

## IHT® | INTERVAL HYPOXIC THERAPY/ TRAINING

Adaptation to interval normobaric hypoxia has been demonstrated to provide beneficial results in a wide spectrum of diseases and health related conditions.

The principle of **IHT® | Interval Hypoxic Therapy/Training** is based on alternation of multiple brief exposures to normobaric hypoxia (breathing in a hypoxic gas mixture using a mask) and subsequent reoxygenation (normoxia - breathing in ambient air).

**IHT®** regimens are customised individually depending on the **IHT®** purpose and the functional state of the patients.

An **IHT®** session consists of alternating periods of hypoxia (PiO<sub>2</sub> - 9-14 kPa corresponding to 9-14% O<sub>2</sub> at sea level) - reoxygenation, each period lasting 2-15 min, 5-10 periods per each session, one session per day, 10-30 sessions per each course.

### What is hypoxia?

Hypoxia is less oxygen, and hypoxemia is less oxygen in blood. The fact is that almost all of us may and often do experience hypoxia at some time during our daily lives even though we don't realise it.

There are periods of hypoxemia in the pathogenesis of most chronic diseases, especially in the severe forms of the diseases (COPD, bronchial asthma, sleep apnoea, sudden infant's death syndrome (SIDS), cystic fibrosis, heart failure, diabetes, severe anaemia, etc.).

So hypoxemia may be destructive if it is severe and if it lasts a long period of time (days or months). **The destructive effects of hypoxemia are:**

- myocardial hypertrophy (especially of the right ventricle);
- cell damage, etc.

But brief periods of hypoxemia (the same as during the usual **IHT®** session) result in adaptation to hypoxia without destructive effects. The **IHT®** effects are non specific as the effects of exercise training, during which there are also mild to moderate hypoxemia periods, especially in working muscles. So such hypoxemia is really physiological. Moreover, such adaptation creates some beneficial protective effects.

### The known examples of beneficial effects are:

- the increase of maximal expiratory airflow;
- the increase of lung diffusion capacity;
- the increase of the external breathing efficiency;
- the increase of the blood oxygen capacity (erythropoetin, haemoglobin);
- the increase of the antioxidant capacity in blood and tissues;
- the increase of the vascularisation in different organs (skin and myometrium for this current state);
- changes in the activity of the transcription factors (NF-kB, AP1 and Sp1) in the heart and the brain;



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Charles Houston, the world known authority in high altitude medicine, suggests that adaptation to hypoxia is a classical example of Selye's General Adaptation Syndrome [1]. Hypoxia stimulates prompt alarm responses and resistance - "struggle" responses.

**The struggle responses are:**

- increased lung ventilation (rate and depth of breathing);
- increased heart rate and output;
- increased circulating red blood cells;
- decreased blood flow to nonessential parts and increased in the brain and the heart;
- enzymatic changes permitting some anaerobic work;

If hypoxia is not too severe, the body acclimatises by slowly replacing these "struggle" responses with those that are more sustainable [1].

There are some experimental and clinical studies demonstrating the improved efficiency of oxygen transport and utilisation. The increase of peak external airflow, lung diffusion capacity and external breathing efficiency after the **IHT**<sup>®</sup> course result in the increase of partial pressure of oxygen (PaO<sub>2</sub>) and oxygen saturation (SaO<sub>2</sub>) in the arterial blood [2, 3]. The significant increase (45-50%) of the erythropoetin level in the blood serum was demonstrated after 5 IHT sessions [4]. EPO stimulates an increase in red blood cells and haemoglobin formation, which is an important part of adaptation to hypoxia. Such changes in the oxygen transport system explain the possibilities to increase the exercise tolerance by **IHT**<sup>®</sup>.

Significant is the increased capacity of various antioxidant systems in the organism and the decreased activity of main systems generating active oxygen species [5, 6].

In animal experiments **IHT**<sup>®</sup> protects the brain of rats from oxidative stress induced by the neurotoxin 1-metil-4-phenyltetrahydropyridine (MPTP) and prevents development of corresponding behavioural disturbance [7].

The cardio protective effects of **IHT**<sup>®</sup> have been demonstrated in both animals [8] and humans [9].



