Pneumonol. Alergol. Pol. 2006, 74, 1-1

DEFINITION OF AIRWAY OBSTRUCTION[1]

Piotr Boros MD PhD
Lung Function Lab,
National TB & Lung Diseases Research Institute,
Warsaw, Poland

An obstructive ventilatory defect is defined as the disproportional reduction of maximal airflow from the lung in relation to the maximal volume (i.e. VC) that can be displaced from the lungs. It implies airway narrowing during exhalation and is expressed by a reduced FEV1/VC ratio. The lower limit of normal (LNN) should be based on the healthy population study, and for adults is usually set at the 5th percentile level of the predicted value.

In the purpose of achieving the best diagnostic value (highest sensitivity) the measurement of slow VC (inspiratory or expiratory) instead of FVC should be used for a more correct estimate of the FEV1/VC ratio.

The earliest change associated with airflow obstruction in small airways is thought to be a slowing in the terminal portion of the spirogram, even when the initial part of the spirogram is barely affected. This slowing of expiratory flow is most obviously reflected in a concave shape on the flow-volume curve. Quantitatively, it is reflected in a proportionally greater reduction in the instantaneous flow measured after 75% of the FVC has been exhaled (FEF75%) or in mean expiratory flow between 25% and 75% of FVC than in FEV1. However, abnormalities in these mid-range flow measurements during a forced exhalation are not specific for small airway disease in individual patients. As airway disease becomes more advanced and/or more central airways become involved, timed segments of the spirogram such as the FEV1 will, in general, be reduced out of proportion to the reduction in VC.

Apart from this unusual circumstance, measurement of lung volumes is not mandatory to identify an obstructive defect. It may, however, help to disclose underlying disease and its functional consequences. For example, an increase in TLC, RV or the RV/TLC ratio above the upper limits of natural variability may suggest the presence of emphysema, bronchial asthma or other obstructive diseases, as well as the degree of lung hyperinflation.

Airflow resistance is rarely used to identify airflow obstruction in clinical practice. It is more sensitive for detecting narrowing of extrathoracic or large central intrathoracic airways than of more peripheral intrathoracic airways. It may be useful in patients who are unable to perform a maximal forced expiratory manoeuvre.

[1] Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R et al. Interpretative strategies for lung function tests. Eur.Respir.J. 2005;26:948-68.

EFFECTS OF HYPOXIA ON THE LUNG CELLS

J. Chorostowska-Wynimko
Laboratory of Molecular Diagnostic,
National Institute of Tuberculosis and Lung Diseases,
Warsaw, Poland

Physiological responses to the hypoxic conditions are complex and involve on the cellular level a range of mechanisms, some occurring within minutes of oxygen deprivation while others more protracted reset a cascade of biosynthetic and physiological programs within the cellular milieu of the lungs. The O2 sensitive events include activation of various transcriptional factors resulting in the highly coordinated changes in the expression/activation of an array of genes redirecting the metabolic and other cellular mechanisms to achieve enhanced cell survival together with functional adaptation to the hypoxic conditions. Added to this interplay is the possibility of genetic polymorphism and protein changes due to the environmental factors that as an effect causes the variability of individual responses to hypoxia. There are number of clinical conditions under which lung cells are exposed to much lower oxygen supply. However, different tissues in the lungs react differently according to their divergent structure and function. Two cell populations in the lung are considered the most prominent and functionally important for the adaptation to hypoxia – pulmonary endothelium and alveolar epithelium. Also, growing evidence suggests that hypoxic conditions may play a direct role in activating lung fibroblasts and therefore inducing pathological pulmonary tissue remodeling.

INTERMITTENT HYPOXIA: BENEFICIAL EFFECTS ON HUMAN RESPIRATION, WHITE BLOOD CELLS AND ANTIOXIDANT STATUS IN PATIENTS WITH BRONCHIAL ASTMA

S.V.Danilyuk[1], T.V. Serebrovskaya[2], G.I. Lysenko[1]
[1] *Ukrainian National Medical Academy of Postgraduate Education, Kiev, Ukraine*
[2] *Bogomoletz Institute of Physiology, Kiev 01024, Ukraine*

Intermittent hypoxia training (IHT) has a marked positive effect in lung pathology. The basic mechanisms underlying the beneficial effects of IHT were elaborated in Ukraine mainly in three areas: regulation of respiration, free radical production and mitochon-

drial respiration. Findings showed that IHT induces increased ventilatory sensitivity to hypoxia as well as other hypoxia-related physiological changes such as increased hematopoiesis, alveolar ventilation and lung diffusion capacity, and alterations in the autonomic nervous system.

