrangement of the blood stream and it's sustaining at the needed level in the vitally important organs (brain, heart). In aged people, PEEP breathing at 10 and 15 mm H_2O causes a decrease in the cerebral hemodynamics. *Conclusions*: Breathing with resistance to exhale leads to the decrease in the microcirculation and function of endothelium in aged people. In addition, reduction of skin blood circulation and dysfunction of endothelium appears with PEEP breathing at 10 and 15 mm H_2O.

PROGNOSTIC FEATURES OF THE EPIDEMIC SITUATION OF TUBERCULOSIS AND ITS CONCOMITANCE WITH HIV INFECTION IN UKRAINE AND IN THE REPUBLIC OF BELARUS

Astrauko A.P.[1], Shtan'ko V.L.[2], Avdonina O.V.[3], Arlindo Valerio Arao de Oliveira[3]

[1]Republican Scientific and Practical Center for Pulmonology and Tuberculosis, Minsk, Belarus; [2]Kiev Municipal center TB hospital, Kiev, Ukraine; [3]State institution «Dnepropetrovsk Medical Academy», Dnepropetrovsk, Ukraine, oksana.avdonina@gmail.com

Aim: To monitor HIV-associated tuberculosis in Ukraine and Belarus for the last 10 years. *Results:* It was shown that the epidemiological indicators of tuberculosis in Ukraine over the last years are swiftly worsening. A negative tendency to increase in destructive forms of tuberculosis incidence is noted; a high percentage of patients with multidrug-resistant forms of tuberculosis is revealed; a number of patients with co-infection TB/ HIV increases. There was a significant exponential increase in HIV- associated tuberculosis in Belarus ($p < 0.001$) with a concentration of co-infections in the Gomel region– 63.0±5.6% (95% CI, 58.3%– 67.7%). In Belarus, one of the main opportunistic infection leading to death among HIV-infected persons is tuberculosis: there was a significant increase in the proportion of TB in the structure of AIDS mortality (from 16.7% in 2001 to 43.2% in 2011). Whether a mathematical simulation technique might be used to predict new cases of tuberculosis and its concomitance in HIV-infected patients was studied. There was a stable trend for increasing number of cases of tuberculosis concurrent with HIV infection in the Dnipropetrovsk region. Results of the study indicate that the application of mathematical simulation technique allow TB doctors and organizers of health to develop specialized care to patients with comorbidity, plan financial costs to take measures that will lead to enhanced TB control in Ukraine and in the Republic of Belarus based on prognostic features of epidemic situation in the regions.

TUBERCULOUS PERIODONTITIS: CLINICAL-LABORATORY AND EPIDEMIOLOGICAL ASPECTS

Avdonina L.I.[1], Priyma N.V.[2], Avdonina O.V.[3], Vayntrub V.F.[1], Khristyan G.Ye.[1], Arlindo Valerio Arao de Oliveira[3]

[1]Polymed Dental Clinic, Dnepropetrovsk, Ukraine, larisa-avdonina@mail.ru;
[2]Crimea State Medical University, Simferopol, Ukraine;
[3]Dnepropetrovsk State Medical Academy, Dnepropetrovsk, Ukraine

To the present day, tuberculous periodontitis is not diagnosed and not present in the classification of tuberculosis. Its microbiological diagnostics is the most complicated as it is performed by investigating small quantities of paucibacillary material. The purpose of work was defining the significance of mycobacterial population variability forms in the clinical picture and epidemiology of tuberculous periodontitis. Comparative analysis of clinical and epidemiological features of tuberculous periodontitis was performed in two groups of patients aged 20 to 70 years over different observation periods from 1980 till 2012. Group A was composed of 258 patients who were observed from 1980 till 1990, and Group B consisted of 250 patients who were examined from 2005 till 2012. Peridental focal points of infection in chronic forms of tuberculous periodontitis were used as the material for the advanced microbiologi-

cal and pathohistological examination. It has been established that in Group A, peridental focal points of infection serve as a reservoir for persisting mycobacteria. The main forms of such mycobacteria are unstable L-phase variants which were found in 50% of the investigated samples. We have noticed that the number of focal points of infection in which the changed mycobacteria forms vegetate tends to increase: L-forms (55,2%) and granular forms in Group B. L-form transformation of mycobacteria and emerging of granular forms is the reason of exacerbations coming up more frequently and persistent course of tuberculous periodontitis. The strains of mycobacteria in peridental focal points of infection susceptible to all antituberculous drugs that were detected 30 years ago has been supplanted by mycobacteria resistant to isoniazid and rifampicin in patients who had not taken antituberculous drugs before. At present, the fact that tuberculous periodontitis in HIV-positive patients can be a prognostic for clinical manifestations of AIDS is a point of interest. The clinical and epidemiological features of tuberculous periodontitis that have been revealed are similar to clinical pathomorphism of extrapulmonary tuberculosis; therefore tuberculous periodontitis can be included in the classification of tuberculosis as a separate nosological entity.

MAINSTREAM CAPNOGRAPHY ANALYSIS AS A TOOL FOR THE ASSESSMENT OF ALVEOLAR VENTILATION EFFECTIVENESS IN CHILDREN WITH BRONCHIAL ASTHMA UNDER INTERMITTENT HYPOXIA TRAINING (IHT)

Bakunovskiy O.M.[1], Serebrovskaya T.V.[1], Nesvitailova K.V.[2], Gavenauskas B.L.[1], Tymoshenko K.R.[3], Mankovska I.M.[1]

[1] Bogomoletz Institute of Physiology, Kiev, Ukraine, sereb@biph.kiev.ua;
[2] Institute of Pediatrics, Obstetrics and Gynecology, Kiev, Ukraine;
[3] Taras Shevchenko National University, Kiev, Ukraine

Capnography is a technique that provides both a waveform and a numerical value for the end-tidal carbon dioxide partial pressure ($P_{ET}CO_2$) during each respiratory cycle. In patients with bronchial asthma the lower CO_2 content in alveolar gas is often observed between attacks compared with healthy people. Clinicians see the cause of hypocapnia in hyperventilatory syndrome and offer special training programs with the use of mainstream analysis to teach patients breathing techniques that reduce the base hypocapnia. However, in clinical practice the mainstream analysis has not yet found a fairly wide use as a diagnostic test for bronchial asthma patients. This study was designed to determine whether the mainstream $P_{ET}CO_2$ measurement can accurately evaluate the effectiveness of alveolar ventilation under IHT in children with bronchial asthma (BA). Two groups of children aged 9–13 years with persistent atopic BA (moderate form, between attacks, without the signs of respiratory insufficiency) participated in the study: experimental group (Gr. I) – 15 children who underwent a two-week IHT (5 min exposures to 12% O_2 with intervening 5 min room air breathing, 4 times a day) alone with traditional medical treatment (anti-inflammatory and spasmolytic drugs), and control group (Gr. II) – 8 children who received the same medical treatment, but without IHT. Most children in both groups had a hyperventilation-induced hypocapnia. The clinical effect of treatment was assessed by physicians who did not participate in the study. The effect "improvement" was registered in 4 (Gr. I) and 3 (Gr. II) patients; the effect "significant improvement" was recorded in 11 (73.3%, Gr. I) and 5 (62.5%, Gr. II) children. IHT program resulted in a significant decline in breath shortness and feelings of chest congestion, the cough was diminished or disappeared, and the amount of sputum was reduced and passed more easily. The attacks of asphyxia disappeared or became more occasional. Exercise tolerance was significantly improved. A decrease in hyperventilation by 26 % and an increase in basal $P_{ET}CO_2$ from hypocapnic (32,3±0,8 mm Hg) to normocapnic range (35,6±0,7 mm Hg, $p<0,05$) was registered in 11 children of Gr.1. The proportion of dead space in the alveolar ventilation diminished by 11, 4 %. Thus, capnography can better assess the IHT effectiveness in children with bronchial astma.

QUALITY OF LIFE IN PATIENTS WITH PULMONARY SARCOIDOSIS

Baradzina H.

Belorussian State Medical University, Minsk, Belarus, baradzina@tut.by

Aim: to investigate the quality of life (QL) in pulmonary sarcoidosis patients compared with QL in patients with tuberculosis and evaluate the influence of good clinical monitoring. We examined 50 patients with sarcoidosis and 40 patients with tuberculosis by "Quality of life - 100". All sarcoidosis patients have

low QL in the following scales: physical health, social relations, independence and emotional status. Total score in these patients was significantly lower than in healthy persons (60.5±4.7, $p<0.01$). Dispnoe, fever, arthritic syndrome have the main influence on QL in sarcoidosis. Total score (42.7±4.5, $p<0.01$) and especially score in physical health scale (33.4±3.8 and 75.8±9.3, $p<0.01$), independence (36.7±4.1 and 56.4±5.8, $p<0.01$), and social relations were significantly lower in tuberculosis than in sarcoidosis. But QL in sarcoidosis compared to tuberculosis was lower in emotions scale (51.7±4.9 and 67.2±6.3, $p<0.01$). All sarcoidosis patients were divided into two groups: 1st group received only basal treatment, 2nd group has additional clinical monitoring by physician during 20 months. Total score of QL in the 1st group increased slightly after treatment but not statistically significant. Total score in the patients of 2nd group has reached 72.4±4.9 and in the emotional status scale - 80.6±7.3. The level of clinical improvement was significantly higher in 2nd group (improving of lung function, small number of relapses). *Conclusion*: In spite of better physical health, sarcoidosis patients have much more psychological problems than in tuberculosis, and physicians must take this circumstance into consideration in the every day activity. Clinical monitoring and good compliance can positively impact on the QL in sarcoidosis.

IS THERE CORRELATION BETWEEN LUNG FUNCTION PARAMETERS AND THE LENGTH OF INDUSTRIAL WORK RECORD IN POTASH MINE?

Baradzina H., G.Hurevich, V. Denisevich

Belorussian State Medical University, Republic Scientific-Practical Center of Pulmonology and Phthisiology, Minsk, Belarus; baradzina@tut.by

Exposition to industrial factors in coal mine is firmly correlated with lung function parameters in miners. The impact of the length of industrial work record of service in potash mine on the lung function has not been so far well investigated. *Aim:* To evaluate the correlation between the lung function characteristics and the industrial work record of service in potash mine. *Materials and methods:* We examined 111 potash miners of Soligorsk (average age 36.1 yrs) by spirometry. I group included 21 miners with the record of service less than 10 yrs; II group (n=52) has the record of service from 10 to 20 yrs, and III group consisted of 38 miners with the record of service more than 20 yrs. *Results:* In average, lung function parameters were absolutely normal. There are no significant differences between groups. We found only a slight tendency to increase of lung function disturbance rate with the length of industrial work record.

Table. Lung function parameters of miners with different exposition to industrial factors.

Groups of miners	VC,%	FVC,%	$FEV_{1,}$ %	$MEV_{75,}$ %
Group I	98.1±14.6	111.9±15.9	107.5±14.2	99.1±10.4
Group II	97.1±11.6	99.3±12.8	101.4±12.6	100.7±10.2
Group III	93.9±13.6	95.9±14.8	99.3±13.6	93.2±9.8

Conclusion*:* Despite of influence of industrial aerosols the lung function of miners remained normal for a long time. This is, probably, the result of broncho- and mucolytic effects of potassium salt and absence of microbial contamination of the mine air. Positive effect of the potassium mine microclimate neutralizes the negative impact of industrial aerosols.

CHANGES IN EPITHELIAL BARRIER OF AIRWAYS IN ALLERGY

Barkhina T.G. , Gushchin M.Y., Polner S.A., Golovanova V.E.

Institute of Human Morphology, Institute of Immunology, Moscow, Russia; tbarkhina@yahoo.com

Aim: To compare clinical and morphological data indicating the damage of the mucous membranes of the nose and bronchi in patients with bronchial asthma (BA) and allergic rhinitis (AR). *Materials and methods*: We investigated the scrapings of the mucous membrane of the nasal cavity and bronchobioptates in patients of different ages with AR and BA. Scanning (SEM) and transmission electron microscopy (TEM) were performed. *Results:* The surface of the epithelial cells of the upper and lower respiratory tract of patients with AR and BA tend to have the same changes that, along with clinical data on hyperreactivity of these parts as determined by provocative tests, indicates a common mechanism of epithelium damage. The greatest damage to the exposed ciliated cells (CC) was detected by SEM, and intracellular destruc-

tive processes - by TEM. Significant changes in goblet cells (GC) can enhance its main function. This reaction was more pronounced in the nasal mucosa. Clinical effect after allergen specific immunotherapy (ASIT) in adolescents was morphologically confirmed by demonstration of endocellular regeneration processes in epithelium. *Conclusion*. The intensity of changes in epithelial barrier of airways is directly related to the severity, early onset, dynamics and duration of BA or AR. This whole complex of changes suggests major modifications in the morphology of the airway in response to allergic aggression. Timely basic therapy and ASIT contribute to a better clinical effect, helps to prevent potential complications, and to restore a damaged nose and bronchial mucosa.

THE ALPHA-1-ANTITRYPSIN (AAT) DEFICIENCY IN RESPIRATORY PATIENTS – TARGETED SCREENING PROGRAMS IN POLAND AND CENTRAL EASTERN EUROPE (CEE AAT NETWORK).

Chorostowska-Wynimko J.[1], Kubincova A.[2], Yanev N.[3], Ulmeanu R.[4], Struniawski R.[1], Pobeha P.[2], Kyuchukov N.[3], Deleanu O. [4], Popławska B.[1], Tkacova R.[2], Ivanov Y.[3], Mihaltan F.[4], Valiulis A.[5]

[1]National Institute of Tuberculosis and Lung Diseases in Warsaw, Poland;
[2]Medical Faculty, PJ Safarik University and L Pasteur Univ. Hospital, Kosice, Slovakia, anna.kubincova@upjs.sk;
[3] UMHAT "Dr.G.Stranski" Pleven EAD, Pleven, Bulgaria;
[4]Institute of Pneumophtisiology "Marius Nasta" Bucharest, University of Oradea-Medical Faculty,UMF "Carol Davila"Bucharest, Romania;
[5] Vilnius University Medical Faculty, Vilnius, Lithuania

Inherited alpha-1 antitrypsin deficiency (AATD) is listed among the three most common genetic disorders in Caucasians. It considerably increases the risk of progressive obstructive lung diseases, mostly chronic obstructive pulmonary disease. Data concerning the prevalence of AAT deficiency in general population or respiratory patients in CEE countries are limited or non-existent. The overwhelming majority of individuals with AAT deficiency remains undiagnosed. In 2009 the targeted screening program for Poland has been established offering free access for high-tech AAT diagnostic for all respiratory patients. AAT serum concentration in DBS is measured by nephelometry and PI-phenotype identified by real-time PCR. The PI*S and PI*Z alleles are confirmed by isoelectrofocusing; rare phenotypes identified by direct sequencing. Between late 2009 and 2013 841 samples from respiratory patients were referred for diagnostics. 113 (13.6%) patients demonstrated AAT deficiency phenotypes. Calculated frequencies for main deficiency alleles PI*Z and PI*S were respectively 46.6 per 1000 (95% CI: 32.3-60.8) and PI*S 20,3 per 1000 (95% CI: 10.8-29.8), significantly higher than in general Polish population. Recently, as a result of the LPP Leonardo da Vinci EU program (2011-1-PL-LEO04-197151) "Introducing standards of the best medical practice for the patients with inherited Alpha-1 Antitrypsin Deficiency in Central Eastern Europe" the CEE AAT NETWORK has been established. Between October 2012-January 2013 samples were collected from 328 COPD patients in Poland (n=198), Bulgaria (n=44), Romania (n=26) and Slovakia (n=60). PI*S or PI*Z deficiency alleles were observed respectively in 14 (4,27%) and 30 (9,14 %) patients. There were 6 patients with rare AAT mutations: FM-3, IM-2, Mzbristol-1. In total, any AAT mutation was diagnosed in 48 COPD patients (14,63%). The calculated frequency for PI*Z and PI*S alleles in overall tested population was 46,1 (95% CI: 31,1-60,9) and 15,8 (95% CI: 6,92-24,6), respectively. The AAT gene prevalence calculated by Hardy-Weinberg equilibrium was: 1/1.15 for MM, 1/34 for MS, 1/4011 for SS, 1/12 for MZ, 1/688 for SZ and 1/471 for ZZ. *Conclusion*: Our results confirm the relatively high frequency of AAT deficiency in COPD patients from CEE. This initiative is the very first attempted to establish the diagnostic and scientific collaboration for AATD in CEE.

SOME INDICATORS OF OXIDANT-ANTIOXIDANT HOMEOSTASIS IN PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE COMBINED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Cintar T.P., Fediv O.I., Stupnitska G.Ya.