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The IHT<sup>®</sup> safety has been proven in placebo-controlled studies [2, 6, 10-13], however there exist counter-indications. **Counter-indications to IHT<sup>®</sup> include:**  
all acute somatic and infectious diseases;  
chronic diseases decompensation;  
pregnancy less than 16 weeks;  
pulmonary hypertension (clinical, ECG and/ or echocardiography signs);  
SaO<sub>2</sub> at rest 92% and less;  
age 70 and over (the clinical study of IHT<sup>®</sup> has not been carried out in this age group).

### IHT<sup>®</sup> in Internal Diseases

The results of studies including placebo controlled demonstrated good tolerance and no significant side effects in adults and children with mild and moderate bronchial asthma [10, 14, 15]. The IHT<sup>®</sup> sessions did not result in a lengthy and substantial increase of pulmonary artery pressure and a decrease of peak forces expiratory flow. Nevertheless we consider IHT<sup>®</sup> to be a counter indication for patients with severe bronchial asthma.

Published clinical investigations data suggest the beneficial changes in the bronchial asthma time course after the IHT<sup>®</sup> course. It is suggested that beneficial effects in the course of bronchial asthma occur due to less incidents of respiratory infections and a decrease of bronchial hyperreactivity [14]. At present we analyse the results of a large-scale randomised study “ **IHT<sup>®</sup> in children with recurrent bronchitis and bronchial asthma**”. In the animal experiment on rats IHT<sup>®</sup> has not resulted in the right ventricle hypertrophy [16,17]. The effect of adaptation to interval hypoxia on ischemic and reperfusion arrhythmias has also been studied. The duration of ventricular tachycardia and ventricular fibrillation has decreased more than 2-fold during acute ischemia and more than 3.5-fold during reperfusion compared to control [16]. At the same time adaptation to hypoxia did not increase catalase and superoxidmutase activity in the myocardium though significantly increased initial velocity of Ca transport in the sarcoplasmatic reticulum and increased its tolerance to induced lipid peroxydation and high Ca concentrations [18].

The experimental study performed in the Ottawa University [8] showed a large decrease in the nuclear content of the pro-inflammatory transcription factors (NF-kB, AP-1, Sp1) in the IHT<sup>®</sup> hearts. The data suggest that IHT<sup>®</sup> cardio protection may be caused by an increased anti-inflammatory capacity and decreased susceptibility to stress in preconditioned to hypoxia hearts.



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In clinical study performed on patients with coronary heart disease and stable angina [9] the **IHT**<sup>®</sup> individual regimens were safe even in the patients with severe functional classes of angina. No significant myocardial ischemia (clinical ECG and Echo-cardio graphic data) and cardiac arrhythmia were caused by **IHT**<sup>®</sup> in the patients with 1st and 2nd functional classes of angina. **IHT**<sup>®</sup> safety in aged patients with CHD was proved in the recent placebo controlled study in the University of Innsbruck . The improvement of exercise tolerance after **IHT**<sup>®</sup> in the patients with stable angina is the most important result of the first study (the average exercise threshold growth was 24 Watts). At the same time the double product (heart rate multiply systolic blood pressure) significantly decreased at sub threshold loads [9]. The same double product decrease at sub maximal exercise after **IHT**<sup>®</sup> was observed in the placebo controlled study in healthy students of the University of Innsbruck [11].

Some investigations studied the effect of **IHT**<sup>®</sup> on the levels of lipids in persons with primary hypercholesterolemia [19]. After the IHT course the total cholesterol level significantly decreased due to a decrease of low-density cholesterol. The authors suggest that such IHT influence on lipid metabolism is caused by enhanced cholesterol hydroxylation in hepatocytes (considerable 30%-40% increase of primary bile acids concentration and no changes in ether cholesterol spectre were observed). Mention should be made that there was no comparable control in this study. In our opinion **IHT**<sup>®</sup> can be a part of a rehabilitation program of patients with stable forms of coronary heart disease instead of/ or combined with exercise training, especially in patients with subjective or objective counter indications to exercise training.

Studying the possible effects of **IHT**<sup>®</sup> in females with coronary heart disease combined with climacteric syndrome when substitution hormonal therapy is counter indicative is promising. The increase of ovarian hormone production was demonstrated in placebo controlled study in perimenopausal women with hypoestrogenemia [20].

