

HYPOXIC TRAINING & HYPOXIC THERAPY

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Adaptation to interval normobaric hypoxia has been demonstrated to provide beneficial results in a wide spectrum of diseases and health-related conditions including: primary hypercholesterolemia, essential hypertension, ischemic heart disease (stable angina of effort and rehabilitation after myocardial infarction), neurocirculatory asthenia, idiopathic stress disorders of cardiac rhythm, bronchial asthma, chronic obstructive bronchitis, rheumatoid arthritis, autoimmune thyroiditis, dysfunctional uterine bleeding, chronic salpingo-ophoritis, prevention of early toxicosis, central chorioretinal dystrophy, allergic dermatoses, kinesia, protection of non-compromised tissues from the effect of radiation in the treatment of malignancy.

Adaptation to interval hypoxia is successfully used in surgery (preparation of patients for planned surgery) and in pediatrics (treatment of bronchial asthma and chronic obstructive bronchitis). Beneficial effects of adaptation to hypoxia were demonstrated in treatment of physical fitness loss in otherwise healthy people, training and conditioning of athletes, and altitude pre-acclimation. Concomitant with improving the efficiency of systems responsible for both oxygen transport and oxygen utilization at all levels of the organism, adaptation to interval hypoxia provides a broad spectrum of protective effects.

Interval Hypoxic Training/Hypoxic Therapy (IHT) is based on the principle of cyclic repetitions of brief, normobaric hypoxic episodes and subsequent reoxygenation. The intensity and duration of the hypoxia-reoxygenation cycles may be customized to suit the application of IHT for the treatment and prevention of specific conditions, as well as for general health and as prophylaxis.

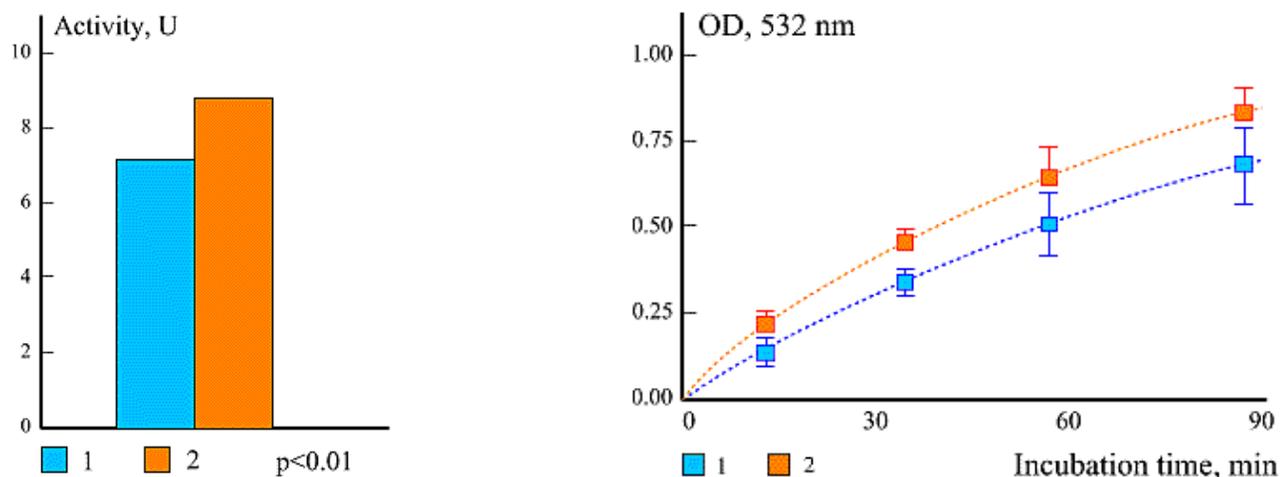
The IHT is mediated by both central control mechanisms (involving primarily the hypothalamo-pituitary-adrenal axis) and numerous local mechanisms (e.g., prostaglandins, opioid peptides, etc.).

Mechanisms of the adaptation to IHT are evident at all levels of the organism (i.e., whole organism, organ systems, organs and tissues, cells, subcellular structures, macromolecules and their microenvironment). While many of these mechanisms remain obscure, some of them have been elucidated and proven experimentally in clinical studies and/or in animal experiments. It is important to note that different mechanisms are active at different stages of the process of adaptation to hypoxia.

Significant among these, the increased capacity of various antioxidant systems in the organism plays an important role in the potentiation of protective mechanisms (Fig. 1) and explains the broad protective capabilities of IHT (Fig. 2).