Bukovinian State Medical University, Chernivtsi, Ukraine; dumanna77@mail.ru

In different countries 3 to 24% of the population suffers from nonalcoholic fatty liver disease (NAFLD). NAFLD is often diagnosed in people aged 40-60 years. It is also known that in this age there is a peak in the incidence of chronic obstructive pulmonary disease (COPD). In this regard, the actual problem

is a combined course of this pathology. *Aim:* To examine the state of oxidant-antioxidant homeostasis in patients with NAFLD combined with COPD. *Material and methods:* The study involved 23 patients with NAFLD combined with COPD (first group) and 18 patients with NAFLD without concomitant COPD (second group). The control group consisted of 20 healthy individuals. It was studied the content of malondialdehyde (MDA), the content of reduced glutathione (RH), glutathione peroxidase (GP) and glutathione -S-transferase (GT) activities in the blood. *Results:* In the first group of patients, the content of MDA was higher than in patients of second group (by 39.6%,) and healthy individuals (by 2.3 times). In addition, there was a significant decrease in RH level in the blood of patients compared with healthy individuals (by 1.8 times - in group 1 and by 1.5 times - in group 2, $p < 0.05$). These changes were accompanied by a compensatory increase in GP and GT activities in both groups of patients. *Conclusion:* Thus, the results indicate the presence of more severe disturbance of oxidant-antioxidant homeostasis in patients with NAFLD combined with COPD, which requires appropriate correction of treatment.

TREATMENT OF THE ADVANCED CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Doboszyńska A.

Pulmonary Clinic, University of Warmia and Mazury in Olsztyn, Poland, anna.doboszynska@wp.pl

COPD is a chronic progressive disease. In the end-stage of the disease, when respiratory failure is developed, a prolonged home oxygen therapy is used. Indications to the prolonged home oxygen therapy in patients with COPD include: $P0_2$ 55 mm Hg or $P0_2$<60 mm Hg with accompanied cor pulmonale or heart failure, or polyglobulia (Hct>55). Home oxygen therapy aims at prolonging patient's life. To achieve this, it is necessary to use oxygen therapy for at least 15 hours per 24 hours.
Another therapy used in the chronic respiratory failure is non-invasive ventilation. Indication to such a treatment in the exacerbations of the chronic respiratory failure is:
– persisting, sever hypoxemia despite oxygen therapy (Pa_{02}/O_2 <50 mm Hg);
– increasing hyperkapnia ($PaCO_2$ > 60 mm Hg);
– respiratory decompensated acidosis with pH<7.30.
Noninvasive mechanical positive pressure ventilation (e.g. respirator of BiPAP type) in the treatment of the acute or exacerbated respiratory failure in the course of COPD brings about several advantages:
– decreases the number of patients requiring intubation;
– decreases the rate of complications resulting from the treatment with invasive mechanical ventilation (e.g. pneumonia);
– decreases in-hospital mortality.

EBUS/TBNA – A CHALLENGE FOR PATHOLOGIST

Domagala-Kulawik J.

Medical University of Warsaw, Department of Pneumonology; domagalakulawik@gmail.com

Endobronchial ultrasound-guided transbronchial needle biopsy (EBUS/TBNA) is a new diagnostic tool useful in hilar or mediastinal lymphadenopathy diagnosis. The alternative method is Endoscopic (EUS) /TBNA. These procedures are performed in the cases of CT-confirmed mediastinal or hilaradenopathy (the diameter of short axis >1 cm). Two main clinical indications for EBUS/TBNA are: lung cancer staging and clinically suspected sarcoidosis. However, many other pathological processes may involve lymph nodes. For aspiration the thin needle, less than 1mm is used. The cell smears are alcohol fixed and hematoxylin- eosin stained. The rapid on site evaluation (ROSE) is possible with immediate diagnosis during bronchoscopy procedure, but in practice the final cytological diagnosis is available after 1-2 days. The wide spectrum of pathological changes in enlarged lymph nodes is recognized by cytopathology: normal cells- lymphocytes and their young forms, reactive inflammatory reaction, unspecific inflammation, granulomatous diseases and the presence of metastatic malignant cells. EBUS/TBNA is useful in lung cancer diagnosis often being the only available material. The best results are obtained in the cases of small cell lung cancer. The distinguishing main types of non small cell lung cancer: squamous cell type from adenocarcinoma is possible in about 60% in classical hematoxylin-eosin staining, but the use

of immunocytochemistry improves the effectiveness of diagnostic. If lymphoproliferative disorder is suspected the flow cytometry analysis of cells is indicated. Tuberculosis remains the common cause of lymphadenopathy. The use of molecular biology in the analysis of TBNA allows for a proper diagnosis of TBC infection. We conclude that EUBS-TBNA may have applications in both benign and malignant lung diseases as a routine examination by the experienced cytopathologist.

EFFECTS OF HEAD-DOWN TILT ON RESPIRATORY CONTROL AND LOAD COMPENSATORY RESPONSES IN RATS

Donina Zh.A.

I.P. Pavlov Institute of Physiology RAS, St.Petersburg, Russia, zdonina@yahoo.com

Aim: To examine the role of vagal afferents in the control of ventilation and compensatory capacity of the respiratory system during short-term head-down tilt (HDT) exposure. The experiments were performed in vagally intact or vagotomized, anesthetized rats. The response of tidal volume (VT), breathing frequency (f), minute lung ventilation (VE), esophageal pressure (Poes), inspiratory occlusion pressure ($P_{0.1}$) were examined at supine position (baseline) and after 30 min HDT-30º exposure. *Results*: There was a significant decrease in VT by 18% and VE by 14% after 30min HDT-30° exposure compared to supine. An increase both resistive by 50% ($p<0.05$) and elastic component by 90% ($p<0.05$) of respiratory resistance was found. On the other hand, it was seen the Poes rising by 116%, which reflects an increase in inspiratory muscle output occurring when respiratory load increases. After bilateral vagotomy, Poes rose only by 65% in comparison to vagal intact animals. Inspiratory occlusion pressure evoked an increase of $P_{0.1}$ in both supine and HDT. In supine, this value rose by 536% ($p<0.01$), whereas in HDT - by 320% ($p<0.05$). *Conclusions*: HDT in anesthetized animals induces ventilatory augmentation accompanied with the rise of the airway resistance due to the increased intrathoracic blood volume. A compensatory capacity of the respiratory system is diminished during short-term exposure at HDT-30º. One of the possible mechanism of such respiratory system compensatory response is the vagal afferent, presumably originating from the slowly adapting lung stretch receptors due to the decreased lung volume under HDT.

ROLE OF HYPOXIA-INDUCIBLE FACTOR 3A (HIF-3α) IN PHYSICAL ENDURANCE OF RATS

Drevytska T, Gavenauskas B, Nosar V, Linnyk O, Drozdovska S, Mankovska I, Dosenko V.

Bogomoletz Institute of Physiology, Kiev, Ukraine

RNA-interference is the novel perspective method for knockdown of the genes involved in different mechanisms of adaptation to physical exercises.One of the crucial factors in this process is hypoxia inducible factor (HIF) that regulates transcription of many target genes encoding proteins that are involved in molecular adaptation to hypoxia. Based on previously data, HIF-3α is considered as negative regulator of HIF-1α and HIF-2α, thereby gene encoding HIF-3α appears to be an attractive target for RNA interference application. The purpose of this study is to examine the effect of HIF-3α silencing on physical endurance of rats. Methods: Experiments were conducted on adult male Fisher rats. All animals were divided into three groups: (1) control (intact animals); (2) endurance training (ET) + scrambled RNA injection; (3) ET + specific HIF-3α siRNA injection. Real-time PCR analysis was performed for quantitative evaluation of HIF-3α, IGF1, GLUT-4 and PDK-1 in m. gastrocnemius and m. soleus. Mitochondrial respiratory function was measured by the polarographic method of Chance and Williams. Results: Knockdown of HIF-3α (expression of mRNA is decreased by 1.7 times in m. soleus and by 2.6 times in m. gastrocnemius) using siRNA increases time of swimming to exhaustion in 1.5 times, but level of NAD- and FAD-dependent oxidative pathways is decreased. Efficiency of phosphorylation and the respiratory control ratio are significantly increased after HIF-3α siRNA treatment.Expression of HIF target genes IGF-1 and GLUT-4was not changed significantly,but PDK-1 expression was increased in m. soleus by 2.1 times. So, HIF-3α silencing increases exercise endurance of rats, efficiency of phosphorylation and the respiratory control ratio. These results might represent a potential therapeutic approach for increase efficacy of athletes endurance training.

ROLE OF ENDOGENOUS INTOXICATION AND NEUTROPHILS IN MECHANISMS OF ACUTE LUNG INJURY IN CASE OF EXPERIMENTAL PERITONITIS

Gerasymchuk M.R., Zayats L.M., Cherkasova V.V. and Vodoslavska N.Y.

Ternopil, Ukraine, Marta_solomea@yahoo.com

The study was carried out on 78 albino Wistar male rats (180-230 g) divided at random into 3 groups. Group 1 consisted of 58 rats with experimental acute diffusive peritonitis (ADP), 2nd group – control group with sterile 0,9% NaCl at equlibrium (n=10) and 3rd intact group (n=10). ADP was induced by intraperitoneal injection of 10% suspension of feces. We analyzed total WBC count, Wet/Dry lung indexes, data of the oxidative and antioxidative systems and endogenous intoxication indexes, light and electron microscopy. Blood samples and lung tissue were obtained in 1, 12, 24 and 48 h after ADP induction. It has been established that after ADP induction was noticed progressive endogenous intoxication with lipid and protein peroxidation and inhibition of antioxidant protection for 24 hours with further exhaustion after the first day of experiment. The most informative and sensitive biomarker of acute lung injury is a coefficient of leukocyte lung regulation. The latter suggests enhanced leukocyte sequestration in respiratory system even on the background of leucopenia, which implies lung injury. Furthermore, lung injury has been confirmed by the analysis of morphological alterations of laboratory rats' lung tissue micro- and ultrastructure.

ADAPTIVE EFFECTS OF INTERVAL HYPOXIA AND HYPEROXIA ON EXERCISE TOLERANCE IN PROFESSIONAL ATHLETES: ROLE OF ROS AND REDOX PATHWAYS

Glazachev O.S.[1], Sazontova T.G. [2], Bolotova A.V. [2], Vdovina I.B. [2], and Arkhipenko Yu.V. [2]

[1]Department of Normal Physiology, I.M. Sechenov First Moscow State Medical University, A.M.Sholokhov Moscow State University for the Humanities, Moscow, Russia, glazachev@mail.ru;
[2]Faculty of Medicine, M.V. Lomonosov Moscow State University, Moscow, Russia.

The pilot study has been performed to demonstrate protective effects of adaptation to interval hypoxia-hyperoxia in eliminating the overtraining syndrome features and enhancing physical capacity in professional athletes. On the first, experimental study on Wistar rats was established that combination of adaptation to physical exercise with adaptation to hypoxia-hyperoxia sessions, not to hypoxia-normoxia, improves tolerance under conditions of acute physical stress. Analysis of free radical processes, antioxidant enzymes and HSP proteins levels revealed that adaptation to hypoxia-hyperoxia provides optimization of both - hypoxic and stress components in systemic response to physical load, that's why in applied studies in 15 young over-trained professional athletes the efficacy of adaptation to 15 hypoxia-hyperoxia sessions with low-intensity sport exercises has been tested. The study results demonstrate improving the functional status, autonomic balance, physical endurance and aerobic performance in athletes with overtraining syndrome. Adaptation to physical loads and its combination with adaptation to variable oxygen levels increases the resistance of membrane structures to free radical oxidation at the expense of excessive activation of antioxidant defense enzymes in the course of physical training, which is partly compensated by adaptation to hypoxia/normoxia and is fully prevented by adaptation to hypoxia/hyperoxia. The combination of two adaptation forms (i.e. direct adaptation to physical loads and cross adaptation to variable oxygen levels) compensates markedly elevated content of HSP proteins in the course of physical training, which is especially well-pronounced during adaptation to hypoxia/hyperoxia. This novel technique is apparently less "physiologically demanding" and more beneficial for the organism.

MORPHOFUNCTIONAL STUDY OF BRONCHIAL ASTHMA WITH EXTRAHOSPITAL PNEUMONIA

Gumeniuk SA[2], Barkhina TG[1], Polner SA[2]., Guschin MY[1].

[1]Institute of Human Morphology, Russia, Moscow; [2]Institute of Immunology, Russia, Moscow; gum-sveta@yandex.ru

Aim: Study of Bronchial Asthma (BA) in conjunction with the extrahospital pneumonias (EP) of different etiopathogenesis and cell-humoral mechanisms. *Materials and methods*: 1241 patients were divided into 3 groups: BA (1), EP (2), BA with EP (3). Morphology: cytological and electron-microscopic methods. *Results:* 7% (86 P) with BA had EP. The patients were divided by severity: mild BA - 19%, medium level - at 55.8%, and severe degree of BA - at 24.4%. A coccal flora was found in sputum. In nasal

secretions we identified different number of lympho- and granulocytes. The most pronounced changes in the cells were observed in group 3. The surface of the epithelial cells of the upper and lower airways had the identical changes and match clinical data. Intensity changes of ciliated cells correlated with the severity of the diseases. The changes were accompanied by a sharp extrusion of goblet cells, which sometimes formed lacuna. These changes led to severe hypoxic and anoxic amendments to the mucous membranes of the respiratory tract. *Conclusion:* Epidemiology, clinical and morphological data of EP with combined pathology of inflammatory disorders have more severe cytological and morphological changes in the upper and lower airways. The group 3 of patients needs an individual approach to the treatment and prevention.

BRONCHIAL ASTHMA AND ALLERGIC RHINITIS IN PATIENTS OF DIFFERENT AGES

Gushchin M.Y., Barkhina T.G., Polner S.A., Gumeniuk S.A.

Institute of Human Morphology, Institute of Immunology, Moscow, Russia; guschin.michail@yandex.ru

Aim: to study the epidemiological, clinical, and morphological features of allergic rhinitis (AR) and bronchial asthma (BA). *Materials and methods:* common clinical, allergological, morphological (cytological and electron-microscopic methods) examination of patients with AR and BA. *Results:* the study was conducted among 685 adolescents with AR and BA between the ages of 14 to 18 years and 870 adults aged 18 to 65 years who were divided into groups. Divided by severity of adults: light level - 23%, medium - at 72%, and severe degree - at 5%. Divided by severity of teenagers: light level - 33,1%, medium - at 42,1%, and severe degree - at 24,8%. In the group of adolescents onset of the diseases occurred mostly from 5 to 15 years, and also a hormonal imbalance was detected that increased the severity of illness at this age. The results of allergological examination in the spectrum of allergens in patients with more severe BA revealed sensibilization to multiple allergen groups. In adolescents with AR and BA, there was found unique clinical and morphological changes in the mucous membranes of the respiratory tract. It was installed expressed morphological changes that have a direct relationship to the severity of the diseases. *Conclusion:* revealed similarities and differences in the clinical course, allergy data and morphological changes in patients of all ages with AR and BA.

SPROMETRY LIMITATIONS – A FEW EXAMPLES

Gutkowski P.

Military Medical Institute, Warsaw, Poland, pgutkowski@wim.mil.pl

Spirometry is the basic method of respiratory function assessment. Several examples of spirometric and plethysmographic measurements performed in adults and children are presented in the paper. The comparison of these measurements indicate that: 1. Spirometry is unable to measure TLC and therefore to diagnose restrictive dysfunction of respiration. 2. In some cases spirometry does not show the airway obstruction. 3. Spirometry may not be sensitive enough to assess bronchodilatation response to beta-agonists nor to assess the bronchocontriction response in bronchoprovocation test. Nevertheless spirometry remains the primary diagnostic tool in pulmonary medicine.

SLEEP DISORDERED BREATHING (SDB) IN CHILDHOOD

Gutkowski P.

Military Medical Institute, Warsaw, Poland, pgutkowski@wim.mil.pl

The natural history and classification of SDB in childhood are to be described in the presentation. The pathomechanisms of SDB and its effects on cardiac and central nervous system are shortly discusses as well as the risk factors of obstructive sleep apnea (OSA) in childhood. In the paper are also given the recent literature examples of OSA impact on the course of bronchial asthma in children on one hand and on impaired behavioral and neurocognitive functions on the other.

THE ROLE OF PULMONARY EDEMA AND SURFACTANT INACTIVATION IN THE PATHOGENESIS OF HCL-INDUSED ACUTE LUNG INJURY

Hryshchuk L.A., Bondarenko Yu.I., Beskyy V.O., Marushchak M.I.

I.Ya. Horbachevsky Ternopil state medical university, Ternopil, Ukraine, hrischuk@ ukr.net

Acute lung injury (ALI) is the major cause of the acute respiratory failure. The aim of this study was to estimate the degree of pulmonary edema and the condition of surfactant metabolism in the dynamics of hydrochloric acid (HCl)-induced ALI. Nonlinear male rats (weight range 200–220 g) were used in all experiments. Were determined the oxygenation index pO2/FiO2 of arterial blood, level of total protein in bronchoalveolar lavage (BAL), Wet-to-Dry ratio and coefficient of stability by R. Pattle. The development of lungs damage in the case of intratracheal instillation of HCl was confirmed by three times increased concentration of protein in BAL after 24 hours of experiment. Elevated calculated ratios of pulmonary edema indicated a significant increasing in the lung tissue edema and pulmonary exudate in all research groups ($p<0, 01$). It was found the progressive decrease in the level of surface activity of pulmonary surfactant system during the first day of observation: significant increase in the level of maximum surface tension and simultaneous decrease in the stability ratio by 45.8%.
Thus, presented data indicate the formation of ALI as a result of lung tissue's edema progression, the accumulation of exudate fluid and hence, impaired oxygenation with the development of hypoxemia. Accumulation of protein-rich fluid in the alveoli is the factor of surfactant inactivation that leads to a decrease in the stability ratio.