Unexpected results were obtained in the pilot study of **IHT**<sup>®</sup> in the patients with non-insulin-dependent diabetes mellitus [3] (tissue hypoxia plays an important role in pathogenesis of this disease). The **IHT**<sup>®</sup> course in the patients with compensated and sub compensated diabetes did not result in the increase of tissue hypoxia, the lactate and pyruvate blood serum levels were used to evaluate the degree of tissue hypoxia. Moreover, in sub compensated patients the lactate and pyruvate levels significantly decreased after **IHT**<sup>®</sup>. According to the data of vibration and taste sensitivity investigations these biochemical changes were combined with less distal sensory polyneuropathy expression [21]. Today we can ascertain that non-insulin-dependent diabetes mellitus is not a counter indication for **IHT**<sup>®</sup>.



Similar can be suggested in terms of patients with rheumatoid arthritis.

The **IHT**<sup>®</sup> safety in the patients with rheumatoid arthritis was proved in preliminary pilot studies. **IHT**<sup>®</sup> did not cause the changes of the disease time course though patients noted a certain antianginal effect and a 2-fold reduction in the morning stiffness duration [22,23].

### **IHT**<sup>®</sup> in surgery-preparation of patients for surgery and anaesthesia

The placebo-controlled study [24] carried out in pregnant women of a high risk group before the planned abdominal delivery showed a decrease both in pre- and post-operation stress-reaction. **IHT**<sup>®</sup> prevented the rise of epinephrine (the epinephrine level had been lower 40% before the operation and 25% after the operation in the IHT group compared to placebo), and the glucose level in blood before and immediately after the operation as well as oxidative stress induced by excessive generation of active oxygen species [6].

**IHT**<sup>®</sup> produced the increase of the erythropoietin level (6.5-3.9 mU/ml before the **IHT**<sup>®</sup> course and 10.1-1.5mU/ml after 15 IHT sessions) [4] and of haemoglobin (5%-15% (6,25) in blood preventing the development of post-operation anaemia.

**IHT**<sup>®</sup> increased the filtration of whole blood as well as erythrocytes [25].

Women who underwent a course of **IHT**<sup>®</sup> prior to the planned abdominal delivery [26] or to uterine myoma surgery [27] displayed an increase (35%-40%) in relative volume of myometrium vasculature accompanied by a decrease in stroma volume. In placebo-controlled studies carried out in apparently healthy persons [12] and patients with climacteric syndrome [13] **IHT**<sup>®</sup> improved their psycho emotional status (the decrease in mental strain and autonomic disorders). In the patients operated on for uterine myoma, wound healing was improved [28]. Each **IHT**<sup>®</sup> session also means the training of respiratory muscles. The **IHT**<sup>®</sup> course was noted to increase peak forced expiratory flow and the lung diffusion capacity [9, 29, 30], which brings the possibility to use **IHT**<sup>®</sup> in the pre-operative period in patients with mild and moderate bronchial asthma and chronic bronchitis without respiratory insufficiency. The studies carried out in volunteer athletes [11] and coronary heart disease patients with stable angina [9] noted that **IHT**<sup>®</sup> significantly decreased heart rate, the double product and pulmonary ventilation at sub maximal exercise compared to placebo. Thus, **IHT**<sup>®</sup> improves the reserves of the organism providing for the economical fulfilment of exercise.

We suggest that the most important indications for **IHT**<sup>®</sup> in planned surgery are the cases of bronchial asthma, chronic bronchitis, and iron deficient anaemia.