In recent years more and more evidence appears that show the absolute necessity of reactive oxygen species (ROS) for the normal vital activity. A burst of oxygen free radicals generated during the initial periods of brief, repetitive hypoxia increases antioxidant activity. Due to IHT, the body's antioxidant defenses increase, cellular membranes become more stable, and improvement of O_2 transport in tissues is evident. Experimental studies suggest that hypoxic training leads to a rearrangement of mitochondrial energy metabolism with increase lipid utilization and a more efficient link between oxidation and phosphorylation as indicated by significantly improved $\Delta ADP/\Delta O$ rations and ADP phosphorylation. It was shown that IHT induces changes within mitochondria, involving NAD-dependent metabolism, which increases the efficiency of oxygen utilization in ATP production. These effects are mediated partly by NO-dependent reactions.

Decennial experience of IHT application to the treatment of bronchial asthma (BA) allows to affirm that human adaptation to IHT is accompanied by a significant increase in the oxygen transport system efficacy, physical working capacity, and the tolerance to episodes of severe hypoxia which occur during acute airflow obstruction. Evaluation of the effect of IHT produced by the method of increasing normobaric hypoxia (three daily 7-minute sessions for 15 days) was carried out in 115 patients with BA. The therapeutic diagnostic complex „Hypotron" (Ukraine), which allowed to determine the individual reactivity of the patient's respiratory system, tolerance to hypoxia, and to choose an optimal program of treatment, was used. Before IHT, regional ventilation heterogeneity and pulmonary circulation has been defined that was impaired with the increase of BA severity. T-immunodeficiency, disimmunoglobulinaemia as well as disturbances in ROS production and antioxidant status were observed. After the course of IHT, an increase in alveolar ventilation and oxygen consumption by 20-30%, two-fold augmentation of the hypoxic ventilatiry response (HVR) slope, the enhance of maximal lung ventilation by 80% and the tolerance to extreme hypoxia by 17-25% was found out. IHT caused the normalization of the number and phagocyting activity of white blood cells. It was shown an increase in neutrophils content from 50 to 65%, a decrease of lymphocytes amount from 39 to 29% and eosinophils percentage from 7 to 3 %. After IHT, a decrease in spontaneous and initiated by hydrogen peroxide blood serum chemiluminescence (by 33 and 41 % respectively) was registered accompanied by a decrease of malon dialdehyde and conjugated dienes concentration (by 31 and 35%, respectively). This effect was accompanied by an enhance of antioxidant enzymes activities in erythrocytes (catalase – by 60%, glutathione peroxidase and glutathione reductase activities – by 20 and 28%, respectively). After IHT, 70% of patients demonstrated a decreased effective drug dose, 15% of patients (mostly young persons) have recovered. Established mechanisms may be responsible for the positive therapeutic effects of IHT in patients with BA.

MODERN SPIROMETRIC EQUIPMENT IN THE PRIMARY CARE SETTING

A. Doboszyńska, J. Serafiński,
Department of the Clinical Nursing
Health Science Faculty, Medical Academy in Warsaw

All current guidelines of the respiratory diseases therapy refer to the results of spirometric tests as the base of disease diagnosis and beginning or modification of the treatment. Therefore, primary care physicians should be able to carry out these tests and properly interpret their results. Currently available spirometers are characterized by the high accuracy, reliability, and simplicity. Properly educated medical staff is able to obtain reliable, repeatable and technically correct results. The simplest device for the assessment of respiratory functioning is peakflowmeter. Regular PEF measurements at home by the patients with obstructive diseases enable to monitor the course of the disease and assess severity of its exacerbations. Spirometry enables more exact assessment of the larger number of parameters and bronchodilatation test. Some of the available devices enable to carry out provocative tests and airway resistance measurements as well as rhinomanometry.

However, one should remember to change measuring head with mouthpiece after each test to prevent infections. The examined patient should breathe into the sterile head-mouthpiece system. Portable spirometers should be equipped with the printer for the results, including flow-volume curve. Very important is a compatibility with computers, enabling data archivization and transmission of the tests results.

EFFECTS OF TRAINING IN NORMOXIA AND HYPOXIA ON MUSCLE TISSUE METABOLIC PARAMETERS AND MITOCHONDRIAL RESPIRATION

B.L.Gavenauskas, I.N. Mankovskaya,
V.I. Nosar., E.V. Rozova, A.I.Nazarenko
Bogomoletz Institute of Physiology, NASU, Kiev, Ukraine