HOW TO TREAT SARCOIDOSIS.

Jarzemska A.[1], Przybylski G.[1], Domagała-Kulawik J.[2]

[1] Lung Diseases Clinical Ward KPCP Bydgoszcz, Poland;
[2] Pneumonology Clinic Medical University of Warsaw, Poland; ajarzemska@wp.pl

Sarcoidosis is a granulomatous disease of unknown cause, ranging from limited to multisystem disorder. About 2/3 patients develop an acute form strongly associated with spontaneous remission, others evolve into chronic course. Persistent sarcoidosis is likely to involve lungs but also other, in practice, any organs. Therefore, with the diffuse and especially with progressive onset, it could be potentially life-threatening. Due to ATS/ERS/WASOG consensus statement- the diagnosis of this disease is based on clinico-radiological findings, supported by histological evidence of noncaseating granulomas obtained by biopsy from involved organs. However, there are not unequivocal recommendations for treatment. Because of the heterogeneous course of the disease, it is not clear when, if at all, to apply therapy. Despite spontaneous remissions some patients have mild forms of this disease and adverse effects of drugs could be potentially worse than expected benefits. Therefore, a specific score of severity of sarcoidosis has just been created to help provide appropriate treatment. An acute form- Lofgren's syndrome, should not be cured with any immunosuppressive agents, as well as many stages of pulmonary or extrapulmonary sarcoidosis with no potentially lethal course. The involvement of heart and nervous system is an indication for immunosuppressive drugs application. Severe renal involvement leading to renal failure (with or without hypercalcemia) is also an indication for treatment. Very rare, but serious complication is hepatic localization of granulomas combined with cholestasis. Usually, liver and spleen localizations are asymptomatic and require no treatment, similarly to bone, cutaneous and other localizations that do not severely impair their function. Taking into account the serious course of some cases of pulmonary and systemic sarcoidosis over the past years, an increasing number of prospective controlled treatment trials have been completed.

EPIGENETIC REGULATION OF OXYGEN SENSING AND ITS IMPACT ON AUTONOMIC FUNCTIONS

Jayasri Nanduri

Institute for Integrative Physiology & Center for Systems Biology of O_2 Sensing, University of Chicago, Chicago, IL. 60637. USA; jnanduri@bsd.uchicago.edu

Recurrent apnea with intermittent hypoxia (IH) is a major clinical problem in preterm infants. Adults who are born preterm exhibit increased incidence of sleep-disordered breathing and hypertension suggesting

that apnea of prematurity predisposes to autonomic dysfunction in adulthood. Here, we demonstrate that adult rats exposed to IH for 10 days in the neonatal period exhibit remarkable cardio-respiratory abnormalities in adulthood manifested as irregular breathing, spontaneous apneas and hypertension. The enhanced hypoxic sensitivity was associated with elevated oxidative stress, downregulation of genes encoding anti-oxidant enzymes, and upregulation of pro-oxidant enzymes in the carotid body and adrenal medulla, which are known to be major regulators of cardio respiratory functions. We examined how perturbations in O_2 levels in neonatal period produce long lasting autonomic abnormalities in adulthood. Emerging evidence suggests that epigenetic mechanisms underlie long-lasting changes in gene expression. Epigenetic changes are heritable modifications of DNA that does not involve changes in DNA primary sequence. Of the different epigenetic mechanisms DNA methylation has been shown to mediate neonatal programming of adult diseases. In general, DNA hypermethylation leads to repression of gene transcription and hypomethylation causes transcriptional activation. Our results showed marked DNA hypermethylation in adult rats exposed to neonatal intermittent hypoxia, which was associated with persistent down regulation of anti-oxidant enzyme genes. Further analysis of the superoxide dismutase 2 (*Sod2)* gene, which encodes the anti-oxidant enzyme Sod2 showed DNA hypermethylation of a single CpG dinucleotide close to the transcription start site. Decitabine, a DNA hypomethylating agent, prevented DNA hypermethylation, oxidative stress, enhanced hypoxic sensitivity, and autonomic dysfunction. These findings implicate a hitherto uncharacterized role for epigenetic modulation of oxygen sensing in mediating neonatal programming of hypoxic sensitivity and the ensuing autonomic dysfunction in adulthood. The current findings are of considerable relevance for understanding the early onset of autonomic dysfunction in adults that were born preterm. Supported by NIH-HLBI grants HL-76537, HL-90554, and HL-86493.

COMPLEX THERAPY OF RECURRENT OBSTRUCTIVE BRONCHITIS COMBINED WITH FOOD ALLERGY IN CHILDREN AGED 1 TO 3 YEARS

Kharchanka A.

Grodno State Medical University, Belarus; kharchanka@mail.ru

Aim: to prove the usefulness of pharmacological correction in babies' recurrent obstructive bronchitis that occurs on a background of food allergy. *Materials and methods:* There were 76 children aged from 1to 3 years under the supervision. All of them suffered from recurrent obstructive bronchitis that occurs on a background of food allergy (to cow's milk protein). These children were cured by usual therapy: antibiotics, short-acting β-adrenergic agonists, theophyllines, H1- histamine blockers, antitussives. It was additionally assigned the probiotic-antagonist "Enterogermina" to 48 children during the course of antibiotic therapy (experimental group). The control group was consisted of 28 children. It was provided physical examination, determination of total immunoglobulin E, calculation of the reactive-protective potential of organism such as: phagocytic index of cell protection, allergic disposition index, lymphocyte-monocyte ratio. *Results:* (1) Diarrhea was registered in 6.4% of cases within the experimental group, and 27% of cases within the control group ($p<0, 05$). (2) The frequency of detection of neutral fat and fatty acids in coprogram of experimental group is lower in comparison with control group by 1,5 and 2,3 times respectively, ($p<0,05$). (3) The level of total Ig E had a downward trend within the experimental group; it has grown by 23 % within control group. (4) Children of experimental group had a real decrease of allergic disposition index and lymphocyte-monocyte ratio in comparison with control group. *Conclusions*. Results of clinical supervision verified by positive shifts in coprogram, blood count, reflecting the state of immunobiological resistance and allergic disposition of organism, allow recommending probiotic "Enterogermina" as accompanying therapy of bronchial obstructive bronchitis in babies.

UNIVERSAL MOBILE ANALYTICAL COMPLEX FOR RESEARCH OF RESPIRATION AND GAS EXCHANGE IN MAN AND ANIMALS

Kislyakov Yu.Ya., Kislyakova L.P., Zaiceva A.Yu., Gulyaev V.I.

Institute for Analytical Instrumentation, Russian Academy of Sciences, St.Petersburg, Russia; yukisl@rambler.ru

Experimental model of universal mobile and compact analytical complex for continuous monitoring of O_2 consumption and CO_2 emissions in breathing humans and laboratory animals has been developed. These

gas exchange parameters are calculated based on the simultaneous recording of expiratory flow rate and partial pressures of oxygen (pO_2) and carbon dioxide (pCO_2) in the exhaled air during each respiratory cycle (for a man), and the dynamics of the partial pressures of O_2 and CO_2 in a metabolic chamber (for animals and other biological objects). An analytical complex, in contrast to existing systems for the control of breathing and gas exchange in humans (EOS-Sprint, ER 800, ER 900, Ergo-line, Oxycon 5, Meta Max 3B, Rapidlab 840, Synthesis 15, Omni 3), has a small size, light weight and measure human respiration and gas exchange immediately during each breathing cycle. It consists of two parts - mobile and stationary. The mobile part includes a sensor unit, electronic converters, microcontroller unit, wireless transmitter and a miniature compact battery. Stationary part includes a wireless receiver and a computer control module. The sensor unit consists of the O_2 sensor (amperometric membrane electrode), the CO_2 sensor (the method of infrared correlation spectroscopy) and expiratory flow rate sensor (differential strain gauge pressure). Wireless transmission of information from the analyzer to the computer provides a radio modem. Computer control module with microcontroller provides calibration, measurement and calculation studied parameters, performance monitoring of all modules of the complex. The computer calculates indicators of the intensity of the gas exchange. The experimental results showed that the mobile analytical complex allows to measure with high precision volumetric expiratory flow rate and the partial pressure of O_2 and CO_2 in the breath of man, as well as the partial pressures of O_2 and CO_2 in a metabolic chamber with the animal (Table 1).

Table 1. Technical characteristics of sensors.

Registered parameters	Range	Error limit of measurement
pO_2, mmHg	0–800	$\pm$0.2 (0–200)
pCO_2, mmHg	0–100	$\pm$0.3
Expiratory flow rate, l / s	0 – 16	$\pm$ 2%

The complex has been tested in human studies during exercise and in studies on laboratory animals in surgical simulation of myocardial infarction and bleeding.

The project was supported by grants of the Program of the Presidium Russian Academy of Sciences “Fundamental Sciences - Medicine”.

MULTISENSORY EDUCATIONAL SYSTEM “ELECTRONIC TONGUE” FOR THE DIAGNOSIS OF THE FUNCTIONAL STATE OF THE HUMAN BODY ON THE CHARACTERISTICS OF EXHALED BREATH CONDENSATE

Kislyakova L.P., Kislyakov Yu.Ya., Zaiceva A.Yu., Gulyaev V.I.

Institute for Analytical Instrumentation, Russian Academy of Sciences, St. Petersburg, Russia, yukisl@rambler.ru

The structure of a learning diagnostic system produced on basis of a new concept of multi-parameter electrochemical analysis, simulating the organization and functioning of biological sensory systems is developed. System features: 1) the use of an array of cross-selective sensors with sensitivity to various chemical components of the medium, 2) evaluation of the measurement results using the methods of handling large volumes of multidimensional data and pattern recognition. Such analysis systems are called “electronic tongue”. They have been successfully used for the diagnosis of patients on integrated electrochemical indicators of urine. The purpose of this study is the development of a learning multisensory analytical system for the diagnosis of the functional state of the human body using indicators of exhaled breath condensate. The diagnostic system is composed of four modules: sample preparation, sensory, measuring and information. Sample preparation module provides a sampling of condensate. The sensor module consists of 6 potentiometric electrodes, each of which has the basic sensitivity of one of H^+, Na^+, K^+, Ca^{++}, NO_3^+, NH_4^+ and the additional cross-sensitivity to other ions and organic components of the condensate. He formed an “image” investigated medium in the form of the composition of the electrode potentials. The measuring module is a precision electronic microprocessor meter output potential sensors (error limit of measurement +0.002 mV, input impedance 10^{13} Ohm). Information module contains a set of data processing techniques derived from the metering unit via telemetry. They realize the functions of the system learning and recognition of multi-dimensional “images” generated by

the sensor module. Studies performed on the subjects showed that each of them has its own individual reproduced "image" of exhaled breath condensate and can be identified on the "image". Changes in the functional state of the subjects are shown in the characteristic changes of the "image". The results indicate efficiency of the described software and application possibilities of the proposed method for the diagnosis of the functional condition of the parameters exhaled breath condensate. The project was supported by grants of the Program of the Presidium Russian Academy of Sciences "Fundamental Sciences - Medicine".

EXPRESSION OF PYRUVATE DEHYDROGENASE KINASE-1 (PDK-1) GENE IN BRAIN-STEM MITOCHONDRIAL DYSFUNCTION DURING ADAPTATION TO INTERMITTENT HYPOXIC AND HYPOXIC-HYPEROXIC TRAINING

Kolesnikova E. E., Drevitskaya T. I., Mankovskaya I. N.

Bogomoletz Institute of Pysiology, Kiev (Ukraine); dr_kolesnikova@mail.ru

It's well known that brain stem as respiration-supporting structure is relatively stable under different physiological conditions. At the same time, deviations of mitochondrial (MT) function at the brainstem nuclei as non-specific reaction at early stage of different disorders could be a cause for the drop in ATP production, enhancement of reactive oxygen species (ROS) production and hence significant shifts in Glu/GABA balance at respiratory rhythm generation. During hypoxia, the induction of pyruvate dehydrogenase kinase-1 (PDK-1), a glycolytic gene, is considered critical for metabolic adaptation to hypoxia through increased conversion of glucose to pyruvate and subsequently to lactate. Simultaneously, forced PDK-1 expression increases ATP levels, attenuates hypoxic ROS generation. We examined the expression of PDK-1 gene in Wistar rats with brainstem MT dysfunction (EMBD, single rotenone injection, 3 mg/kg s.c.) during adaptation to 14-days intermittent hypoxic training (IHT, 15 min hypoxia (12% O_2) with 15 min room air breathing, 5 times a day) and hypoxic-hyperoxic training (IHHT, 5 min hypoxia (12% O_2) with 5 min hyperoxia (30% O_2,) 12 times a day). EMBD was accompanied by the drop in PDK-1 gene expression (by 29%). At the same time, 14-days course of IHT and IHHT enhanced PDK-1 gene expression (by 34% and 40%, respectively, $p<0,05$). After IHT and IHHT, EMBD rats were characterized by significant rise of PDK-1 gene expression (by 35% and 200%, respectively). Our observations suggest that adaptation to IHT and IHHT promotes the expression PDK-1 to maintain ATP production and to prevent toxic ROS production in the brain stem of EMBD rats.

EFFECT OF INTERMITTENT HYPOXIA TRAINING (IHT) ON OXYGEN CONSUMPTION IN ELDERLY PEOPLE WITH AND WITHOUT OBESITY

Korkushko O., Ishchuk V., Shatylo V.

State Institute of Gerontology, Academy of Medical Science of Ukraine, Kyiv; vadishchuk@ukr.net

Obesity is accompanied by a decrease in physical performance due to glycogenolysis disorder that leads to a deficiency of energy substrates and more rapid fatigability during exercise. Many investigations showed cardiovascular chronic hypoxia progression and carbohydrate metabolism disorders in obese humans. Short episodes of breathing with hypoxic gas mixture (5 min) with intervening 5 min room air breathing, 4 times a day (IHT) improve cardiovascular system efficiency, normalize lipid and carbohydrate metabolism, and increase tissue insulin sensitivity. ***Aim:*** To investigate oxygen consumption in elderly people with and without obesity under IHT. ***Methods.*** Two groups of elderly people were examined: Gr. 1 - 15 subjects without obesity (body mass index, BMI = 22.6 ± 0.5 kg/m^2), and Gr. 2 - 20 subjects with obesity (BMI = 32.6±0.5 kg/m^2, $p < 0, 01$). IHT was conducted during 10 days. With the subject seated, normobaric hypoxia (12% O_2) was administered using a devise 'Hypotron' (Ukraine). Oxygen consumption at rest and at 55 W load was studied during bicycle ergometer test by Oxycon-4 (Netherlands) before and after IHT. Exercise power at lactate threshold was also estimated. *Results.* Before IHT, oxygen consumption at rest was higher by 13% in Gr. 1 (5.3 ± 0.2 ml/kg) compared to Gr. 2 (4.6 ± 0.1, $p<0.05$). The same pattern was observed at 55 W load: 18.3 ± 0.8 ml/kg in Gr. 1 against 14.2 ± 0.4 ml/kg in Gr. 2 ($p<0.05$). Exercise power at lactate threshold was 70.0 ± 5.0 W in Gr. 1 and 62.5 ± 3.2 W in Gr. 2 ($p>0.05$). After the IHT course, oxygen consumption did not change in Gr. 1 (5.2 ± 0.2 ml/kg at rest and 17.8 ± 0.9 ml/kg at 55 W load) as well as lactate threshold. In Gr. 2 the tendency to increase the oxygen consumption at rest (4.8 ± 0.1 ml/kg) and at 55 W load (14.7 ± 0.5 ml/kg) was observed.

Exercise power at lactate threshold increased significantly (66.8 ± 2.4 W, $p<0.05$). *Conclusions.* IHT improves tissue oxygen consumption in elderly obese people. This leads to the inclusion of anaerobic mechanism of energy supply during physical load. The results suggest the potential use of IHT in the complex treatment of obese people.

H_2S PROTECTS HEART FROM DEFEROXAMINE-INDUCED CARDIOTOXICITY PREVENTING ROS AND RNS PRODUCTION

Kotsuruba A.V., Korkach Ju. P., Goshovska Y.V., Sagach V.F.