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## REFERENCE

1. Houston C. Going Higher. Oxygen, Man, and Mountains. Fourth Edition. The Mountaineers, Seattle, WA 98134. P. 159-162. 1998.
2. Tkatchouk E.N., Tsvetkova A.M., Grytsenko P.V., Zhou Zhau-Nian, Wu Xiu-Feng, He Li-Qun, Huang Peng-Guo. Effects of interval hypoxic pretraining on response of blood oxygen transport capability to acute hypobaric hypoxia in healthy subjects. The 3rd World congress on mountain medicine and high altitude physiology. May 20th-24th, 1998, Matsumoto, Japan.
3. Sokolov E.I., Davydov A.L., Starkova N.T., Koroleva A.V., Mestergazi G.M., Ehrenburg I.V., Tkatchouk E.N. The effect of the interval hypoxic training on blood oxygen transport indices in the patients with non-insulin-dependent diabetes mellitus. *Hyp. Med. J. V. 5. N 2. P. 17-19. 1997.*
4. Gulyaeva N.V., Tkatchouk E.N. Effects of normobaric hypoxic training on immunoreactive erythropoietin and transferrin levels in blood serum of healthy volunteers. *Hyp. Med. J. V. 6. N 1. P.13-17. 1998.*
5. Sazontova T.G., Tkatchouk E.N., Kolmykova S.N., Ehrenbourg I.V., Meerson F.Z., Arkhipenko Yu.V. Comparative analysis of peroxidation and antioxidant enzymes activities in rat adapted to different regimes of normobaric hypoxia. *Hyp. Med. J. N 4. P. 4-7. 1994.*
6. Pilyavskaya A.N., Adiyatullin A.I., Tkatchouk E.N. Interval hypoxic training in preparation to planned abdominal delivery. 2. Effect on the free radical-mediated oxidation parameters in blood plasma of pregnant women, in umbilical blood and in placenta. *Hyp. Med. J. N 1. P. 14-17. 1997.*
7. Gulyaeva N.V., Stepanichev M.Yu., Onufriev M.V., Sergeev I.V., Mitrokhina O.S., Moiseeva Yu.V., Tkatchouk E.N.. Interval hypoxic training prevents oxidative stress in striatum and locomotor disturbances in rat model of parkinsonism. *Progress in Alzheimer's and Parkinson's Diseases* edited by Fisher et al., Plenum Press, New York, 1998.
8. Fliss H., Ehrenburg I.V., Gulyaeva N.V., Tkatchouk E.N. Effects of in vivo hypoxic preconditioning on transcription factors and protein kinase C activity in rat heart. XIII World Congress of Cardiology, Rio de Janeiro, Brazil, P. 1157-1161, 26-30 April 1998.
9. Erenbourg I.V. Adaptation to interval normobaric hypoxia increases the endurance of physical loads in the patients with coronary heart disease and stable angina. In book J.R.Sutton, C.S.Houston, G.Coates "Hypoxia and brain". 9th International Hypoxia Symposium at Lake Louise, Canada, February 14-18, P. 321, 1995.
10. Haluszka J., Zaremba-Czereyski J., Tkatchouk E.N., Ehrenburg I.V., Gulyaeva N.V., Willim G., Baran B. Interval normobaric hypoxic training - a new perspective of treatment in children suffering from bronchial asthma. *J. Invest. Allergology & Clinical Immunology. V. 7. P. 531. 1997.*
11. Burtscher M., Tsvetkova A.M., Tkatchouk E.N., Brauchle G., Mitterbauer G., Gulyaeva N.V., Kofler W. Beneficial effects of short term hypoxia. 11th International Hypoxia Symposium at Jasper, Canada. P. 108, 1999.