A little is known about the effects of intermittent hypoxic training (IHT) on muscle structure and respira-

tion at endurance training (ET). The aim of this study was to compare muscle tissue adaptations induced by ET combined with IHT to those occurring with ET only at the same relative workload. The rats were divided into 4 groups, defined as follows: G_1-control; G2- ET: rats were swimming with a load which corresponded to 70-75% VO_2 max for 4 weeks with duration 30 min/day; G3- IHT: rats were breathing with hypoxic mixture containing 12 % O_2 for 15 min with 15-min rest intervals, 5 times daily; G4-ET+IHT: rats underwent the IHT sessions, as in G3, combined with exercise sessions, as in G2, for the last 2 weeks of ET. It was shown that muscle PO_2 (PmO_2) and capillary density maximally increased in G4. The testing intensive workload led to the lesser shifts in PmO_2, blood and muscle pH, and muscle metabolic parameters (lactate and pyruvate concentration, lactate/pyruvate and NAD/NADH ratios, succinate dehydrogenase activity) in G4 than in G2 and G3. ET+IHT induced a greater increase in the numerical density, the surface density, and size of muscle mitochondria compared to the similar effects of ET. Whereas ET without IHT stimulated preferential structural adaptation of the subsarcolemmal mitochondria, ET+IHT affect on both the subsarcolemmal and intermyofibrillar mitochondria and led to a mostly expressed increase in the values of mitochondrial respiration control and ADP/O ratio under α-ketoglutarate oxidation compared to those values under succinate oxidation. Combination of ET with IHT is found to be the most productive model for stimulating of mitochondrial biogenesis and increasing of the NADH-dependent oxidation pathway role in muscle energy production.

Airway Reactivity Assessment

P. Gutkowski
Lung Physiology Dept., The Children's Memorial Health Institute, Warsaw, Poland

Many patients with intrathoracic airway obstruction show spontaneous variability in the degree of obstruction. This is indicative of an increased susceptibility of the patient to environmental stimuli that cause acute airway narrowing.
Variable airway obstruction can be mimicked in the laboratory by challenge tests with bronchoconstrictive stimuli of various natures. This enables to measure the degree of the airway responsiveness of the subject to a particular agent.
Airway hyperresponsiveness refers to an exaggerated response to the bronchoconstrictor. This is reflected by an increased sensitivity to the stimulus, which is usually accompanied by an excessive severity of the induced obstructive response.
In the presentation are discussed, according to European Respiratory Society guidelines, the indications and contra-indications to the challenge tests, the safety requirements, the different laboratory protocols of non-specific tests and the modes of analysis and interpretation of the results.

Effects of Training in Normoxia and Hypoxia on Muscle Tissue Metabolic Parameters and Mitochondrial Respiration

B.L.Gavenauskas, I.N. Mankovskaya, V.I. Nosar., E.V. Rozova, A.I.Nazarenko
Bogomoletz Institute of Physiology, NASU, Kiev, Ukraine

A little is known about the effects of intermittent hypoxic training (IHT) on muscle structure and respiration at endurance training (ET). The aim of this study was to compare muscle tissue adaptations induced by ET combined with IHT to those occurring with ET only at the same relative workload. The rats were divided into 4 groups, defined as follows: G_1-control; G_2- ET: rats were swimming with a load which corresponded to 70-75% VO_2 max for 4 weeks with duration 30 min/day; G_3- IHT: rats were breathing with hypoxic mixture containing 12 % O_2 for 15 min with 15-min rest intervals, 5 times daily; G_4-ET+IHT: rats underwent the IHT sessions, as in G3, combined with exercise sessions, as in G_2, for the last 2 weeks of ET. It was shown that muscle PO_2 (P_mO_2) and capillary density maximally increased in G_4. The testing intensive workload led to the lesser shifts in PmO_2, blood and muscle pH, and muscle metabolic parameters (lactate and pyruvate concentration, lactate/pyruvate and NAD/NADH ratios, succinate dehydrogenase activity) in G_4 than in G_2 and G_3. ET+IHT induced a greater increase in the numerical density, the surface density, and size of muscle mitochondria compared to the similar effects of ET. Whereas ET without IHT stimulated preferential structural adaptation of the subsarcolemmal mitochondria, ET+IHT affect on both the subsarcolemmal and intermyofibrillar mitochondria and led to a mostly expressed increase in the values of mitochondrial respiration control and ADP/O ratio under α-ketoglutarate oxidation compared to those values under succinate oxidation. Combination of ET with IHT is found to be the most productive model for stimulating of mitochondrial biogenesis and increasing of the NADH-dependent oxidation pathway role in muscle energy production.

ADAPTATION ABILITY EFFECTS OF EXERCISE ADAPTATION ABILITY EFFECTS OF EXERCISE – AND HYPOXIC – TRAINING PROGRAM IN ELDERLY SUBJECTS

O.V. Korkushko, V.B. Shatilo, Yu. T. Yaroshenko, V.A. Ishchuk

Institute of Gerontology of the Academy of Medical Sciences of Ukraine, Kiev.