Bogomoletz Institute of Physiolology NASU, Kyiv, Ukraine; toliko49@uk.net

Objective. Hydrogen sulfide (H_2S) has been shown to protect against oxidative stress injury and inflammation in various hypoxia-induced insult models. However, it remains unknown whether H_2S protects rat cardiomyocytes against chemical hypoxia-induced damage. We hypothesized that deferoxamine (DFO), an iron chelator and activator of the hypoxia-inducible factor-1alpha (HIF-1α), would provide cardiotoxicity by oxidative (ROS) and nitrosative (RNS) stress activation in an in vivo model of ischemia in part through inhibition of the cardiac H_2S availability. *Model.* Deferoxamine mesylate salt (Sigma Cat # D9533) was injected intraperitoneally 15mg/100g for 2 days to adult rats. *Main outcome measures*. Content of H_2S, H_2O_2, NO_2^- , NO_3^- and urea, as well as ROS ($*O_2^-$ and *OH) and RNS (NO) generation rate were determined in hearts tissue homogenate of control and DFO-pretreated rats. NO generation rate was calculated by cNOS (eNOS+nNOS) and iNOS activity of NO de novo synthesis pathways. Oxygenation index ([nitrite]1000/([nitrate]+[urea], RNS/ROS ratio and % cNOS in total NOS (cNOS+iNOS) activity were calculated in both groups. *Results.* H_2S content in DFO-pretreated heart homogenates was dramatically decreased (from 12.01±1.71nmol/mg protein to 1.15 ± 0.14nmol/mg protein) simultaneously with dramatic increasing of ROS ($*O_2^-$ from 4.02 ±0.97 r.u. to 13.09 ±2.34 r.u., *OH from 0.92±0.15 r.u. to 16.85 ±3.78 r.u.) and RNS (cNOS from 6.38 ±3.76 pmol/min/mg protein to 35.71 ± 3.76 pmol/min/mg protein, iNOS from 1.28 ±0.36 pmol/min/mg protein to 13.71 ±1.56 pmol/min/mg protein, nitrite from 359.01±22.6 to 1906.83±440.4 pmol/mg protein, nitrate from 12.96±0.75 to 45.28 ±9.05nmol/mg protein. Total NO generative activity of NOS raised from 7.63±1.5 pmol/min/mg protein to 49.42 ±5.32 pmol/min/mg protein. In addition, oxygenation index in DFO pretreated hearts was markedly increased (from 3.49 ±0.53 r.u. to 13.51±2.17 r.u.). H_2O_2 pool, % cNOS and RNS/ROS ratio were not affected. *Conclusions*. Our findings showed that exposure of rats to hypoxia mimetic agent DFO for 48 h induces both dramatic decreases in H_2S level and nitrosamine and oxidative stress in heart tissues, suggesting protective effect of endogenously generated H_2S in normoxic heart condition against stress and inflammatory factors. Taken together, our findings suggest for the first time that H_2S may protect cardiomyocytes against ROS- and RNS-induced injuries and inflammatory responses through inhibition of ROS- and RNS-activated pathways, mainly by peroxynitrite (under excess NO and $*O_2^-$) formation.

CHANGES OF THE PARAMETERS OF THE PLASMATIC COMPONENT OF THE HEMOSTATIC SYSTEM IN PATIENTS WITH BRONCHIAL ASTHMA

Kovalenko S.V.[1], Dorofeev A.E.[2]

[1]Bukovinian State Medical University, [2]Donets'k National Medical University; dorofeyev@med.finfort.com

Introduction. An indisputable role in the development of the chronic inflammatory process in the bronchopulmonary apparatus is played by disturbances in the system of hemostasis. *The object of the research.* To study the specific characteristics of the hemocoagulating component of the system of hemostasis in patients with bronchial asthma (BA). *Material and methods.* Have been estimated the total anticoagulating blood potential according to the level of plasma fibrinogen; the activity of antithrombin III (ATIII), Hageman-dependent fibrinolysis, total (TFA), nonenzymatic (NFA) and enzymatic (EFA) fibrinolytic activity of the blood, the potential activity of plasminogen (PAPG); a quantitative evaluation of the activity of factor XIII (fibrinases) in 50 patients with asthma. *The experimental findings.* It has been found an increased level of fibrinogen. While investigating the NFA level increase was registered as a result of anelevation of its share within the TFA pattern. The potential activity of plasminogen did not increase significantly compared with healthy persons. The activity of antiplazmin was reliably decreased

in BA patients. There occurred an activation of the clotting blood system in case of a BA exacerbation, as a consequence – an increase of the ATIII level, decrease of the level Hageman-dependent factor, a reliable increase of factor XIII. *Conclusions.* The signs of marked blood hypercoagulation are observed in patients with BA at the time of an exacerbation.

NICOTINE DEPENDENCE AND MOTIVATION TO QUIT SMOKING IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

Królikowski K., [1] Domagała-Kulawik J.[2] , Chądzyński R.[2]; Mąka A.[4] ,and Opolski G.[3]

[1]Cancer Epidemiology and Prevention Department, Centre and Institute of Oncology, Warsaw, Poland, biuro@szpitalujazdowski.pl;
[2]Department of Pneumonology, Medical University of Warsaw, Warsaw, Poland;
[3]Chair and Department of Cardiology, Medical University of Warsaw, Warsaw, Poland;
[4]Students' Scientific 'alveolus' of Department of Pulmonology and Allergology, Medical University of Warsaw

Introduction: The percentage of smokers in Poland is 33.5% among adult men and 21.0% of adult women, which is, respectively, 5.2 and 3.5 million people. Diseases of tobacco are the cause of many deaths. These include patients with acute myocardial infarction. *Objectives:* The aim of this study was to assess the degree of dependence and the strength of motivation to quit smoking of patients hospitalized with acute myocardial infarction (AMI) as compared to asymptomatic smokers and analysis of the results with regard to demographic data and disease severity. *Method:* The surveys: motivation test to quit smoking and Fagerström test (tF) was performed in 32 patients-current smokers hospitalized for AMI. The control group consisted of 32 "healthy" cigarette smokers. In addition to the clinical examination and questionnaire regarding addiction, each patient was carried out anti-smoking advice by the rules. *Results*: The majority of patients reported the first episode of the AMI, dominated transmural infarction. Fagerström test mean score in the group of men did not differ between patients and healthy controls and ranged from 5.84 to 5.72. In the women patients group with AMI, Fagerstrom test average was 2.6 and 6.1 in the group of healthy subjects. In the particular case of the patients with AMI observed a strong dependence of the simultaneous strong motivation in patients with a first myocardial infarction with coexisting hypertension. *Conclusions:* Patients with AMI (especially women) have an average degree of dependence and high motivation to quit smoking. Strong biological and psychological dependence was observed in men. These observations point to the need to include patients with AMI to specialist care.

PECULIARITIES OF TUBERCULOSIS EPIDEMIOLOGY IN RURAL POPULATION

Kryvanos P., Sinkov G., Baradzina H.

Belorussian State Medical University, Minsk, Belarus, krivonos_pavel@list.ru

Aim. To study peculiarities of tuberculosis epidemiology of rural population in region of Minsk. *Methods.* We used report forms of the official statistics and made comparative analysis of tuberculosis cases in rural and urban population of Minsk region during 2007-20011. *Results*. We revealed common conformities of tuberculosis prevalence in urban and rural population. Tuberculosis morbidity of rural population exceeded analogous data of urban population 1,7 – 1,8 times and corresponded to average data in the country. Morbidity of female tuberculosis in rural population was 1,6 times higher as compared with urban population; male tuberculosis morbidity 1,5-2 times accordingly. We revealed reliable differences in morbidity data of some age groups. The highest tuberculosis morbidity was registered in males of 35-55 years, in females of 25-40 years. Risk to fall ill with tuberculosis decreases with age in urban population and increases in rural population. Incidence rate of tuberculosis in urban males and females of 65 years age are the same. But rural females older than 65 years fall ill with tuberculosis 1,7 times more offer as compared with males. *Conclusion.* Modern unfortunate tuberculosis situation as in Minsk region also in the country depends high morbidity in rural population. Revealed differences of some age groups of rural population require following study.

BACILLI SHEDDING SIGNIFICANCE IN DIFFERENTIAL DIAGNOSTICS OF LUNG TUBERCULOSIS AND CANCER

Kryvanos P.,Tamashakina G.

Belorussian State Medical University, Scientific Practical Centre for Pulmonology and hthisiology, Minsk, Belarus, krivonos_pavel@list.ru

Aim. To study bacilli shedding character in patients with lung tuberculosis and cancer. *Methods*. We analyses the results of complex examination of 80 patients with new detected lung cancer in clinic of Scientific Practical Centre for Pulmonology and Phthisiology in 2007-2011 years. *Results*. We detected mycobacterium tuberculosis in sputum of 13 (16.1%) patients, 7 of them had tuberculosis formerly – 2-10 years ago. 10 patients had central cancer and 3 patients - peripheral lung cancer. Most of patients (11 persons) had advanced (3-4 stage) lung cancer forms. Lung cancer diagnosis was confirmed with bronchoscopy and morphological studies of bioptats in all the cases. 9 patients had localized lung cancer in zone of post tuberculosis changes. Only 1 patient had profuse and frequent bacilli shedding; 7 patients had single or dual bacilli shedding; 5 patients had second bacilli shedding in 5-10 months. 12 patients had drug resistance. 3 patients had active tuberculosis and lung cancer simultaneously; 3 patients had cancer on back –ground of chronic tuberculosis; 2 patients had tuberculosis reactivation thanks to tumor. *Summary.* Physicians interpret MBT detection in sputum or post tuberculosis changes in tuberculosis favour during the differential diagnosis process. The further examination is conducted only in aggravation of clinical and roentgen data of illness.

STATE OF RESPIRATORY MUSCLES (RM) IN MEN WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Lemeschewskij A., Nedzvedz M., Makarevich A., Lemiasheuskaya S.

Belorussian State Medical University, Minsk, Belarus, lemechby@gmail.com

Background. It is necessary to introduce new methods of assessment of RM. *Aim:* to investigate the RM status by echography and compare results with histological data. *Material and Methods:* We obtained the indices (ultrasonic): homogeneity (H), structural density (SD), echogenicity (E) in units. We carried out histological research of bioptic material of intOAM. Research was made in 20 pts: 1st group (10 – 1st COPD stage; mean age – 55 yrs; FEV_1 – 79%; BMI – 24kg/m^2); 2nd group (10 – 2nd COPD stage, age – 59 yrs; FEV_1 – 59%; BMI – 24kg/m^2); control group - 12 pts. *Results:* There have been areas of myolysis, in which we found cell proliferation of perimiysium, "ingrowth" of fatty tissue between myofibrils (MF). There is interstitial sclerosis around the individual MF and bundles, sections "contractions" of MF. Among the relatively preserved MF was found deep dystrophic one with protein granules of different sizes in the appearance of the sarcoplasm. The atrophy and crimp of muscular fibrils with the phenomena of "contractions" of MF was observed predominantly in the 2nd group. Increasing of COPD severity was associated with significant enhancing of "contractions" ($r=0.72$), destruction of MF ($r=0.69$) and proliferation of fibroblasts ($r=0.52$). We detected the presence of negative correlations between H, SD and intensity of sclerosis manifestations ($r=-0.39$ and $r=-0.51$ respectively; $p<0.05$). Meanwhile the E was higher in these pts and correlated directly ($r=0.48$; $p<0.05$). The E of intOAM correlated in the 2nd group with fat mass index ($r=0.62$). This may indicate the accumulation of intramuscular fat in the second stage. *Conclusion:* The proposed echodensitometric parameters reflect the degenerative processes occurring in the RM.

IMPACT OF DIFFERENT FACTORS ON BONE MINERAL DENSITY IN MEN WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

Lemiasheuskaya S.

Belorussian State Medical University, Minsk, Belarus, lemsvby@gmail.com

Background: COPD is often associated with the systemic extra pulmonary effects such as osteoporosis. *Aim:* to study the likelihood of low bone mineral density in male patients with COPD. *Material and Methods:* We examined 92 COPD male patients aged 40 – 70 years. BMD was measured in spine (L_1-

L_4) and femoral necks (FN) using DEXA. *Results:* The index of "odds ratio" (OR) was 4.14 with the confidence interval (CL) (95%CI, 3.12-5.51) in patients with the presence of exacerbations in the year 3 and more. The likelihood of reduction in BMD with COPD significantly increase in patients with disease duration 10 years or more (OR, 7.34; 95% CI, 5.41-9.95); work related to hazardous occupational factors – OR, 2.30 (95% CI, 1.63-3.24); smoking – OR, 5.25 (95% CI, 3.20-8.35); the presence of emphysema in the X-ray – OR, 3.11 (95% CI, 2.37-4.06). Age 57 years and over - the probability increases 5.25 times (95% CI, 3.90-7.07). The likelihood of lower BMD in the 2nd stages COPD is 2.18 (95% CI, 1.36-3.50) and in the 3rd stage is greatly increase – OR, 10.91 (95% CI, 6.98-17.05). The presence of hypoxia (SpO_2%) significantly increases the risk of secondary reduction of BMD in COPD - OR 15, (95% CI 10.05-22.38). *Conclusion:* Factors that increase the likelihood of reducing the BMD in male patients in age 40-70 years are the frequency and type of exacerbations, age, duration and severity of disease, the presence of occupational factors, emphysema and hypoxia.

EFFECT OF INTERMITTENT NORMOBARIC HYPOXIA ON TOTAL OXYGEN CONSUMPTION AND EFFICIENCY OF CARDIO-RESPIRATORY MECHANISMS OF OXYGEN SUPPLY IN PATIENTS WITH CHRONIC PULMONARY DISEASES

Levashov M.I., Berezovskii V.A., Saphonov S.L., Chaka E.G., Yanko R.V.

Bogomoletz Institute of Physiology, Kiev, Ukraine, levashov@biph.kiev.ua

Intermittent normobaric hypoxic training (INGT) is one of the effective non-pharmacological methods for care and rehabilitation of patients with chronic pulmonary diseases. The total oxygen consumption (OC) and main indices characterizing the efficiency of cardio-respiratory mechanisms of oxygen supply were studied in 103 adult high-risk chronic obstructive pulmonary diseases patients. The 1st group of patients received only conventional treatment. The 2nd group received the same treatment in combination with INGT. INGT comprised of a daily 90 minute sessions in chamber "Orotron" for 2 weeks under such environmental parameters: PO_2 - 147-160 hPa, relative humidity - 60-70%, ambient temperature - 16-18°C and content of light negative ions - up to 6000 per cm^3. The heterogeneity of OC dynamic of both the amplitude and direction was observed in 2nd group of patients after INGT. The pattern and degree of changes were dependent on the initial level of OC. In this regard the 2nd group of patients was divided into three subgroups: 2a - 33% of patients had a normal value of OC, 2b - 53% of patients had a lower value and 2c - 14% of patients had a higher value of OC. INGT did not change OC but improved the efficiency of hemodynamic mechanisms of oxygen supply in patients subgroup 2a. The total OC and efficiency of respiratory mechanisms of oxygen supply moderately increased in patients subgroup 2b. The value of OC decreased to normal level in patients subgroup 2c, but respiratory and hemodynamic mechanisms of oxygen transport remained highly effective. It was concluded that INGT normalized OC in patients with chronic pulmonary diseases.

THE MODERN SPIROMETRY: CHALLENGES AND RESPONSES

Lopata V.A.[1], Myasnyi I.S.[2], Zabrodska L.V. [1]

[1]Bogomoletz Institute of Physiology, Kiev, Ukraine, v.lopata@meta.ua;
[2]Clinical Hospital "Feofaniya", Kiev, Ukraine

The aim of study was to discuss the spirometry problems and offer their solutions. Spirometry is a medical technology that combined methodological, metrological and informational aspects. Modern microprocessor spirometers have reached their limit - the requirements of ATS/ERS standard and have a reserve to improve their performance. This, however, doesn't solve all problems of spirometry. They are designated mainly in methodological and informational support: (1) Algorithms for interpreting the results of spirometric tests based only on the parameters of FVC, FEV1 and Tiffeneau' index, whereas flow rates parameters of the forced expiratory "flow-volume" loop don't participate in the diagnostic conclusion formation. (2) Too great a role of subjective factors (operator training and patient cooperation) in the conduct of forced spirometry. (3) Spirometric testing software isn't standardized. For these problems solving, we have developed:

- the prospective requirements for spirometers;
- algorithm for interpreting the results of spirometric tests, taking into account the values of MEF25, MEF50, MEF75 and FEF25-75 of forced expiration;
- the requirements for the unified spirometry software;

- scenes of animation programs to encourage patients with forced expiratory maneuvers.

For the further development of the spirometry it's necessary to: (1) put into practice a patient incentive programs ; (2) develop the interpretation algorithms that take into account parameters of forced expiration flow rates for deeper and more objective assessment of breathing function as a result of spirometry; (3) create the dynamics standards of methodological, metrological and informational support for spirometry with a mandatory upgrade every 3 years.