Figure 1: Activity of superoxide dismutase in the brain of rats (1-control, 2-IHT)

Figure 2: Lipid peroxidation in brain homogenates (thiobarbituric acid-reactive material) (1-control, 2-IHT)



Thus, IHT exerts its action via initiation or *de novo* formation of potent adaptive mechanisms at different levels of the organism. This is precisely the characteristic that allows the use of IHT as an important component of therapeutic and/or prophylactic measures. Counter-indications of IHT include all acute somatic and infectious diseases; chronic disease decompensation; pregnancy less than 16 weeks; pulmonary hypertension (clinical, ECG and/or echocardiographic signs); SaO₂ at rest 92% and less; age 70 and over.

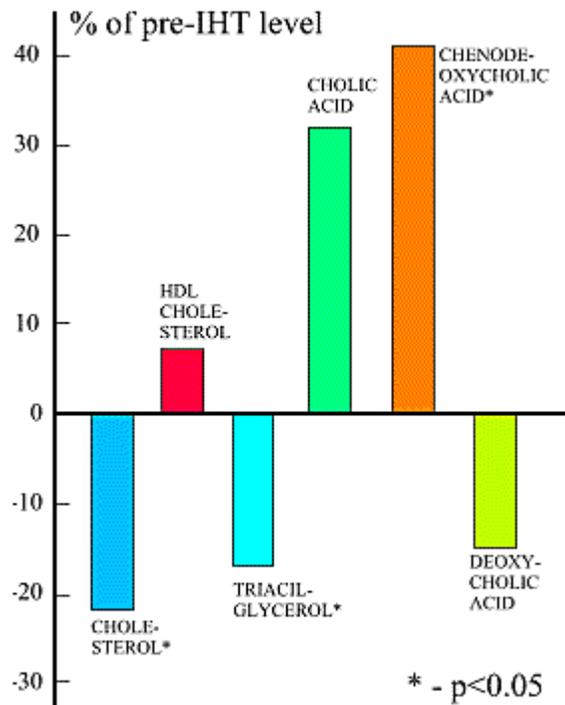
Hypercholesterolemia

IHT considerably decreases levels of total cholesterol and triglycerides in blood serum and reduces the index of atherogenicity.

In addition, the IHT exerts a hypotensive effect, decreases nicotine dependence, and, by virtue of its hypocholesterolemic effect, it can be used to counteract certain risk factors of ischemic heart disease (Fig. 3).

Figure 3

Effects of IHT on lipid metabolism in patients with primary hypercholesterolemia



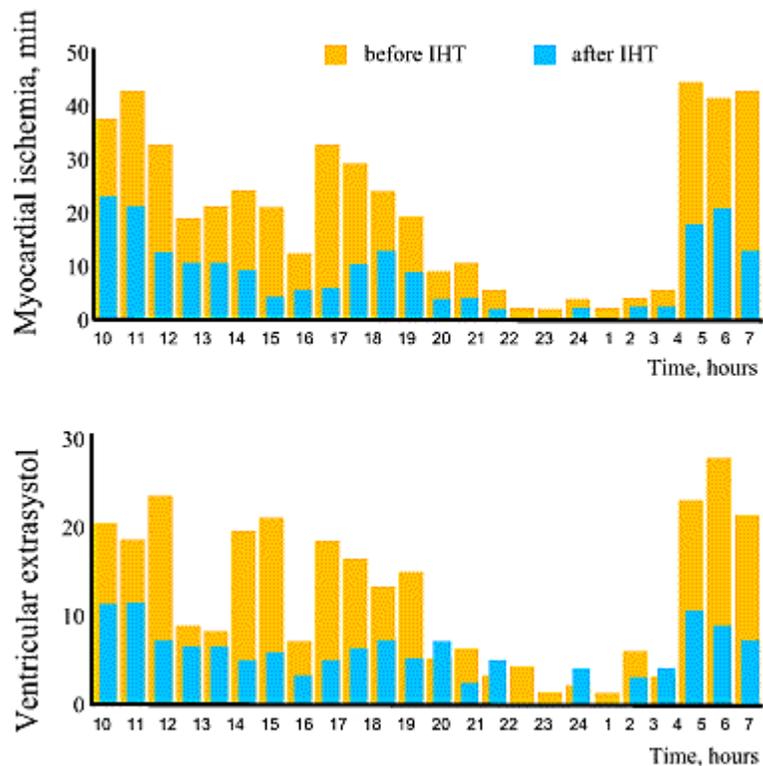
Ischemic heart disease (IHD)

After a course of IHT, patients with IHD who have had previous myocardial infarction and/or who have stable angina of effort display less frequent anginal attacks and an improved tolerance for exercise. They also display an increased of threshold potency of the threshold double product (HR x BPS) at the threshold load that correlates with the maximum oxygen uptake by the myocardium, while under a standard load the value of the double product decreases.

At rest, both heart rate and the minute ventilation are decreased, breathing efficiency is increased, and oxygen consumption reduces. In addition, 24-hour ECG monitoring reveals a reduction in the amount and duration of both painful and silent periods of myocardial ischemia (Fig.4).