In 137 healthy, elderly subjects, aged from 60 to 74 years an exercise stress test (EST) – 10 min 100 W and hypoxic stress test (HST) – 10 min inhalation of 12% oxygen have been performed.

The decrease of tolerance to above was found in 62% and 61% of subjects, respectively.

In subjects with EST – intolerance significant fatigue manifestations in 5-10 min loading were found: increase of the arterial blood pressure (ABP) to 220/110 mmHg, high lactate content and reduced blood glucose level, utmost an increase of the sympathetic activity (LF/HF ratio) and a decrease of the blood plasma cortisol level was found.

In subjects with low tolerance to fall of SaO2 below 80% symptom like dizziness was present.

In 32 elderly subjects with low EST- tolerance the study was undertaken on the efficacy of three months training according the dynamic aerobic exercise training program (DAETP). The DAETP consisted of 4 to 6 training sessions weekly with a use of 30-min exercise at 90 % of individual anaerobic threshold (AT).

In other 20 elderly subjects with low ERS- and HST- tolerance the efficacy of a 3-week intermittent hypoxia training program (NHTP) was studied. The INHTP consisted of 10 to 15 training sessions daily, 25-min each. The session included four cycles of 5 min breathing 12-14 % O2 gas mixture and 5 min breathing atmospheric air (21 % O2).

The adaptation effect of dynamic aerobic exercise training program (DAETP) was demonstrated through:

- Increased of sub maximal exercise performance (VO_2max atmospheric level).
- Less increased systolic ABP and heart rate and sympathetic activity index (LF/HF ratio) at 10 min EST.
- Reduction of ABP, heart rate and minute ventilation at exercise of 25W or 50W.

The adaptation effect of intermittent hypoxia training program (INHTP) was demonstrated though:

- Increase of sub maximal exercise performance (VO_2 max atm. level)
- Reduction of ABP, heart rate and minute ventilation at exercise of 25W or 50W.
- Improvement of endothelial function in the reactive hyperemia test,
- Less significant decrease of SaO2 at 10-min HST,
- Fair tolerability after training course,

Conclusion: The authors concluded that properly selection of individual modes of dynamic aerobic exercise training program (DAETP) or intermittent hypoxia training program(INHTP) are safe for elderly subjects without severe diseases.

The result observed at both types of training leads to an increase of organism – tolerance to various stress stimulations in elderly aging people.

HYPOXIA AND ENDOTHELIAL FUNCTION IN AGING

O.V. Korkushko, V.Yu. Lishnevskaya, E.O. Asanov, A.V. Pisaruk, N.D. Chebotarev, G.V. Duzhak

Institute of Gerontology of the Academy of Medical Science, Kiev, Ukraine

In aging, the organism resistance to hypoxia is reduced due to morphological and functional changes. Of certain importance is the functional state of the endothelium through which a regulation of the vascular tone, including micro vessels, is accomplished. The endothelium is a site in which the vasodilatory and vasoconstrictor factors are synthesized under influence of various humoral and mechanic factors. It has been shown that endothelium injury results in the disturbance of a balance of the vascular tone regulators. Endothelial dysfunction leads to an increase of the vascular wall receptors sensitivity to vasoconstrictor influences.

Hence is our interest in studying a role of the endothelial dysfunction in reducing organism resistance to hypoxia in aging.

Study subjects and methods: The study involved essentially healthy people, between the ages of 20 and 70 years (16 persons in each decade).

The isocapnic normobaric hypoxia was induced via inhaling gaseous mixture with reduced oxygen content (12% O_2 i 88% N_2) during 10 min. The SpO_2, heart rate and arterial pressure were registered on the monitor YuM-300, YuTAS Firm (Ukraine).

For studying epithelial function, the volume blood flow rate was measured at base level and at the peak of reactive hyperemia, using laser flow meter (BLF 21D, Transonic S., Inc., USA) placed on the inner part of the arm. Reactive hyperemia was created by tightening shoulder vessels for 3 min by a tone meter, with the cuff pressure reading non-exceeding 50 mm Hg. Measured was also the maximal volume blood flow rate and the time interval for blood flow reversal to initial level. This test characterizes the epithelium capacity for endothelial relaxation factors synthesis and reflects the endothelium functional state (patent of Ukraine 46415).