DYNAMICS OF RESPIRATORY MUSCLE CHANGES DURING CHRONIC OBSTRCTIVE PULMONARY DISEASE PROGRESSION

Makarevich A. [1], S. Lemeshevskaya[1], A. Poctavcev[1], A. Lemeshevsky[2], M. Nedvedz[3]

Belorussian State Medical University: [1] - Department of Internal Medicine; [2] - Department of General Surgery; [3] - Department of Pathologic Anatomy, Minsk, Belarus, makae@bsmu.by

Background The pathological changes of respiratory muscles (RM) during chronic obstructive pulmonary disease (COPD) progresses have not been studied in details yet. *The aim* was to assess RM status in COPD patients with different stages and detect the relationship between echodensitometric and morphological changes in RM. *Methods***.** All 152 COPD male patients were divided according to the severity: $COPD_1$ (mild: age - 55 yrs, FEV_1 - 85%) – $COPD_2$ (moderate: age - 57 yrs, FEV_1 -55%) - $COPD_3$ (severe: age – 60 yrs, FEV_1-33%). We studied the following muscles of inspiration (sternocleidomastoid, scalenus anterior, external intercostals) and expiration (abdominal internal oblique, abdominal external oblique, rectus abdominis, transversus abdominis and internal intercostals). The status of RM was detected in these groups both by using the echodensitometry indices (echogenicity - IE; homogeneity - H and structure density - ISD) and morphological material of abdominal internal oblique muscle (which was received during inguinal herniotomy). *Results***.** In COPD, the tendency to increase of the indices of homogeneity (IH) and) was detected (due to hypertrophy of RM), while IE reacted differently. In moderate COPD IH and ISD were decreased, while IE was increased (due to fatty infiltration and sclerosis of RM according to our parallel morphologic data). In severe COPD IH and ISD rose against the background of IE decrease (due to reduction of fatty mass and intensification of RM sclerosis). *Conclusion* The proposed echodensitometric parameters reflect in a complex way the dynamics of the degenerative processes occurring in RM during COPD progression.

MITOCHONDRIAL DYNAMICS IN OXYGEN-GLUCOSE DEPRIVATION ON A MODEL OF CULTIVATED HIPPOCAMPAL SLICES

Malieieva G.V., Lushnikova I.V., Skibo G.G.

Bogomoletz Institute of Physiology, Kiev, Ukraine, li@biph.kiev.ua

Ischemia injury is one of the most common death reasons in Ukraine and in a whole world. At the cells level stroke characterized by oxygen and glucose supply loose that cause energy failure and neurdegeneration. Mitochondrais are the key organelles of cell energy homeostasis. In order to discover dynamics of energy metabolism in ischemia damage we have been focused on investigation of mitochondrial functioning after 30-min oxygen-glucose deprivation (OGD) and reoxygenation 1 and 4 hours. We have done a comparison analyze of active mitochondrial activity of hippocampal pyramidal neurons and glial cells of CA1 and CA3 areas using fluorescent dyer MitoTracker Orange. In the present study it was determined that pyramidal neurons and glial cells have different dynamics of mitochondrial activity. Hippocampal pyramidal neurons have demonstarated the increasing of activity during first hour and the decreasing for four hours after OGD. Glial cells increased their mitochondrial activity fourth hours after start of reoxygenation, comparing with first hour. This indicates a specific activation of pyramidal neurons in response to the OGD, which, however, can not be maintained for a long time. For glial cells is characteristic of a more prolonged and sustained increase in mitochondrial activity. Thus, it can be assumed that the more resistant glial cells are able to some extent, to modulate the function of neurons in a lack of oxygen and glucose.

INTERMITTENT HYPOXIA-HYPEROXIA, A NEW MODE OF ADAPTIVE TRAINING IN CORRECTION OF LUNG MITOCHONDRIAL DYSFUNCTION

Mankovska I., Gonchar O., Steshenko N.

Department of Hypoxic States, Bogomoletz Institute of Physiology, Kyiv, Ukraine, ogonchar@yandex.ru

Hypoxic and hyperoxic therapy has a various application in traditional and alternative medicine for the treatment and prophylaxis of various pathological syndromes. Glutathione (GSH), GSH-related enzymes as well as MnSOD play an important role in preventing of lung mitochondrial dysfunction following oxidative stress injury. However, its role in forming of compensatory-adaptive responses to hypoxia/hyperoxia is unclear. It was explored a new mode of adaptive training, which combines periods of hypoxia and hyperoxia (H/H) and is characterized by upregulation of adaptive ROS signals compared to classical intermittent hypoxic training. The purpose of this study was to determine the influence of repetitive moderate sessions of hypoxia and hyperoxia on pro-/antioxidant homeostasis in lung mitochondria of rats exposed to acute severe hypoxia. It was shown that H/H pretreatment [5 cycles of 5 min hypoxia (10% O_2 in N_2) alternated with 5 min hyperoxia (30% O_2 in N_2) daily for two weeks] reduced the acute hypoxia-induced basal and stimulated *in vitro* lipid peroxidation, increased the GSH/GSSG ratio, and decreased the GSSG content. The enhancement in the level of GSH and activities of MnSOD, glutathione peroxidase and glutathione reductase in comparison with acute hypoxia as well as the maintenance of glutathione-S-transferase activity at control level confirm that mitochondrial protection during H/H may be mediated through the modulation of mitochondrial antioxidant levels. In lung H/H training caused the increase in MnSOD protein synthesis, at the same time, no changes in mRNA MnSOD expression was registered. This study supports the viewpoint that moderate periodic generation of free radical signal during changes in the oxygen level causes the induction of antioxidant enzyme protein synthesis that may be an important trigger for specific adaptations.

CONTENT OF ANTIMICROBIAL PEPTIDES IN OROPHARINGEAL SECRETIONS OF CHILDREN SUFFERING FROM ACUTE RESPIRATORY DISEASES

Marushko Yu., Melnikov O., Movchan O., Lysovets O.

Bogomoletz National Medical University, Kyiv, Ukraine, Pr-Marushko@yandex.ru

Today the studying of children local immunity of oropharingeal secretions that often suffer from acute respiratory diseases is a matter of current interest. Antimicrobial peptides, especially defensins, are the first link of antiinfectious defense. Their level in children is almost not studied. The aim of the work: to study features of acute respiratory diseases (ARD) course and human β -defenses level in oropharingeal secretions (OS) in children of different age suffering from chronic tonsillitis. 30 children that suffered from ARD and chronic tonsillitis aged from 4 to 12 were examined. The level of human β -defenses in OS during non acute period was investigated. Clinical, immunological and statistical methods were used. The level of human β -defensins in OS of children that suffered from ARD aged from 4 to7 years is much smaller than in OS of the children with the same diseases aged from 8 to 12 years. It is 0,85 (0,12-2,25) mkg/ml and 4,8 (0,26-9,88) mkg/ml. The level of defenses in children aged from 4 to 7 is smaller than minimal level, when human β -defenses can demonstrate their antimicrobial activity. Clinically, the group of children that suffer from ARD aged from 4 to 7 is characterized by higher frequency of ARD and exacerbation of chronic tonsillitis, 11 children (73,3%) aged from 4 to 7 had bacteriologically confirmed bowels dysbiosis. During bacteriological studying of tonsils swab St. aureus was found in 9 children (60 %) aged from 4 to 7 and in 7 children aged from 8 to 12 (46,7 %). They showed smallest levels of human β-defensins: 0,46 (0,12- 0,59) mkg/ml and 2,61 (0,26 – 5,94) mkg/ml relatively. Thus, we determined that children who suffer from ARD and chronic tonsillitis have low level of human β -defensins in OS. That is more pronounced in the younger age group (from 4 to 7 years). It can explain high frequency of ARD of children under school age.

FUNGAL CONTAMINATION OF PREMISES AS A RISK FACTOR FOR RESPIRATORY ALLERGY

Maslova L.

Belorussian Medical Academy of Postgraduate Education, Minsk, Belarus, allergo@tut.by

Background: Currently, moulds are among the unconditional risk of allergic rhinitis and asthma, in closed rooms. The inhabitants of modern cities, especially children, spend a significant part of their time indoors. Our objective was to determine the structure of mycobiota indoor and its impact on respiratory allergy development. *Methods***:** questionnaire to assess the living conditions of patients, suggest fungal infection, visual examination of lesions of microscopic fungi, mycological examination of premises, sampling locations of the alleged mold damage, the selection of fungi in culture. Evaluation of 174 patients living in the fungal contamination included a medical history of life and disease, allergic history, physical examination, skin allergotesting, blood samples for determination of specific IgE to the major inhalation allergens. *Results*: Mycological analysis of the isolates showed a high degree of microscopic fungi spores sample contamination, dominated genera Penicillium, Cladosporium, Aspergillus, Ulocladium. A total of 174 people living in the areas affected by fungi, 59 of them (33.9%) have a sensitization to fungal allergens, including thresholds specific Ig E. Almost half of the sensitized patients (16.7%) were sensitized to several species of fungi. 174 residents of the surveyed areas were affected by the fungus, and 33 people (19%) had a diagnosis of asthma. Asthma fungal installed in 21 patients, 6 of whom had isolated fungal sensitization, 15 - sensitization to fungal allergens combined with sensitization to house dust mite allergens. *Conclusion*: Among the patients living in a residential area where the growth of fungi took place, there were increased sensitivity to fungal allergens in isolation or in combination with other types of sensitization. There is a need of residential patients with fungal sensitizationis inspection, the development of measures for the indoor fungi elimination. When moulds induce the early type of hypersensitivity specific immunotherapy should be used as the primary method of pathogenetic therapy.

SYMPATHETIC-ADRENAL SYSTEM AT PSYCHO-EMOTIONAL STRESS UNDER HYPOXIA IN AGING

Osmak E.D.

D.F. Chebotarev State Institute of Gerontology of the NationalAcademy of Medical Sciences of Ukraine, Kiev

The onset of CNS changes in aging creates the prerequisites for reducing of the resistance to psycho-emotional stress influences. Age changes of the sympathetic-adrenal system present the key mechanism of age-dependent disturbances in adaptation to various factors including hypoxia and psycho-emotional stress. Our earlier investigations have shown that during aging there develops a more marked reaction of the sympathetic-adrenal system to the hypoxic stress. In literature there is lack of data about the peculiarities of adaptation to psycho-emotional stress under hypoxia in old age. We have tried to elucidate the reaction of the sympathetic-adrenal system to psycho-emotional stress under hypoxia in the old age. The study included 15 young and 25 essentially healthy elderly people in the age range from 60 to 74 years. Normobaric hypoxia was induced by the inhalation of gas mixture with low oxygen content (12% of O_2 and 88% of N_2) during 20 min. Blood plasma catecholamine concentrations were measured at the basal state and at 20^{th} min of hypoxia. To reproduce the state of psycho-emotional stress, we used the laboratory model of psycho-emotional strain developed by A.A. Polyakov, N.F. Prokopenko and A.V. Pisaruk. Psycho-emotional stress at normoxic conditions caused a typical universal reaction to stress which is mediated by activation of sympathetic-adrenal system in all study groups. The increase in blood adrenalin content was observed in young subjects and both catecholamines (adrenalin and noradrenalin) - in old persons. Under hypoxic conditions the psycho-emotional load did not lead to further activation of the sympathetic-adrenal system in young subjects. On the contrary, in elderly subjects the combined action of psycho-emotional and hypoxic stress led to more marked reactions of the sympathetic-adrenal system in comparison with their young counterparts. *Conclusions*. In aging there develops a more pronounced reaction of the sympathetic-adrenal system to psycho-emotional stress. Combination of psycho-emotional and hypoxic stresses leads to more pronounced activation of sympathetic-adrenal system in elderly versus young people.

PULMONARY ALVEOLAR MICROLITHIASIS: REPORT OF 2 CASES

Patil P.V.[1], Gaude G.S.[2], Paramjyothi G.[1], Jain R.[1], Kaur K.[1]

1Navodaya Medical College, Raichur -584103. 2J.N. Medical College, Belgaum - 590010. India. docpvpatil@gmail.com

Pulmonary Alveolar Microlithiasis (PAM) is a rare pulmonary disease of unknown aetiology and pathogenesis, characterized by diffuse microliths in the alveoli. We report 2 cases of PAM encountered by us in last 16 years. Case 1: A 40 years male presented with cough and expectoration and progressive exertion dyspnoea since 6 months. He gave history of occasionally bringing sand like particles in the sputum. Sputum AFB was repeatedly negative. The RA test, LE cell phenomenon and ANA tests were also negative. The sputum examination revealed sand like particles to be microliths. Fiberoptic transbronchial lung biopsy showed calcified spherules (microliths) in alveoli. Case 2: A 22 years female presented with cough with scanty expectoration and dyspnoea since 3 years. The patient was treated in rural area as a case of pulmonary tuberculosis (PTB) based on chest X ray (CXR). However sputum was negative for AFB on repeated examination. Later the patient was referred to our hospital where the CXR and high resolution computed tomography (HRCT) –findings were suggestive of PAM. The above 2 cases are being presented for their rarity. Such cases are often under-diagnosed and treated as PTB in rural setup. Facilities for genetic studies to detect the mutation in SCL34A2 gene, which encodes a type IIb sodium dependent phosphate transporter, are not available in our setup.

THE ROLE OF POLY(ADP-RIBOSE) POLYMERASE-1 (PARP-1) IN CONCANAVALIN A (CONA) INDUCED MICROCIRCULATION DISTURBANCES IN MOUSE LIVER

Pavlovych S.I., Martynova T.V., Makogon N.V., Grushka N.G., Sukhina V.S., Bryzgina T.M., Yanchii R.I.

Bogomoletz Institute of Physiology, Kyiv, Ukraine, spavl@biph.kiev.ua

Experimental hepatitis induced by polyclonal T lymphocyte activator ConA closely mimics pathological features of immune-mediated liver diseases, such as microcirculatory disturbances leading to tissue hypoxia. This is a good and convenient model for studying the mechanisms of autoimmune hepatitis, particularly mediated by nuclear enzyme PARP-1. It participates in DNA repair and regulates transcription factors. Excessive activation of PARP-1 has been shown to contribute to some inflammatory disorders. Here we examined the effect of PARP-1 inhibitor 4-hydroxyquinazoline (4-HQN) on ConA-induced liver microcirculation disturbances to estimate the involvement of PARP-1 in the development of hepatic tissue hypoxia. ConA administration resulted in hepatitis with pathological changes in liver vascular system which caused acute tissue hypoxia. Hypervolemia, microvessel enlargement, stasis, hemolysis, thrombosis, vessel wall damage and perivascular edema were observed. The vascular injury was accompanied with the enhanced neutrophilic infiltration in the liver and with intensified superoxide production by activated neutrophils. These changes caused oxidative stress and increased lipid peroxidation (estimated by the level of malondialdehyde in the liver). The treatment of mice with 4-HQN (2h before ConA) decreased the total score of liver vascular injury (sum of scores for microvessel enlargement, hypervolemia, thrombosis, vessel wall damage and perivascular edema), $P < 0.001$. 4-HQN administration significantly reduced diffuse and focal neutrophilic infiltration in Con A-induced hepatitis and attenuated hepatic oxidative stress. These results suggest that PARP-1 plays an important role in pathogenesis of immune-mediated hepatic vascular damage and support the potential therapeutic application of PARP inhibitors in the treatment of hypoxic liver injury.

SYSTEMIC CONDITION OF SOME INFLAMMATORY MEDIATORS IN PATIENTS WITH BRONCHIAL ASTHMA AND WAYS OF THEIR CORRECTION

Pobedjonna G.P., Shuper V.O.

Lugansk state medical university, Lugansk, Ukraine, g-pobeda@ukr.net

Cytokines (CK), in particular, interleukins (IL) play a significant role in the development of chronic inflammation in bronchi of patients with Bronchial Asthma (BA). The purpose of work: to study IL-1β, IL-4, IL-8, IL-10, TNF-α contents in blood serum (BS) and condensate of moisture of expiratory air (CMEA) in patients with BA of different severity with exacerbation; to define the directions of their

correction. Materials and methods. 222 patients with BA were studied including those with mild degree - 107 (group I), moderate degree - 74 (group II), severe degree - 41 (group III). IL-1β, IL-4, IL-8, IL-10, TNF-α were studied in CMEA and BS by enzyme immunoassay method.
Results. In group I IL-1β, IL-4 were increased in BS and CMEA. In group II IL-1β, TNF-α, IL-8, IL-4 were increased almost doubled of the norm in BS and CMEA. IL-10 in BS was around the norm, and in CMEA - significantly higher. In group III IL-1β, IL-4 TNF-α in BS and CMEA were significantly higher than norm; IL-8 in CMEA was higher than in BS, IL-10 in BS and CMEA was close to norm.
Conclusions. After basic treatment the studied cytokines in patients of II and III groups didn't become normal in BS and CMEA. Medications with pleotropic effects which aren't contraindicated in BA should be added for correction of cytokines.

SENSING CHANGES IN OXYGEN CONTENT: THE ROLE IN HEALTH AND DISEASE

Pokorski Mieczyslaw

Department of Respiratory Research, Medical Research Center, Polish Academy of Sciences, Warsaw, Poland, m_pokorski@hotmail.com

Oxygen is indispensible for life, as its molecule participates in energy metabolism in mitochondrial electron transport chain. Sensing changes in oxygen is thus a vital homeostatic function of the organism. Oxygen is basically sensed by the sensory organ of the carotid body located at the bifurcation of the common carotid artery. The organ produces a powerful defensive chemoreflex consisting of lung hyperventilation in response to reductions in O_2. The innate mechanisms of carotid body function are still unknown and are subject of intensive research; in particular the role of a spate of neurotransmitters and/or ionic channels in the organ's receptor neurons, called chemoreceptor cells or Type I cells, is unsettled. The assessment of carotid body function consists of taking the ventilatory responses to hypoxia (HVR) and hyperoxia. Clinical usefulness of these tests is subject to debate. In health, the HVR may be used to predict the ability to adaptively respond to hypoxia, e.g., during strenuous exercise, which comes down to the prediction of safety of hypoxic episodes which someone may encounter. In disease, the HVR may be used to predict, e.g., if supplemental oxygen given to patients in case of emergency or in chronic respiratory disease would diminish ventilation. The hypoxic ventilatory response, and thus the ability to deliver oxygen through the aged lungs, also is crucially important during the aging process. Interestingly, despite severe structural and ultrastructural changes in the aged lungs, the response to hypoxia is well preserved. Therefore, in advanced, but healthy, old age the central and peripheral neural respiratory drive is able to compensate for the morphological lung tissue decline. The lecture will end up with the hints on the newest theories concerning the detection of oxygen changes along the hyperoxia-hypoxia continuum, having to do with the transient receptor potential channels.