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12. Akopov G.P., Petrova E.P., Orlova M.A., Glazachev O.S., Tkatchouk E.N. The effect of interval hypoxic training on the psychophysiological status of healthy subjects. *Hyp. Med. J.* Vol. 5, N 2. P.20-22. 1997.
13. Bailina M.I., Roshchina E.S., Gulyaeva N.V., Akopov G.P., Petrova E.P., Tkatchouk E.N. influence of the interval hypoxic training on psychophysiological state of patients with climacteric syndrome. *Hyp. Med. J. V. 6. N 4. C. 161-164.* 1998.
14. Geppé N.A., Kurchatova T.V., Dairova R.A., Tkatchouk E.N., Farobina E.G. Interval hypoxic training in bronchial asthma in children. *Hyp. Med. J. V. 3. N 3. P.11-14.* 1995.
15. Geppé N.A., Kourchakova T.V., Karashtina O.V., Kirilchenko M.G. The response of cardiovascular system in bronchial asthma patients to the dosed hypoxic exposure evaluated by ECHO-CG method. *Hyp. Med. J. V. 6. N 3. P. 131-133.* 1998.
16. Belkina L.M., Budanova O.P., Tkatchouk E.N., Saltykova V.A., Shimkovich M.V., Ehrenbourg I.V., Meerson F.Z. The antiarrhythmic effect of adaptation to normobaric hypoxia in local ischemia and reperfusion of the myocardium. *Hyp.Med. J. V. 3. N 1. P.15-17.* 1995.
17. Rakusan K., Ehrenburg I.V., Gulyaeva N.V., Tkatchouk E.N. The effect of intermittent normobaric hypoxia on myocardial structure in rats. *Hyp.Med. J. V. 5. N 3. P.3-8.* 1997.
18. Sazontova T.G., Tkatchouk E.N., Golantzova N.E., Ehrenbourg I.V., Meerson F.Z., Arkhipenko Yu. V. The state of sarcoplasmic reticulum Ca-Pump and the activity of myocardial antioxidant defence in adaptation to normobaric hypoxia. *Hyp. Med. J. V.3. N 3. P. 5-8.* 1995.
19. Lyapkov B.G., Kondrynskaya I.I., Ehrenburg I.V., Gorbachenkov A.A. On the mechanisms of interval hypoxic training effect on lipid (cholesterol) metabolism in primary hypercholesterolemia. *Hyp. Med.J. V. 1. N 4. P. 12-13.* 1993.
20. Bailina M.I., Roshchina E.S., Gulyaeva N.V., Tkatchouk E.N. The effect of the interval hypoxic training on hormonal status in perimenopausal women. *Hyp. Med. J. V. 5. N 4. P.14-17.* 1997.
21. Sokolov E.I., Starkova N.T., Davydov A.L., Koroleva A.V., Tkatchouk E.N., Tsvetkova A.M., Lyapkov B.G., Ehrenburg I.V. The effect of interval hypoxic training on the vibration sensitivity of patients with non-insulin-dependent diabetes mellitus complicated with distal neuropathy. *Hyp. Med. J. V. 3. N 4. P.15-18.* 1995.
22. Kotlyarova L.A., Stepanova E.N., Tkatchouk E.N., Ehrenbourg I.V., Kondrynskaya I.I., Gorbachenkov A.A. The immune state of the patients with rheumatoid arthritis in the interval hypoxic training. *Hyp. Med. J. V. 2. N 4. P.11-12.* 1994.
23. Kotliarova L.A., Ehrenbourg I.V., Kondrynskaya I.I., Gorbachenkov A.A. Interval hypoxic therapy in complex treatment of rheumatoid arthritis. *Hyp. Med. J. V. 1. N 1. P.-18.* 1993.
24. Adiyatulin A.I., Pilyavskaya A.N., Pilyavsky B.G., Tkatchouk E.N. Interval hypoxic training in planned abdominal delivery. 1. Effects on epinephrine and glucose levels in blood plasma before and after surgery. *Hyp. Med. J.Vo.4. N 4. P.23-25.*1996.



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25. Kondrykinskaya I., Ehrenbourg I.V., Redchits E.G., Gorbachenkov A.A. Blood cell content and filtration rate before and after interval hypoxic training. Hyp. Med. J. Vol .1. N 2. P.22-23. 1993.
26. Rakusan K., Ehrenburg I.V., Gylyaeva N.V., Tkatchouk E.N. The effect of intermittent normobaric hypoxia on vascularization of human myometrium. Microvascular Research 58, P. 200-203. 1999.
27. E.N.Tkatchouk. Histological changes in the uterus and skin in gynaecological patients after a course of interval hypoxic training. Hyp. Med. J. Vol.1. N 1. P.19-21.1993.
28. Tkatchouk E.N. Effectiveness of interval hypoxic training in surgery: prevention of postoperative uterine myoma complications. Hyp. Med. J. Vo1. N 3. P.17-21.1993.
29. Tkatchouk E.N. Prevention of postoperative complications in gynaecology with interval hypoxic training. Hyp. Med. J. Vol.2. N 2. P.50-51. 1994.
30. Tomalak W., Haluszka J., Baran B., Ehrenburg I.V., Tkatchouk E.N. Alteration of breathing pattern by hypoxic stimuli in children undergoing interval hypoxic training. Hyp. Med. J. Vol. 6. N 3. P. 128-130. 1998.



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