Studies were carried out at the initial state and on 10 min of hypoxic mixture breathing.
Results: The present investigation shows that in aging there develop disturbances at a level of the microcirculatory vessel link. Indicative of this is the significant decrease of skin volume blood flow rate and the tissue perfusion state in micro vessels. With increased age, the pronouncement and the duration of reactive hyperemia at the breathing of both, the air and the hypoxic mixture, decrease. On the one hand, this indicates suppression of the release of endothelial vasodilators in response to the damaging factor (hypoxia) influence. On the other hand, this may be associated with vasoconstriction of peripheral vessels in elderly people under hypoxic action due to more pronounced sympathic-adrenal influences.
Conclusions:
1. In aging there develops a dysfunction of the epithelium at a level of the microcirculatory vascular link.
2. Hypoxia causes epithelium dysfunction, being more marked in aging.
3. The epithelial dysfunction, developing in elderly people due to hypoxic mixture breathing, leads to microcirculatory disturbances.

SPECIFIC ASPECTS OF SPIROMETRY SOFTWARE

V. Lopata, Sensor Systems Ltd., Kiev, Ukraine

The modern spirometrical study is impossible without automated processing of their results, up to the diagnostic conclusion. The most important element of such processing and the most intensive factor of the spirometer's improvement is spirometry software.
Specific of software, defined by specific of spirometrical study, have following aspects:
1. The microprocessor spirometers with unified meterological channels, has a different variants of the microprocessor technology using. In the first variant processing of information is realized by personal computer. In the second variant microprocessor controller with limited resource programmed to processing of most informative diagnostic tests. Such devices, equipped by LCD and thermal printer, are oriented on use in the largest network of the medical institutions and in „home medicine".
2. The methodical base of modern spirometry is study of forced expiration. Using of this method requires from patient active cooperation, and from software:
- correct estimation of the criteria of tests adequacy;
- selection of the best attempt from executed tests;
- exception of artifacts, appearing in process of the forced expiration.

3. In modern spirometry exists many systems of normatives, got by different researcher with using of the different equipment. This circumstance provides, sometimes, contradictions in diagnostic conclusions. The problem of software is objectivity of normative base and statistical processing of databases, actual for proved medicine.
4. Depending on purposes of the spirometer, program of patient identifications must have a different granularity. For instance, to obligatory parameters for normative calculation (sex, age, growing, weight), can be entered additional (race, professional factors of the risk, dependency from smoking etc.).
5. Program of spirometry results archiving must take into account resource of used microprocessor device and satisfy different requests – from short-term keeping of 10-20 tests to creation of permanent archive of several thousand tests in card files, grouped by miscellaneous criteria (age, sex, diagnostic conclusion etc.).
6. The Important element of software is the algorithm of metrological procedures, providing:
- adduction of the inspired volume to expired volume (have in mind a difference of temperature and relative humidity of the air in these maneuver);
- measurement of dosed air volumes (1 l or 3 l);
- verification of processing by ensemble of typical test signal.

7. Software development for spirometry has a special actuality in connection with intensive development of the telemetrically diagnostic systems. Telemetrically technology of respiration monitoring (telespirometry) provide the analysis, compression and archiving of information, as well as artifacts exception, particularly multiple in field conditions, under influence of the moving of patient and/or measuring sensors.
The specific telespirometry – equipped of a connection channel between medical center and patient require the development of additional programs for interpreting the patient's data, essential for diagnostic conclusions and therapeutic recommendations.

USEFULNES OF SPIROMETRIC MEASUREMENT – VIDEO PRESENTATION.

W. Lubiński
Department of Internal Medicine, Pneumonology and Allergology, Military Institute of Health Service of Poland

Spirometry is an effort-dependent test that requires careful instruction and the cooperation of the test subject. Inability to perform acceptable maneuvers may be due to poor subject motivation or failure to understand instructions. Physical impairment and young age (eg, children < 5 years of age) may also limit the subject's ability to perform spirometric maneuvers. These limitations do not preclude attempting spirometry but should be noted and taken into consideration when the results are interpreted. Technicians should have docu-

mented training, with continued competency assessments in spirometry administration and recognition of causes for errors encountered in the testing process. Measures of air flow and volume are indicators of lung health and these non-invasive tests can be done in the physician's office with a spirometer, a device used to measure lung health.
The results of spirometry should meet the following criteria for number of trials, acceptability, and reproducibility. The acceptability criteria should be applied before reproducibility is checked.
A minimum of 3 acceptable FVC maneuvers should be performed. If a subject is unable to perform a single acceptable maneuver after 8 attempts, testing may be discontinued. However, after additional instruction and demonstration, more maneuvers may be performed depending on the subject's clinical condition and tolerance. A minimum exhalation time of 6 seconds is recommended, unless there is an obvious plateau of reasonable duration (no volume change for at least 1 second) or the subject cannot or should not continue to exhale further. Acceptability: A good 'start-of-test' includes: an extrapolated volume of < or = 5% of the FVC or 150 mL, whichever is greater; no hesitation or false start; a rapid start to rise time. No cough, especially during the first second of the maneuver. No early termination of exhalation. No maneuver should be eliminated solely because of early termination. The FEV1 from such maneuvers may be valid, and the volume expired may be an estimate of the true FVC, although the FEV1/FVC and FEF25-75% may be overestimated. Reproducibility: The two largest FVCs from acceptable maneuvers should not vary by more than 0.200 L, and the two largest FEV1s from acceptable maneuvers should not vary by more than 0.200 L.