PHASE CHANGES IN ENERGY METABOLISM DURING RECOVERY AFTER HYPOXIA OR STRESS

Portnichenko V.I.[1], Nosar V.I.[2], Portnychenko A.G.[1], Pavlovich S.I.[2], and Mankovskaya I.N.[2]

[1]International Centre for Astronomical, Medical and Ecological Research, NAS of Ukraine, Kyiv; [2]Bogomoletz Institute of Physiology, NAS of Ukraine, Kyiv, Ukraine, vport@biph.kiev.ua

Patterns of energy metabolism changes during hypoxia or stress are poorly characterized and understood. Male Wistar rats were exposed to periodic hypobaric hypoxia (PHH, 5600 m, 1 h, 6 séances every 3 days), acute hypoxia (5600 m, 3 h), or stress (6 h immobilization daily, 2 weeks). During recovery period, oxygen consumption (VO_2), pattern of respiration, body temperature (Tm), mitochondrial respiration by Chance, HIF-1α and HIF-3α gene expression were determined. Four phases of metabolic changes were identified. The first phase, hypometabolic (up to 7 days), is characterized by decrease in VO_2 and Tm, induction of HIF-1α and HIF-3α with delayed transitory stimulation of metabolism in response to each séance of hypoxia. It was found that during above-mentioned phase the mitochondrial complex II was significantly activated. During the second (transitional) phase the metabolic shifts were developed. In the third (hypermetabolic, 7-12 day or more) phase, metabolism was intensified that accompanied by VO_2 enhancement and the mitochondrial complex I activation. The fourth phase of primary adaptation (after 5 séances of PHH or 2 week of stress) was characterized by the normalization of VO_2 and Tm, expression of HIF-1α and HIF-3α, mitochondrial respiration, the increase in NAD-dependent oxidation of carbohydrate and lipid substrates. Thus, we identified four general patterns of the rebuilding in energy metabolism during periodic, acute hypoxic episodes and stress.

CELLULAR AND MOLECULAR BASIS OF ACUTE O_2 SENSING AND ITS PHYSIOLOGICAL CONSEQUENCES

Prabhakar Nanduri R.

Institute for Integrative Physiology & Center for Systems Biology of O_2 Sensing, University of Chicago, Chicago, IL, USA, nprabhak@medicine.bsd.uchicago.edu

The carotid body is a sensory organ for detecting arterial blood O_2 levels and reflexly mediates systemic cardiac, vascular and respiratory responses to hypoxia. Sensory discharge of the carotid body is low under normoxia and dramatically increases in response to even modest hypoxia. Type I (also called glomus) cells, the site of O_2 sensing in the carotid body, express haem oxygenase-2 and cystathionine-γ-lyase, the enzymes which catalyze the generation of gaseous messengers carbon monoxide (CO) and hydrogen sulfide (H_2S), respectively. Physiological studies have shown that CO is an inhibitory gas messenger, which contributes to the low sensory activity during normoxia, whereas H_2S is excitatory and critical for sensory stimulation by hypoxia. Hypoxia increases H_2S generation in the carotid body, which requires redox-dependent interaction of cystathionine-γ-lyase with haem oxygenase-2, which generates CO. The transcriptional activators, hypoxia-inducible factors 1 and 2 (HIF-1 and HIF-2) constitute important molecular underpinning of hypoxic sensing by the carotid body. Recent studies demonstrate that redox balance determined by mutual antagonism between HIF-1α and HIF-2α isoforms defines the *set point* for hypoxic sensing by the carotid body. Emerging evidence suggest that developmental programming of the carotid body response to hypoxia involves epigenetic changes, e.g., DNAmethylation of genes encoding redox-regulating enzymes. Available evidence implicates heightened carotid body chemo-reflex in the progression of autonomic morbidities associated with cardiorespiratory diseases, such as sleep-disordered breathing with apnoea, which causes intermittent hypoxia (IH). Exposing rodents to chronic IH leads to sensitization of the carotid body response to acute hypoxia and induces sensory long-term facilitation and these effects are mediated by altering the redox state. Analysis of the systemic responses revealed that rodents exposed to chronic IH exhibit: a) more number of spontaneous apneas (cessation of breathing greater than 2-3 breaths), b) elevated baseline and augmented sympathetic nerve response to hypoxia, c) augmented catecholamine secretion from adrenal medulla, d) hypertension and e) elevated ROS levels in central and peripheral nervous system. Remarkably, selective ablation of the carotid body, while preserving the carotid baroreceptor function, prevents IH-evoked systemic and cellular responses.
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THE INFLUENCE OF HYPERINFLATION AND SYSTEMIC INFLAMMATION ON THE 6 MINUTE WALKING DISTANCE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Przybyłowski T., Rubinsztajn R., Maskey-Warzęchowska M., Paplińska-Goryca M., Nejman-Gryz P., Karwat K., Chazan R.

Department of Internal Medicine, Pneumonology and Allergology, Warsaw Medical University, Poland, przyb@amwaw.edu.pl

Dyspnea and impaired exercise tolerance are frequent in patients with chronic obstructive pulmonary disease (COPD). Hyperinflation contributes to exercise intolerance by its negative impact on lung mechanics. The aim of the study was to evaluate the influence of hyperinflation on the 6 minute walking distance and the markers of systemic inflammation in patients with COPD. The study group consisted of 149 patients with stable COPD (61F, 88M) aged 68±8.8 yrs in all stages of severity. All the patients underwent spirometry and bodypletysmography with bronchial reversibility testing. Hyperinflation was defined as RV%TLC > 48% and > 126% predicted. The 6 minute walking test (6MWT) was performed in accordance with the ATS recommendations. The following serum inflammatory markers were evaluated: C-reactive protein, IL-6, IL-8, TNF alpha, CC16, adiponectin and resistin. The patients were divided into group A (patients without hyperinflation, n=53) and group B (patients with hyperinflation, n=96). Table 1 presents significant differences in the results of the 6 MWT between the two groups.

	Group A	Group B	p
Distance (m)	472.2±102.6	401.5±108.9	0.0003
Distance (% pred.)	98.0±20.3	84.3±20.5	0.0001
HR at rest (min^{-1})	74.2±10.9	80.4±10.5	0.0008
Baseline SpO_2 (%)	94.8±2.3	93.8±2.7	0.01
SpO_2 6 min (%)	90.5±5.8	88.5±6.5	0.01
Post-6MWT dyspnea (Borg scale)	1.5±1.5	2.3±1.9	0.01

We found significant positive correlations between 6 MWD and serum IL-8 (R=-0.2,p=0.02), IL-6 (R= -0.3, p=0.002), TNF alpha (R=-0.2, p=0.04) and C-reactive protein (R=-0.2, p=0.03); SpO_2 6 min and resistine (R=0.2, p=0.006), CC16 (R=0.2, p=0.03); RV%TLC and IL6 (R=0.2, p=0.007) in the group as a whole. Conclusions: (1) Hyperinflation has a negative influence on exercise tolerance in COPD patients. (2) Systemic inflammation may also deteriorate exercise tolerance in COPD patients.

GUINEA-PIG BLOOD SERUM INTERLEUKIN-6 ACTIVITY IN THE DYNAMICS OF EXPERIMENTAL BRONCHIAL ASTHMA DEVELOPMENT

Regeda M.S., Kolishetska M.A., Sementsiv N.G.

Danylo Halytsky Lviv National Medical University, Lviv, Ukraine, marta.kolishetska@gmail.com

Bronchial asthma is a common respiratory illness which affects people of all ages at any given time. Cytokines play a critical role in the orchestration of chronic inflammation in all diseases, including asthma and chronic obstructive pulmonary disease.

The aim of our research is to investigate some changes in activity of anti-inflammatory cytokine - Interleukin 6 (IL-6) in the blood serum of guinea-pigs in the dynamics of experimental bronchial asthma (BA) development. *Research materials and methods*. Researches were carried out on 60 guinea-pigs (males). The weight of each one was 180-220g. They were divided into 5 groups for 12 animals in each of them. Intact guinea-pigs formed the first group (control). Animals with an experimental BA (5^{th} day) were among the second group. Among the third group there were guinea-pigs with an experimental BA (19^{th} day). The fourth group consisted of animals with an experimental BA (26^{th} day) and the last fifth group included guinea-pigs with an experimental BA (33^{rd} day). Experimental model of bronchial asthma was restored on guinea-pigs by the V.I. Babych method (1979). Euthanasia of animals was carried out by the way of decapitation followed the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (1985). The IL-6 concentration in the blood serum was defined for all groups of guinea-pigs. It was made using hard-phase immune-enzyme analysis (ELISA), by means of the test-system "Diaclone" (France). Numerical results were adapted with static method using Student's criteria. *Research results and discussing.* During the experimental researches some changes in activity of Interleukin-6 in the dynamics of BA development was observed. So, after 5 days guinea-pigs had increased their index by 39,7% ($p<=0,05$) in comparison with control indexes. Then, on 19^{th} day of experiment, the increasing of such index was noticed on 88,2% ($p<=0,05$) concerning the first group. The same index was noticed concerning the intact animals (by 88,2% ($p<=0,05$)). In the latest term, on 33^{rd} day, the highest increasing of this anti-inflammatory factor was observed. It was higher by 122 % ($p<=0,05$) in regarding to healthy animals. Consequently, the research of anti-inflammatory cytokine IL-6 in the blood serum of guinea-pigs during BA showed its great increasing. It is evidence of considerable activity of immune inflammation and its direct participation in pathogenesis on the assumption of such bronchial-pulmonary disease.

SOME POSSIBILITIES OF ELIMINATION OF THE ULTRASTRUCTURAL PREREQUISITES UNDER EXPERIMENTAL PNEUMOSCLEROSIS DEVELOPMENT

Rozova E.V.

Bogomoletz Institute of Physiology, Kiev, Ukraine, erozova@ukr.net

The development of pneumosclerosis under experimental pneumonia and some possibilities of its prevention were studied on adult Wistar rates. Due to peculiar structure of lung tissue, the chronisation of

acute pneumonia and the development of pneumosclerosis accompanied not only with collagen fibers germination in connective lung tissue, but to an even grater degree with disturbances of air-blood barrier with epithelium desquamation, significant cell reaction with destruction of capillaries wall endothelium and pronounced mitochondrial dysfunction. All these processes lead to hyperhydration of lung tissue and/or intra-alveolar edema origin even during 4 and 6 weeks after pneumonia simulation. Different modification of traditional therapy not always could prevent of pneumosclerosis development. In our investigations it was shown that exogenously entered phospholipids in liposomal form proved a pronounced positive effect on ultrastructure of lung tissue under acute pneumonia, consists, first of all, in a substantial decrease of edema symptoms. We have also shown that the same positive effect may reveal in the case of pneumonia chronisation. It was argued that employment of natural phosphatidylcholin (lecithin) in liposomal form in combined therapy of experimental pneumonia lead to normalization of ultrastructure of lung tissue: decreasing of destructive processes, hyperhydration and intra-alveolar edema, mitochondrial dysfunction. Simultaneously, the number of sections with collagen fibers spreading and hyalinosis in lung tissue decreased after 4 weeks of pneumonia modeling on 35% and after 6 weeks - on 75%. Thus, the effectiveness of treatment of chronic experimental pneumonia essentially increased with employment of phospholipids in liposomal form.

INFLUENCE OF PSYCHOLOGICAL FEATURES OF CHILDREN ON THE PARAMETERS OF EXTERNAL BREATHING

Roubuts T., Kharitonava A.

Grodno State Medical University, Belarus, roubuts_60@mail.ru

The act of breathing is considered to be a means of expression in the sphere of interpersonal relations as well as a means of evidence of the inner state of an individual. *The aim* of our research was to study the influence of the psychological peculiarities of a child's organism on the parameters of the function of the external breathing. *Material and methods***.** The psychological investigation and the study of the function of the external breathing of 148 practically healthy children with the help of the spirometer were carried out. The children were 12,05±2,51 years of age in average. *Results.* The children are divided into the following groups according to the type of the temperament: phlegmatic type – 34,2%, sanguinic type – 24,4%, intermediate – 30,5%, choleric type – 7,3%, melancholic type – 3,7%. The decreasing of FVC at the children with melancholic type ($F=2,561$, $p<0,05$) was revealed. It was also revealed that there is a negative correlation dependence between schizoid dissocial type and the value FEV_1 ($r=-0,283$, $p<0,000$ and $r=-0,264$, $p<0,001$, accordingly), proneness to conflict and FVC ($r=-0,270$, $p<0,001$), positive - between conformism, stress level and IT ($r=0,279$, $p<0,001$ and $r=0,211$, $p<0,01$, accordingly). *Conclusion.* The schizoid and dissocial type of the child's temperament can be accompanied by the obstructive violation of the function of external breathing. Conformism and stress states are accompanied by the restrictive violation of the external breathing.

UNDERGROUND WORKING ENVIRONMENT PROVOKES LUNG DISEASES DEVELOPMENT

Rybina T., Amelchenko E., Omelyanenko-Gonulal O.

Clinical Laboratory of Occupational Diseases, Republican Scientific and Practical Center of Hygiene, Minsk, Belarus, oxanamackiewicz@yahoo.com

Background: Morbidity with temporary disability is the main parameter, characterizing health status of workers with occupational aerosol exposure. Unhealthy and dangerous working conditions, their long-term exposure upon workers promote risk factors of occupational lung diseases development. We analyzed morbidity with temporary disability (MTD) of the workers with lung diseases working in underground conditions within the period of 7 years. *Materials and methods:* Study included 2 groups: 1st group – workers with underground working environment (n=30383), 2nd group – workers without underground working conditions (n= 5536). Groups were divided into 5 age subgroups. Length of service of the workers with respiratory diseases was calculated on the basis of morbidity with temporary disability. *Results:* Upper respiratory tract infections developed in 1st group workers at mean age 36,1 years old and length of service in underground conditions - 11,6 years. Control group developed upper respiratory tract infections in older age - 39,6 years old ($p<0,05$). We didn't reveal statistical difference

in comparison of morbidity of workers with influenza and pneumonia. Mean age of the workers with temporary disability due to the upper respiratory tract diseases - 38,1 years old. Length of service in underground conditions – 13,7 years. 2nd group workers data demonstrated older age – 43,2 years old (t=3,09; p<0,05). *Conclusion***:** Medical prophylaxis measures should be provided first of all in workers with length of service in underground conditions 5-15 years.

THE INFLUENCE OF HYPERINFLATION ON BODY COMPOSITION AND CYTOKINE PROFILE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Rubinsztajn R. , Przybyłowski T., Maskey-Warzęchowska M., Paplińska-Goryca, Gryz P-N, Karwat K., Chazan R.

Department of Internal Medicine, Pneumonology and Allergology, Warsaw Medical University, Poland, przyb@amwaw.edu.pl

Body composition is an important prognostic factor in patients with COPD. The decrease in fat free mass **(**FFM), muscle mass (MM) and increase in visceral fat is associated with an elevated secretion of cytokines which promote systemic inflammation. The aim of the study was to evaluate body composition and the cytokine profile in patients with COPD in relation with the presence of hyperinflation. The study group consisted of 149 patients (61F, 88M) with stable COPD in all stages of severity aged 68±8.8 yrs with a mean FEV1 55.9±18.9 % predicted. All the patients underwent spirometry and bodypletysmography with bronchial reversibility testing. Hyperinflation was defined as RV%TLC > 48% and > 126% predicted. Body composition was analyzed by bioimpedance. The following serum inflammatory markers were evaluated: C-reactive protein, IL-6, IL-8, TNF alpha, CC16, adiponectin and resistin. Hyperinflation was found in 96 patients (group A) and it was more frequent in women than men (49/61 vs. 47/88, p<0.001). BMI and age in this group were comparable to those in patients without hyperinflation (group B). Table presents significant differences in body composition between both groups.