Peculiarities of the respiratory link of oxygen-transport system in children related to the rate of morpho functional development

I.M. Mankovska[1], O.M. Bakunovskiy[1], E.V. Moiseenko[1], E.E. Kolesnikova[1], L.V.Kvashnina[2], M.I. Velichko[2]
[1] *Bogomoletz Institute of Physiology of NAS, Ukraine*
[2] *Institute of Pediatrics, Midwifery and Gynecology of AMS, Ukraine*

The data analysis of the screening anthropometric study of 258 children of the primary school age (6-9 years old) revealed differences in the rate of their physical development and significant discrepancies in their biological and calendar age. There were determined three groups of children which characterized by different rate of morph functional development: with normal rate, accelerated rate and decelerated rate of the development. Such division on the groups was corresponded to the results of functional tests with physical loading (running with a maximal speed on 30 m under the control of the heart and respiratory rate before the start and after the finish on 1st, 3rd, 5th, 10th minutes).
The aim of the examination was to test the functional state of the respiratory link of oxygen-transport system in children of the primary school age in health and bronchial-lung pathology related to their morph functional development. In this study there were applicated the methods of spirography, regional reography of the lungs, respiratory gas analysis, oxyhemometry.
The study of the functional state of the respiratory link of oxygen-transport system established the control values of the respiratory and gas exchange parameters in children with normal rate of the morph functional development. The functional state of respiratory link in the group with decelerated rate of the development was characterized by the decreased indices of the volume and ventilatory parameters of the lungs connected with a significant mosaic of the ratio between respiration and circulation in different regions of the lung. The data analysis in the group with bronchial-lung pathology (reconvalescention) after pneumonia, chronic bronchitis) elicited some peculiarities in the pathophysiology in children with different rate of the morph functional development. There was a decreased efficacy of alveolar ventilation, altered structure of respiratory cycle under increased discrepancy between ventilation and circulation in the separate regions of lungs in children with the decelerated rate of morph functional development. In children with normal and accelerated rate of development the functional state of respiratory link of oxygen-transport system allowed to engage reserve mechanisms which promoted more effective oxygen transport to tissues.
It was concluded that there were an irregularity at the morph functional development in children of 6-9 years old which accompanied by different time of the forming of oxygen transport-system determined the efficacy of the compensatory mechanisms realizing under hypoxia, especially, under lung pathology.

Comparative characteristics of the morphofunctional state of lung and heart tissues at acute and interval hypoxia

K.V.Rozova, I.N. Mankovskaya
A.A.Bogomolets Institute of Physiology National Academy of Sciences of Ukraine, Kiev

The morphofunctional state of lung and heart tissues of 20 adult male Wistar rats was investigated under acute hypoxic hypoxia (AHH) and interval hypoxic hypoxia (IHH). AHH was created by inhaling a gas mixture containing 12% O2 in N2 during 30 min, intermittent regime implicated 3-times per day breathing

by similar gas mixtures during 15 min with 15-min rest periods for 2 weeks. The morphological studies were carried out by an electron-microscopic method using morpho- and stereo metric analysis. The results testify that for the lung tissue AHH is more harmful factor, than for myocardium, because of edema development. Hypoxia designed in the interval mode affected the investigated tissues differently. It was revealed that the first 15 min of IHH were accompanied by the insignificant changes in ultrastructure of lungs including both the signs of edema and mitochondria structure injuries while myocardium appeared practically intact. The first 15-min normoxic interval did not substantially affect the morphofunctional state of the lung tissue but changed considerably the myocardium ultrastructure: there was demonstrated the sharp swelling of myofibrils and the regional edema of cardiomyocytes. At the same time, there was shown that the cardial mitochondria structure and capillary endothelium were completely preserved. An increase of multipleness of hypoxic influences within the range of one session of IHH has significantly destructed the layers of air-blood barrier (ABB) and the surfactant system of lung. The first full session of IHH affected the heart tissue structure less significantly: there was demonstrated swelling and loss of regularity of myofibrils while mitochondria and capillary endothelium remain mostly unchanged. The 2-week IHH has a normalizing effect on the morphofunctional state of the lung tissue. This effect expressed in: 1) diminishing of the changed mitochondria amount; 2) partial normalization of the surfactant system functioning with the reserve surfactant appearance; 3) absence of erythrocytes in alveoli; 4) diminishing of signs of edema in ABB. The positive effect of IHH on myocardium was also established expressing in an increased number of mitochondria, practical disappearance of swelling and destruction of myofibrils. So, our experiments have shown the expressed organ specificity in cellular reactions both to AHH and IHH and the possibility of preferential negative effects of hypoxic training on the morphofunctional state of lungs. It was shown that the most affected tissue under acute hypoxia or hypoxic part of IHH is the lung tissue while myocardium is the most vulnerable under deoxygenating.

ROLE OF GENETIC FACTORS IN THE ADAPTATION TO INTERMITTENT HYPOXIA

T.V. Serebrovskaya, I.N. Mankovskaya, E.V. Moiseenko, T.I. Drevytska

Department of Hypoxic States, Bogomoletz Institute of Physiology, Ukrainian Academy of Sciences, Kiev.

Overwhelming majority of the adaptation processes to hypoxia are based on transcriptional regulation by hypoxia-inducible factors – HIFs (HIF-1, HIF-2, HIF-3). Now it is well-known that HIF targets include genes involved in energy metabolism, vasomotor control, erythroporsis, angiogenesis, apoptosis etc. HIFs are activated at physiologically relevant oxygen levels, ensuring fast and adequate response to hypoxia. We investigated the role of these factors in human and animal adaptation to intermittent hypoxia training (IHT). Recently the allele polymorphism of oxygen-dependent degradation domain (ODD) of HIF-1? has been described. It consists in the replacement of cytosine for thymine in 1744 location ($C^{1744}\rightarrow T$). The physiological significance of such replacement is obscure. In the investigation of humans we tried to verify whether HIF-1α polymorphism in exon 12 may identify individual features of adaptation to IHT (inhalation of 12% O_2, 5 min, 5 times daily with 5 min breaks during 14 days). The distribution of HIF-1α genotypes for $C^{1744}\rightarrow T$ in 26 healthy elderly subjects (60.7±8,7yr) were studied by using the polymerase chain reaction and restriction analysis. We detected that all subjects from the group had ?/? genotype. Meanwhile, the broad spectrum of adaptive reactions to IHT was observed, from the best adaptation up to deadaptation. These results suggest that the $C^{1744}\rightarrow T$ polymorphism in HIF-1α does not contribute to individual peculiarities of adaptation to IHT. Because the activity of HIF-1α is regulated by multiple steps including the transcriptional level, the effect of the polymorphism in exon 12 on the adaptive reactions remains to be elucidated.

In experiments of rats the mRNA levels of HIF-1α, HIF-1β, HIF-2α, and HIF-3α subunits were detected in lung, heart, kidneys and m. gastrocnemius during normoxia, acute hypoxia (12% O_2, two hours) and IHT. During normoxia, the mRNA expression of all HIF subunits was found in all tissues, but the greatest level of expression was observed in lung and kidneys. During acute hypoxia, the mRNA expression of HIF-3α gene increased significantly in heart, lung and kidneys, and the tendency to augmentation of HIF-2α mRNA level was observed. IHT mostly modulated the expression of HIF-3α subunit in response to acute hypoxia. Our results suggest that induction of HIF-units at the transcriptional level may play significant role in adaptation to intermittent hypoxia.

CIRCADIAN RHYTHM OF VENTILATORY RESPONSE TO PROGRESSIVE HYPOXIA AND HYPERCAPNIA IN HEALTHY YOUNG MEN

M.Siekierka[(1)], M.Tafil-Klawe[(1)], W.Adamczyk[(1)], J.J.Klawe[(2)]

[(1)] Department of Human Physiology

[(2)] Department of Hygiene and Epidemiology, Collegium Medicum in Bydgoszcz, Nicolas Copernicus University in Toruń

Rhythmicity is a ubiquitous biological phenomenon. The purpose of the present study was to evaluate the

circadian rhythm of ventilatory response to progressive isocapnic hypoxia and hypercapnia in healthy young subjects. Fifty six healthy men, 18-30 years old, were involved in the study. The rebreathing technique – progressive isocapnic hypoxia and progressive hyperoxic hypercapnia – was used to measure hypoxic and hypercapnic chemoreflex reactivity. All measurements were performed every 3 hours in the course of 24 hours. The ventilatory response to isocapnic hypoxia was analyzed as the relationship (slope) of MV/SaO2 – minute ventilation/arterial blood oxygen saturation) and as the relationship (slope) occlusion pressure (P0.1)/arterial blood oxygen saturation. The ventilatory response to hyperoxic hypercapnia was analyzed as the relationship (slope) of MV/PetCO2 (end-tidal CO2) and as the relationship (slope) occlusion pressure (P0.1)/end-tidal CO2.
The maximal ventilatory response to hypoxia was observed at 12.00: slope of MV/SaO2 = -3.09+/- 1.8, slope P0.1/SaO2 = -0.82+/-0.9. The lowest values were found at 18.00: -1.76 and –0.56, respectively and at 6.00: -2.44 and – 0.59. The ventilatory response to hypercapnia reminds stable during 24 hours – without significant differences in the course of 24 hours.
Circadian changes of hypoxic reactivity may be important in pathophysiological hypoxemic conditions, suggesting a direction of further investigations.