	Hyperinflation (+) group A	Hyperinflation (-) group B	P
Total body water (kg)	36.5±8.0	40.9±7.8	0.0006
Fat free mass (kg)	49.4±10.2	55.9±10.7	0.0003
Body fat (%)	32.5±7.9	28.8±8.1	0.008
Muscle mass (kg)	47.6±10.6	52.4±10.3	0.0005
Height (cm)	163.9±8.9	168.8±8.2	0.0007

We found significantly higher serum concentrations of inflammatory markers in group A: IL-6 – 6.4±10.9 vs. 3.6±4.2 pg/ml, p=0.004; resistin – 9.3±4.2 vs. 7.6 ±2.4 ng/ml, p=0.02, CRP 4.1±2.3 vs. 2.9±2.1 mg/l, p=0.04, respectively. Conclusions: (1) Although BMI in COPD patients with lung hyperinflation is not different when compared to non-hyperinflated patients, patients with hyperinflation have a lower FFM, TBW, MM and a higher proportion of fat tissue. (2) Hyperinflation is associated with systemic inflammation and could therefore be a negative prognostic factor in COPD patients

INHIBITION OF H_2S-SYNTHESING ENZYME CYSTATIONINE-GAMMA-LYASE PROTECTS HEART FROM REPERFUSION INJURY

Sagach V.F., Shimanskaya T.V., Goshovska Y.V.

Circulation Department, Bogomoletz Institute of Physiology, Kyiv, Ukraine, vsagach@biph.kiev.ua

Purpose: Hydrogen sulfide (H_2S) is an endogenously generated gaseous transmitter. It is produced in cardiovascular system from amino acid L-cysteine by cystathionine-gamma-lyase (CSE) enzyme. Recent studies demonstrate controversial results of exogenously applied H_2S donors. Among others H_2S exerts toxic effect at mitochondrial respiration and cardioprotective properties. Thus, mechanism of H_2S action is not fully understandable. The aim of the present study was to investigate the modulation of H_2S synthesis in heart ischemia-reperfusion model. *Methods*: Rat hearts of control group was perfused by Langendorf preparation and submitted to 20 min of non-flow ischemia followed by 40 min of reperfusion (I/R protocol). Second group of animals was pretreated with precursor of H_2S synthesis L-cysteine in dose of 121 mg per kg (intraperitoneal injection 30 min before I/R protocol). The third group was

treated with inhibitor of CSE DL-propargyl glycine (PAG) in dose of 11.3 mg per kg intraperitoneally 10 min before L-cysteine injection and underwent I/R protocol. Registration of left ventricular developed pressure (LVDP), end-diastolic pressure (EDP), dP/dt and coronary flow was performed. Oxygen cost of myocardial work (OCMW) was expressed as the ratio of the oxygen consumption and the heart work (the product of the LVDP and the heart rate). *Results*: L-cysteine protected hears from reperfusion injury improving cardiodynamic parameters restoration after ischemia. At the 10^{th} min of reperfusion LVDP averaged 52% comparing to 42% in control. L-cysteine prevented appearance of postischemic contraction and dramatic coronary flow reduction in early period of reperfusion: EDP averaged 34 mmHg comparing to 43 mmHg in control. This protective action of L-cysteine was not attenuated by the CSE inhibitor PAG. In third group recovering of cardiac contractile activity was even greater then in second group. At the 10^{th} min of reperfusion LVDP averaged 105% and EDP averaged 3 mmHg comparing to 43 mmHg in control group. Other parameters showed the same pattern of recovery including OCMW which at 10^{th} min of reperfusion averaged 216% in second group and 134% in third group comparing to 239% in control group. These data indicate more effective oxygen utilization by ischemic myocardium under L-cysteine and PAG pretreatment. *Conclusion*: Our data demonstrate that L-cysteine improves heart contractile activity recovery after prolonged ischemia. L-cysteine in combination with PAG protects hearts from ischemia-reperfusion injury and prevents non-effective oxygen utilization by ischemic myocardium.

PROTEASOME ACTIVITY CHANGES AFTER FOCAL ISCHEMIA

Savchuk O.I., Goncharov S.V., Dosenko V.E., Skibo G.G.

Bogomoletz Institute of Physiology, Kiev, Ukraine, floweringbowl@ukr.net

Stroke is the third leading cause of mortality and a major cause of functional disability among the older people worldwide. The aim of our study was to investigate proteasomal activity in rats with focal cerebral ischemia in the locus of damage and in risk zone. *Materials and methods*. Experiments were performed on 42 adult male Wistar rats, weighing 280-320 g, animals were divided in 6 groups – №1 control (sham operated, 7 rats) and №2 experimental (7 rats) with 6 hours of reperfusion, №3 control (7 rats) and №4 experimental (7 rats) with 24 hours of reperfusion, №5 control (7 rats) and №6 experimental (7 rats) with 72 hours of reperfusion. Ischemic Stroke was modeled by transient occlusion of the middle cerebral artery according to the method of Koizumi J., et al. (1986), which lasted 60 minutes. Evaluation of ischemic damage was performed 6, 24 and 72 hours after restoration of blood flow. To confirm the specificity of proteasomal hydrolysis we added to the samples selective inhibitors of the proteasome -laktatcystyn-beta-lactone or Mg-132 at a concentration of 5 mM. *Results*. Three types of proteasomal proteolytic activity were measured in brain tissue: chemotrypsin-like (CTL), trypsin-like (TL) and peptidylglutamyl peptide-hydrolase (PGPH). Shifts in proteasomal activity in the result of ischemia were found ambiguous. The TL activity of proteasome in ischemic brain regions decreased by 2 times compared with controls ($P = 0.045$) in groups №2, 6, but increased by 11 times compared with controls ($P>0.05$) in group №4, but increased by 6 times in group №3. CTL activity decreased by 1.2 times compared to the control ($P = 0.037$) in groups № 2, 6, but increased by 2 times compared with controls ($P>0.05$) in group №4. PGPH activity decreased by 3 times compared to the control ($P = 0.037$) in groups № 2, 4, this type of activity was not significantly changed with either the control or with the risk zone in groups №1, 3, 5, 6. *Conclusions*. Proteasomal proteolysis is significantly reduced in a result of focal brain ischemia during the first 6 hr of reperfusion with subsequent increase observed starting from 24 hr.

FEATURES OF THE KIDNEY INFLAMMATION AND THE LEVEL OF ENDOGENOUS INTOXICATION IN ACUTE LUNGS INGURY IN EXPERIMENT

Sas P.A.

Ternopil state medical university named after I. Ya. Horbachevskiy, Ternopil, Ukraine, sas_lesia@mail.ru

Purpose – to determine features of the kidney inflammation progression during acute lungs injury (ALI). Simulated acute lung injury experiments were performed on white rats by introducing to the trachea HCl, pH 1,2 at a dose of 1.0 ml·kg-1 at inhalation. Animals of the experimental group withdrew from the

experiment at 2, 6, 12 and 24 hours. In kidney tissues there was determined the content of TBA-active lipid peroxidation processes products, in serum – endogenous intoxication level using data on middle molecular weight of different fractions (MMW 254-280). Studies have shown that the lipid free radical oxidation is significantly intensified, what is evidenced by a significant increase in TBA-active products of lipid peroxidation, which was increased at 1.79 times ($p<0.001$) in 6 hours. After 12 h, these figures declined by 12.6% ($p<0,05$), but did not reach the control level. After 24 h they exceeded the level of control by 76.7% ($p<0,001$). Content of MMW also increased up to 6 hours of observation, somewhat decreased to 12 hours, and increased again to 24 hours. Thus, during ALI the inflammation is significantly increased in the kidneys. The content MMW varies in proportion to it and shows derangement of secretary function. Reducing the content of these indexes to 12 h indicates obviously the development of adaptive-compensatory processes in the body. However, after 24 h the depletion occurs.

INSPIRATORY MUSCLE RESISTANCE TO FATIGUE DURING SIMULATED AIRWAY OBSTRUCTION

Segizbaeva M.O., Aleksandrova N.P.

I.P.Pavlov Institute of Physiology, RAS, St. Petersburg, Russia, marina@infran.ru

Respiratory muscle fatigue can develop during simulated airway obstruction. The aim of this study was to characterize the pattern of inspiratory muscle fatigue and to assess the resistance to fatigue of diaphragm (D), parasternal (PS), sternocleidomastoid (SM) and scalene (SC). 6 healthy untrained subjects participated in this study. To identify signs of inspiratory muscles fatigue development electromyographic activity of D, PS, SCM and SC was recorded during 5-min exercise with loaded breathing ($40\ cm\ H_2O \cdot s \cdot l^{-1}$) . The before-to-after exercise measurements of maximal inspiratory pressure (MIP) and EMG power spectrum changes were performed. Maximal inspiratory pressure declined about 12 % after exercise test compared with control, whereas the peak magnitude of integrated electrical activity of D, PS, SCM and SC during post-exercise Muller's maneuver was significantly greater than in pre-exercise test in all subjects. The extent of inspiratory muscles fatigue was evaluated by analysis of shift in centroid frequency (f_c) of EMG power spectrum. All subjects demonstrated a significant reduction in f_c of PS, SCM and SC. Frequency f_c of D was not changed. Diaphragm is more resistant to fatigue during obstructive breathing compared with PS, SCM and SC. The data suggest that the reduction of maximum inspiratory pressure in chronic obstructive pulmonary disease also caused primarily by the weakening of the accessory muscles, while the weakness of the diaphragm may occur in the later stages of the disease. The functional failure of accessory muscles is an additional factor, which, along with the additional breathing resistance increases the load on the diaphragm, promoting its fatigue and reduced respiratory reserve.

TUBERCULOSIS IN MEDICAL WORKERS

Semashko O.B.,Tsygankova O.A.,Pankratova Yu.Yu.,Germenchuk I.A..

Belorussian State Medical University, Minsk, Belarus, olga.semashko.83@mail.ru

According to the Belorussian Center of Medical Technologies, Computer Systems, Administration and Management of Health (BelCMT), the respiratory tuberculosis (RT) in healthcare providers takes up third place yearly in Republic of Belarus. During last 10 years 152 professional patients were revealed among medical workers. 125 of them (82%) have respiratory tuberculosis. They were occupied in TB dispensary and deal with patients, suffered from tuberculosis, which also include persons discharging bacteria, or contaminated substance. Respiratory tuberculosis (RT) was frequently diagnosed in hospital aide – 42%, nurses – 35%. Doctors morbidity was about 17% and medical technologists ones – 6%. We studied features of RT development (according to medical documentation) in 32 patients. Selection was made using casual selection method. In all cases overload at work was associated with unfavorable accommodation facilities: one-room apartment with other family members, a hostel room with 6-8 people or a communicating room. Short length of service before RT was diagnosed attracts attention: 25 people (78%) felt ill in the range from half a year till 4 years of work, 9 (28%) of them -in the range of half a year till one and half a year. The occupational disease was established in most cases in 1-2 years after

the treatment onset (90,6%), and in 9,4% of cases in 6 and more years. Some patients were not inspected by Medical Rehabilitation Expert Board(MREB), since after treatment they came back to former work. Percent of disability were established in cases of disease reccurrence.The II-III group of disability and 60-80% of disability were established when an infiltrative form of tuberculosis with a disintegration and BK+ phase, a resection of part of a lung took place. Thus, it is necessary to employ injured medics in due time and to direct them on MREB for drawing up PRP (Patients Rehabilitation Program) and activity restriction extent definition.

LESSONS FROM TWENTY YEARS' INVESTIGATION OF INTERMITTENT HYPOXIA: PRINCIPLES AND PRACTICES

Serebrovskaya T.V.

Bogomoletz Institute of Physiology NASU, Kiev, Ukraine, sereb@biph.kiev.ua

Widespread use of the intermittent hypoxic training/treatment (IHT) methods in sports, military and medical practice during recent decades has provoked a discussion: "What is 'intermittent hypoxia'? Does it play pathogenic roles in disease states, such as sleep-disordered breathing, chronic pulmonary disease, cardiovascular disease, and cancer? Or, quite to the contrary, does exposure to intermittent hypoxia induce protective responses?" (Semenza, 2011). In contrast to studies from the former Soviet Union countries that emphasized mainly the beneficial effects of IHT on an organism, intermittent hypoxia research in Western Europe and North America was primarily focused on the detrimental effects associated with sleep apnea. However, during the past decade, such a gap of division between East and West is progressively shrinking, and mutual understanding on what "intermittent hypoxia" means, becomes clearer. Potential mechanisms underlying both beneficial and adverse effects of IHT have been described. Basic investigations led to the proliferation of various methods of IHT exposure, the development of different medical equipments – hypoxicators – for its implementation in sport practice, military operations and also for clinical application. However, wide array of different protocols and measurements makes the results difficult to harmonize. The questions that arise are, what are the key mechanisms determining the adaptive versus maladaptive nature of different paradigms of intermittent hypoxia, and, what molecular pathways are mediating the observed pathological or physiological response (Prabhakar, 2012)? Until now there is no exact evidence about the precise mechanism for switching adaptive or maladaptive responses to hypoxic impact. Besides, there is no exact answer on the practical question of what dose and regimen of hypoxic impact could be mostly beneficial for animals and humans. Wide spectrum of protocols for IHT is represented now in literature showing both effects. Meanwhile, the mode of hypoxic influence (depth, duration, and intermittence) appeared to be critical for the determination of healing or harmful result. Therefore, special purposeful investigations are needed to elucidate basic mechanisms of different IHT effects depending on the modality of hypoxic stimuli and elaborate most effective and safe regimen for the introduction in human practice.

MODERN TRENDS IN THE TREATMENT OF COPD, COMBINED WITH OSTEOARTHROSIS

Skiba T.A.

Lugansk state medical University, Ukraine

COPD is one of the most common human diseases, which, according to the WHO data, affects 0,8% of the population of the planet, mainly persons over the age of 40, with the excess of incidence rate among men (0,9%)than among women (0.7%). In recent years, the importance of such factors of COPD pathogeneses, as hypoxemia and hypercapnia, increases and leads to limitation of physical activity, increasing of body mass index as unfavorable prognostic factor for life, and in the future – to development of systemic effects of disease, such as progressive cachexia, secondary anemia, systemic inflammation, systemic osteoporosis as a basis for the osteoarthrosis (OA) development. In patients older than 40 years the comorbidity of COPD and OA occurs quite often. In turn, OA is a common pathology, especially in people of middle and elderly age, which significantly reduces the quality of life of the patients, thus makes its important medico-social value. The degree of severity, functional changes and progression

of disease in patients with COPD and OA are at least partly connected with level of chronic inflammation. The coexistence of COPD, which is accompanied by a systemic inflammation, with OA, in the progression of which the influence of the mediators of inflammation was also revealed, requires careful consideration to search for ways of rational treatment of COPD and OA combination. At the present time the physical rehabilitation has a significant role in the treatment of COPD; it should increase the tolerance of the patient for physical loads, slow down the fall of the respiratory volumes and improve the social adaptation of the patient. Accompanying of OA with COPD, especially with the defeat of the large joints and pain syndrome, can significantly limit the recovery capability of the patient and degrade the quality of his life. That is why the determination of ways of pharmacological correction of the revealed pathogenic factors and directions of medical rehabilitation of patients with a combination of COPD and OA has a considerable practical importance.

APPLICATION OF INTERMITTENT HYPOXIC TRAINING FOR THE AMELIORATION OF BALNEOTHERAPEUTIC COMPLEX SPA TRUSKAVETS EFFECTS ON IMMUNE SYSTEM

Starodub A.G., Barylyak L.G., Popovych I.L.

Bogomolets Institute of Physiology, Kyiv, Ukraine, i.popovych@ukr.net

Children with chronic pyelonephritis and concomitant chronic bronchitis being at balneotherapeutic complex spa Truskavets were subjected to additional IHT course using the apparatus Hypoxytron- Simplex (Kiev). Such treatment prevented in some cases the reduction of Stange test and the concomitant reduction of CD8-T cells, caused the increase in blood serum immunoglobulins G, A, M content and serum and saliva lysozyme content with normalizing of circulating immune complexes. IHT also potentiated the stimulatory effect of balneotherapy on the activity, the intensity and completeness of phagocytosis by neutrophils in blood culture Staph. aureus. IHT did not significantly affect other parameters of immunity.

HYDROGEN SULFIDE AS ENDOGENOUS MODULATOR OF CA^{2+}-SENSITIVE MITOCHONDRIAL PERMEABILITY TRANSITION PORE IN ADULT AND OLD RAT HEART

Strutynska N.A., Semenykhina O.M., Kotsuruba A.V., Dobrovolsky F.V., Sagach V.F.