definition of restrictive ventilatory disorders

Tadeusz M Zielonka
Clinic of Lung Diseases, Medical University in Warsaw

For many years a decrease of vital capacity (VC) measured by spirometry has been the criterion of restrictive pattern. Currently a decrease of VC is no longer sufficient for the diagnosis of a restrictive pulmonary defect and the measurement of the total lung capacity (TLC) by whole-body plethysmography or helium dilution is necessary. Spirometry is not sufficiently sensitive to detect the restrictive pulmonary impairment in many patients, since in majority of cases it turns out to be a pseudorestriction. Pseudorestrictive defects (i.e. VC reduction with correct or even increased TLC) often occur with obstructive diseases, with increased FRC. The VC reduction is provoked by increase of RV.
Spirometry tests require effort on the part of the subject, prompted by directions from the technician. Each FVC maneuver requires maximal effort during three maximal inhalations and exhalations. The upper/lower limit of normal value should be defined as 5/95 percentile. Restrictive ventilatory impairment is observed not only in pulmonary diseases but also in pleural, neuromuscular or hepatic diseases, in thorax malformation etc. Many patients with restrictve diseases such as interstitial lung diseases have normal value of FVC and TLC but decrease of diffusing capacity, compliance or blood gas abnormalities is demonstrated. Spirometry is very useful at excluding a restrictive defect.

ZABURZENIA CZYNNOŚCIOWE UKŁADU ODDECHOWEGO U CHORYCH NA MIASTENIĘ

[1] T.M. Zielonka, [2] A. Kostera-Pruszczyk, [2] B. Ryniewicz, [1] P. Korczyński, [2] B. Szyluk, [2] A. Kamińska, [1] R. Chazan
[1] Katedra i Klinika Chorób Wewnętrznych, Pneumonologii i Alergologii AM w Warszawie,
[2] Klinika Neurologii Akademii Medycznej w Warszawie

Miastenia to choroba, w której dochodzi do osłabienia przepony i mięśni oddechowych klatki piersiowej z zaburzeniem wentylacji o typie restrykcji. Celem pracy była ocena czynnościowa układu oddechowego u chorych na miastenię. Zbadano 70 chorych (50 kobiet i 20 mężczyzn) w wieku 7-82 lat (średnia 32,5). Tylko 3 badanych paliło papierosy. Chorych podzielono na dwie grupy: I w wieku do 18 lat (n=24) i II powyżej 18 lat (n=46). Wszyscy chorzy mieli wykonaną spirometrię i pletyzmografię z oceną oporu oskrzelowego, RV i TLC. Zmniejszenie VC poniżej 80% sugerujące restrykcję obserwowano u 34% chorych (średnia VC=87% wartości należnej). Ocena TLC potwierdziła restrykcyjny typ zaburzeń wentylacji tylko u 11% chorych (średnia TLC=98%). Zmniejszenie VC spowodowane było przede wszystkim zwiększeniem RV stwierdzanym u 54% badanych (średnia RV-128%). Zwiększenie RV stwierdzono aż u 74% chorych w I grupie (średnie RV=147%) i u 40% w II grupie (średnia RV=118%). Tylko u 4% chorych stwierdzono w spirometrii obturację mierzoną zmniejszeniem FEV1%VC<70%, ale u 37% chorych zwiększony był opór oskrzelowy. Zmniejszenie PEF stwierdzono u 50% (średni PEF=74%). U chorych na miastenię rzeczywisty restrykcyjny typ zaburzeń czynnościowych jest rzadko stwierdzany. Zmniejszenie VC obserwowane u tych chorych wynika głównie z czynnościowej restrykcji spowodowanej zwiększeniem RV. Najczęściej obserwowanym zaburzeniem czynnościowym układu oddechowego szczególnie młodych chorych na miastenię jest zwiększenie RV. Znacznie rzadziej jednak zwiększone jest FRC. Często również występuje zmniejszenie PEF i zwiększenie oporu oskrzelowego. Spirometria nie jest optymalną metodą do oceny zmian czynnościowych u chorych na miastenię i warto także oceniać TLC, RV i opór oskrzelowy.