Bogomoletz Institute of Physiology, Kyiv, Ukraine , natalystrutynska@inbox.ru

Introduction. Hydrogen sulfide (H_2S) is an endogenous gaseous mediator, produced by de novo synthesis in mammalian tissues during cysteine metabolism. It is known three H_2S synthesized enzymes – cystathionine β-synthase (CBS), cystathionine γ-lyase (CSE) and 3-mercaptopyruvate sulfurtransferase (MPST). H_2S and NO are key regulators of several cell processes and organ functions under both normal and pathological conditions. Mitochondrial permeability transition pore (mPTP) opening causes mitochondrial membrane potential collapse that leads to mitochondrial dysfunction and apoptosis in aging heart. The role of H_2S in mitochondrial function regulation is now receiving increasing attention. The present study aims to clarify the mechanisms underlying the cardioprotective effects of H_2S in aging rats. *Methods***.** In the isolated from the adult and old rat hearts mitochondria, we studied the intramitochondrial H_2S pools simultaneously with production of ROS ($*O_2^-$ and *OH-radicals generation, H_2O_2, uric acid, MDA and DK pools) production of RNS (activity of cNOS and iNOS, NO_2^-, GSNO and protein nitrosothiol pools) and arginase II activity. In experiments *in vivo* and *in vitro* we studied the effects of both H_2S donor (NaHS) and precursor of de novo synthesis (L-cysteine) on the sensitivity of isolated from the adult and old rat hearts mitochondria mPTP opening to its natural inductor, Ca^{2+} by mitochondria swelling. *Results***.** For production of H_2S in physiological concentrations we used donor H_2S - NaHS in concentration 10^{-6} - 10^{-5} mol/l. NaHS used in these concentrations exerted the inhibiting effect on the Ca^{2+}-induced mPTP opening in adult hearts (corresponding values of such effect were 31 and 77%, respectively), while in old hearts the protector effect of NaHS was observed only at its concentration of 10^{-5} mol/l. A specific inhibitor of K_{ATP}-channels, 5-hydroxydecanoate (5-HD; 10^{-4} mol/l) decreased the both Ca^{2+}- independent and Ca^{2+}-induced mitochondrial swelling in the presence of NaHS (10^{-10} and 10^{-5} mol/l), indicating the contribution of these channels to the H_2S-dependent inhibition of mPTP transition in both adult and old rat hearts mitochondria. In experiments *in vivo*, single intraperitoneal injections of

NaHS (10^{-4} mol/kg) or L-cysteine (10^{-3} mol/kg) resulted in a decrease in the sensitivity of mPTP of its Ca^{2+} induced opening in both adult and old rat hearts. In experiments *in vivo* propargylglycine (10^{-4} mol/kg), specific blocker of H_2S de novo synthesis by cystathionine-γ-lyase, increase the sensitivity of Ca^{2+} induced mPTP opening in old hearts. The results showed that in heart mitochondria isolated from the old rat H_2S pool was decreased to 47% of control value, as well as NO_2^- (31%) and GSNO (56%) pools and cNOS activity (51%). In contrast, iNOS activity was increaset to 168% of control value, as well as ROS generation ($*O_2^-$ – 308%, *OH – 288%) and pools of H_2O_2 (197%), uric acid (1042%), MDA (284%), DK (1059%) and protein nitrosothiol (697%). *Conclusion*. We demonstrated that endogenous H_2S may be include in the control of the Ca^{2+}-induced mPTP opening in heart mitochondria isolated from the adult and old rat. Concentration of H_2S in mitochondria of old rat hearts was dramatically decreased thereby resulted in increasing of sensitivity of mPTP to Ca^{2+}. Thease changes were accompanied by oxidative (ROS) and nitrosative (RNS) stress activation. Thus, endogenous H_2S may exerted the protective effect on the Ca^{2+}-induced mPTP opening by incresing Ca^{2+}-dependent constitutive NO de novo synthesis by cNOS and by inhibition of ROS and RNS formation .

ANTITOXIC EFFECT OF ADAPTATION TO HYPOXIA AND HYPEROXIA: REDOX SIGNALING AND PHYSICAL ENDURANCE IN THE MODEL OF LOW DOSE INTOXICATION BY CHROMIUM AND BENZENE

Stryapko N.V., Sazontova T.G., Hajrullina A.A., Vdovina I.B., Kulikov A.N., Arkhipenko Yu.V.

Faculty of Medicine, M.V. Lomonosov Moscow State University, arkhipenko@fbm.msu.ru

The aim of this study was to evaluate the possibility of non-medicamentous prevention of toxicant-induced damage. We used the rat model of intoxication by potassium bichromate and benzene developed on the basis of data obtained with employees exposed to low doses of toxicants or inhabitants from environmentally neglected zones. New model of the adaptation to hypoxia and hyperoxia is capable of antioxidant system and energy metabolism activation. We investigated the effect of chronic intoxication with a mixture of benzene and potassium bichromate on physical endurance, behavior parameters, the intensity of oxidation processes, the activity of antioxidant enzymes, level of heat shock proteins (HSPs) and hypoxia induced factor (HIF-1α) on male Wistar rats. It was found that preliminary adaptation to hypoxia and hyperoxia (alternately by 3-5 min, in total 1 hour daily during 7 days) can prevent disorders caused by intoxication: decrease of physical endurance, animal weight reduction, increased oxidative stress and concentration of transcription factor HIF-1α and HSPs. Conclusion: preliminary respiration with hypoxia and hyperoxia can be used as preventive method of toxic damage.

DETERMINATION OF ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH AND WITHOUT DIABETES MELLITUS TYPE II BY THE CONTENT OF ENDOTHELIAL CELLS IN BLOOD

Stupnitska G.Ya., Fediv O.I.

Bukovinian State Medical University, Chernivtsi, Ukraine, dumanna77@mail.ru

In recent years, chronic obstructive pulmonary disease (COPD) is regarded as systemic inflammation with the presence of comorbidities that significantly affects the course of the underlying disease. We studied the role of the functional state of endothelium in systemic effects of COPD with the presence of comorbidities, in particular cardiovascular diseases and diabetes mellitus type II (DM II). *The aim* of the work: to estimate the content of blood circulating endothelial cells as an indicator of endothelial dysfunction in COPD patients with and without concomitant DM II. *Materials and methods*. The study involved 20 patients with COPD, combined with DM II, and 25 COPD patients without concomitant diabetes. The control group consisted of 20 healthy individuals. Number of circulating endothelial cells was determined by the method of Hladovec J., that assumes the isolation of endothelial cells with platelets with subsequent deposition of platelet adenothindiphosphate. *Results*. In the group of patients with COPD combined with type II DM, the content of circulating endothelial cells in blood was higher ($12,5 \pm 2,1 \times 10^4$/l) than in patients without concomitant diabetes ($6,0 \pm 0,9 \times 10^4$/l, $p < 0.05$) and healthy individuals ($3,5 \pm 0,9 \times 10^4$/l, $p < 0.05$). *Conclusion*. Thus, higher level of endothelial cells desquamation in blood indicated the presence of endothelial dysfunction, particularly with concomitant DM type II.

CLINICAL COURSE AND TREATMENT OF BRONCHIAL ASTHMA IN THE ELDERLY

Svintsitskyy A.S.
Bogomolets National Medical University, Kyiv, Ukraine, sasnmu@mail.ru

Bronchial asthma is a common disease in the elderly. According to epidemiological data, the prevalence of asthma in elderly patients (EP) is about 5 to 15%. In this study we examined 186 patients with bronchial asthma aged over 60 years. Allergens from focal infections (chronic bronchitis, pneumonia) played leading role in hyperresponsiveness formation and asthma development in EP. Genetic predisposition was less common, EP mainly had infectious-allergic form of asthma due to inflammatory lung diseases. The most important features of asthma clinical course in EP were comorbidity, nonspecific manifestations of the disease, age-related changes in respiratory organs, depletion of adaptive mechanisms, rapid deterioration at late start of treatment, frequent development of complications caused both by the disease and treatment.
Based on our observations and literature data, principles of asthma treatment in EP are:

- immunotherapy in most EP is not used;
- to prescribe drugs with optimal effect and the lowest probability of adverse events;
- to give priority to inhalation of anti-inflammatory drugs and bronchodilatators;
- to select the optimal inhaler (without reference to the asthma clinical course severity) accordingly to lung function ventilation parameters;
- to optimize methods of drugs administration (basic therapy includes use of inhalers, spacers; nebulizers are used at exacerbation of disease);
- to follow the rules of possible complications prevention (oral hygiene, etc.);
- to educate patients to implement the treatment recommendations;
- to treat comorbidities, exclude drugs that can affect the course of asthma.

THE CHILDREN'S INCIDENCE OF ASTHMA IN GRODNO ACCORDING TO A LONG-TERM MONITORING

Tomchyk N.V.
State Medical Universit, Grodno, Belarus, natallianv@tut.by

According to epidemiological studies the incidence of bronchial asthma among children is 5-10%, but, according to statistical reports, this index is much lower. The purpose of the work is to assess the dynamics of asthma incidence in Grodno in 2000 to 2012. General and primary asthma incidence was studied among children in Grodno at the age of 0-17 years in 2000 to 2012 according to the statistics. It has been found the reduction in overall asthma incidence from 10,1 in 2000 to 6,1 in 2012 per 1000 children ($p < 0,001$) in the background of chronic allergic respiratory diseases during the same period. It is noted the decline of the indicator of primary incidence from 1,6 in 2000 to 0,5 in 2012 per 1000 children ($p < 0,005$). It has been found an increase in the overall asthma incidence of children aged 15-17 from 12,1 in 2000 to 37,1 in 2012 per 1000 children, $p < 0,001$. In addition, this group of children marked the increase in the number of boys suffering from asthma from 14,2 in 2000 to 49,4 in 2012 per 1000 children, $p < 0,001$. Conclusions: It was established the decrease in general and primary asthma incidence in children in the city of Grodno. The older the child, the higher the frequency of this pathology is observed. Among teenagers bronchial asthma is more often found in boys.

RAT RESPIRATORY FUNCTION AFTER HYPEROXIC GAS MIXTURE IMPACT

Yanko R.V., Chaka E.G., Litovka I.G. and Levashov M.I.
Bogomoletz Institute of Physiology, Kiev, Ukraine, biolag@ukr.net

Hyperoxic gas mixture (HGM) is widely used in the clinic for the treatment of diseases. However, it is known that with increasing levels of partial pressure of oxygen and duration of its effects may develop various pathological processes. Our purpose is to examine the changes of morphological and biochemical indicators of lung respiratory section of adult rats after exposure to HGM. The investigation of HGM (40% oxygen) influence was performed within 1 hour during 14 days to 24 male Wistar rats age of 12 months. Histological preparations from the lung tissue were made by the standard method. The concentra-

tion of total oxyproline was determined photometrically. In rats exposed to HGM, there is occurred the tendency to reduce the area of transversal cut to alveolus (7%). The average width and depth to alveolus remained at the control level. Width of the entrance to the alveolus and the total width of respiratory bronchioles, alveolar ducts and sacs in the experimental group of animals significantly increased by 21 and 25% accordingly. So there is an increase of respiratory bronchioles airiness and alveolar ducts, but decrease of alveolar surface area and alveolus airiness, after the exposure to HGM. Experimental rats revealed a significant increase in the number of collagen fibers, interalveolar septum thickness (41%) and the concentration of total oxyproline (29%) in the lungs. Therefore, breathing the gas mixture of 40% oxygen reduces the total alveolar surface area, increases the mass of connective tissue in lungs which leads to the reduction of gas exchange rate and ventilation in adult rats.

CHOLESTEROL LEVEL AS A MARKER OF COMMUNITY-ACQUIRED PNEUMONIA (CAP) SEVERITY

Yatsevich O. N[1]., Alekseychik D. S.[2]

[1]Department of Internal Diseases N 1 Belorussian State Medical University, Minsk, o-n-y@yandex.ru; [2]Central distrik polyclinic № 3, Minsk

Background: The knowledge regarding lipid biomarkers in CAP still remains limited. *The aim:* We investigated the level of cholesterol in immunocompromised CAP patients. *Methods:* 365 hospitalized CAP patients were retrospectively enrolled to the study and assigned to one of the two groups. The 1st group included 140 patients under 45 years of age with moderate and severe CAP (mean age: 32±8; 82% severe CAP and 18% moderate CAP). The 2nd group - 225 patients over 45 years of age with moderate and severe CAP (mean age: 63±1; 90% severe CAP and 10% moderate CAP). *Results:* Cholesterol level in patients with severe pneumonia appeared to be lower than those in patients with moderate pneumonia (3.8±1.0 mmol/L in patients under 45 years old and 4.3±0.9 mmol/L in patients over 45 years old) vs (4.7±0.8 mmol/L and 5.09±1.0 mmol/L respectively). We found the different cholesterol levels in patient with moderate and severe CAP. The hypo-and normocholesterolemia in patients of the 1st group was detected in 73% of those with moderate CAP and in 92 % with severe CAP, in patients of the 2nd group – in 56.6% and 86% respectively ($p<0.05$). We analyzed 22 medical records of the deceased patients. Cholesterol level was considerably decreased in non-survivors - 2.3±0.5 mmol/L ($p<0.05$). Probably this could be related to the increased cholesterol use for the leukocytes membrane building. *Conclusions:* Cholesterol level was significantly decreased in patients over 45 years old versus patients under 45 years old with the similar CAP severity. Cholesterol value was significantly lower in severe CAP patients in comparison with the moderate CAP patients. Thus, cholesterol level could be a simple marker of CAP severity.

OCCUPATIONAL TUBERCULOSIS (TB) AS THE DISEASE OF MEDICAL PERSONALS

Zienkow L.N., Aleksa E.N.

Grodno State Medical University, Grodno, Belarus, alex_helen2001@mail.ru

Background. Pulmonary TB takes a leading place among all occupational diseases of medical staff in the Grodno region of Belarus. 32 patients with TB are registered in the regional center of Pathology. This is 85% of the total number of occupational diseases in medical staff. *The aim* of study was the analysis of the incidence of occupational TB cases. *Material and Methods.* All the 30 observed patients were women, age varied from 25 till 35 years (in 70% of cases) as well as the length of work varied from 6 till 15 years. There were 15 nurses, 13 physicians, 2 laboratory assistants and 2 nurses among these patients. 30 patients worked in TB hospitals and only 2 persons were from other hospitals. *Results.* Focal pulmonary TB was established in most of the patients (86%). Surgical treatment was performed in four patients. The disability group was established in 8 patients. Two patients died from pulmonary TB. It should be noticed that 3-4 of new cases of TB were diagnosed annually in the Grodno region. The exogenous and endogenous risk factors of occupational TB were: a high virulence and drug resistance of mycobacteria TB, unfavorable work conditions with high level of chronic psychoemotional or physical stress, nonphysiological conditions (night duties, uncomfortable psychological climate) and other factors. *Conclusions.* The important measures for

the prevention of occupational TB among medical personals are the following: regular periodic medical examinations, following the strict measures of infectious control and improvement of work conditions.

THE IN VIVO AND IN VITRO BLOOD OXYGEN-BINDING PROPERTIES MODIFICATION BY DIFFERENT NITRIC OXIDE DONORS

Zinchuk V.V., Stepuro T.L., Khodosovsky M.N.
Grodno Medical State University, Grodno, Belarus

It is known, that the donors of nitric oxide (NO) – sodium nitroprusside (SNP), nitroglycerine (NG), can protect liver against ischemia/reperfusion injury decreasing lipid peroxidation, improving antioxidant status and transaminase activity. Including the role of NO in the hemoglobin oxygen affinity regulation we aimed to investigate in vivo and in vitro the possibilities of modification of blood oxygen-binding properties by different NO donors. Infusion of SNP (2, 5 mg/kg) or NG (1, 5 microg/kg) was performed in rabbit hepatic ischemia(30min)/reperfusion(120min) model in vivo. The in vitro experiments were performed with rabbit venous blood, which was incubated during 30 or 60 min with different NO donors: SNP, NG, molsidomine (Mls), S-nitroso cysteine (CysSNO), S-nitroso-N-acetylpenicillamine (SNAP), S-nitrosoalbumin (AlbSNO). Indices of blood oxygen transport ($p50_{act}$, $p50_{stand}$, pCO_2, pH, etc.) were measured. There is determined, that NG infusion in vivo experiments leads to decrease of hepatic venous blood $p50_{act}$ on 5 mmHg ($p<0,05$) at the end of reperfusion concerning rabbits without NG. SNP administration for animals reduces $p50_{stand}$ in the blood on 4,5 mm Hg ($p<0,05$) on the 120 min of reperfusion. The in vitro investigation has shown, that none of the NO donors changed the $p50_{act}$, but $p50_{stand}$ was reduced by CysSNO and SNAP on 2,8 ($p<0,05$) and 3,3 ($p<0,05$) mm Hg, respectively. Thus modification of blood oxygen-binding properties depends of NO donor's structure, metabolism, peroxynitrite formation and environment of experiment.

TOLERANCE TO HYPOXIA

Zubieta-Calleja, GR, Ardaya G, Zubieta N, Paulev PE and Zubieta-Castillo, G.
High Altitude Pulmonary and Pathology Institute IPPA, La Paz, Bolivia. zubieta@altitudeclinic.com

People living at sea level have poor tolerance to hypoxia. In striking contrast, humans experiencing hypoxia at high altitude live very well. How is it possible for man to tolerate extreme hypoxia at high altitude? In this article we propose a hypothesis that potentially explains the tolerance to hypoxia at high altitude. Close examination of values of hemoglobin and PaCO2 for an altitude of 3510 m demonstrate that an increase in hemoglobin (Hb) and a decrease in arterial carbon dioxide tension (PaCO2) are two essential changes that occur on high altitude exposure. We propose a formula:

$$Tolerance\ to\ Hypoxia = \frac{Hb}{PaCO2} \times 3.01$$

We present evidence that the relationship between Hb and PaCO2 explains the tolerance to hypoxia at high altitude. (Presented in part at the Leh Symposium and the Global Hypoxia Summit in New Dehli India Aug3-9, 2012).