Figure 4

Myocardial ischemia duration and ventricular extrasystoles frequency during a 24-hour Holter ECG monitoring before and after IHT in patients with ischemic heart disease



IHT has a pronounced anti-arrhythmic effect and may be used in patients with symptomatic extrasystole associated with psycho-emotional states.

Gynecological diseases

IHT has been established to have beneficial effects on juvenile dysfunctional uterine bleeding. Bleeding was stopped and blood hemoglobin rose. Urinary pregnandiol and the number of keratotic cells in vaginal smears were increased. IHT normalized the course and outcome of labor in these women through stabilization of blood pressure, decrease in edema, decrease in the mean duration of delivery, and abolishment of afterbirth complications and residual manifestations of gestosis. It also normalizes the principal parameters of platelet hemostasis in pregnant women with gestosis: ADP- and epinephrine-induced platelet aggregation decreases and the level of fibrin degradation products diminishes (from 7.82 ± 0.01 to 2.56 ± 0.02 mg/l).

Preparation of patients for surgery and anesthesia

IHT can be beneficial in the preparation of patients for anesthesia and surgery. Women who underwent a course of IHT prior to surgery for uterine myoma displayed an increase in relative volume of myometrium vasculature accompanied by a decrease in stroma volume (Table 1), an improvement of blood and oxygen supply to the myometrium, and an improvement of their psycho-emotional status, including decreases in both mental strain and autonomic disorders. Wound healing also was improved in patients operated for uterine myoma (Table 2).

Table 1.
Uterine stereometric indices
in gynecological patients:
effect of IHT before surgery.

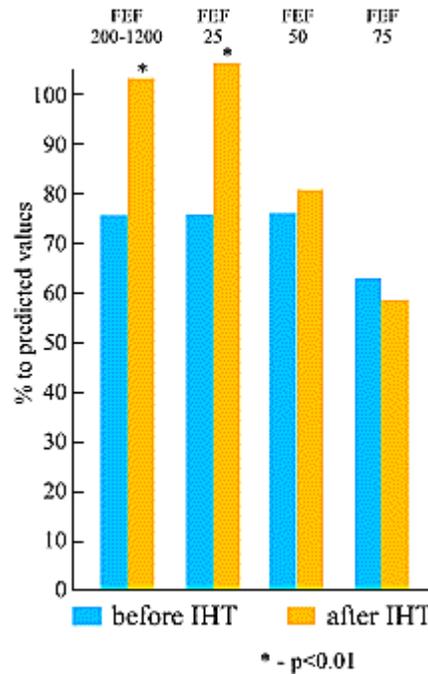
| The group of patients | The relative volume, % M± S.E.M. | | |
|----------------------------------|----------------------------------|------------|-----------------|
| | Blood Vessels | Stroma | Muscle elements |
| Patients after the course of IHT | 8.13±0.21 | 20.09±0.33 | 71.78±0.38 |
| Control group | 6.01±0.18 | 21.36±0.31 | 72.63±0.27 |
| P | <0.001 | <0.01 | >0.05 |

Table 2.
Stereometric analysis of skin
in patients after gynecological
surgery: effect of IHT before surgery.

| The group of patients | The relative volume, % M± S.E.M. | | |
|----------------------------------|----------------------------------|------------|---------------|
| | Epidermis | Derma | Blood Vessels |
| Patients after the course of IHT | 28.76±0.66 | 65.09±0.98 | 6.15±0.32 |
| Control group | 28.97±1.43 | 67.48±1.52 | 3.54±0.30 |
| P | >0.05 | >0.05 | <0.001 |

An IHT-induced improvement in the function of external respiration suggests the usefulness of preoperative IHT for patients with initial forms of broncho-obstructive diseases or with impaired external respiration (Fig. 5).

Figure 5
The changes of forced
expiratory flow (FEF) rates
in gynecological patients



Chronic bronchitis and bronchial asthma

IHT is an effective treatment for chronic obstructive bronchitis and bronchial asthma in both adults and children. Clinical efficiency was observed in approximately 80% of patients with atopic bronchial asthma and in approximately 70% of patients with bacterial asthma and chronic obstructive bronchitis. On average the positive clinical effect has been seen to persist for a period of 4 months.

In bronchial asthma clinical recovery is usually accompanied by improved external respiration and reduction of bronchial hyperreactivity. The good clinical results observed in atopic bronchial asthma in children are accompanied by a decrease in circulating immune complexes and restoration of the initially reduced content of blood immunoglobulin M (Table 3).

An adaptation to hypoxia is accompanied by the improvement of respiration and circulation in patients with chronic obstructive bronchitis. The available data supports benefits of using the IHT in treatment programs of patients with bronchial asthma (excluding hormone-dependent asthma) and chronic obstructive bronchitis without initial manifestations of chronic respiratory insufficiency.

Table 3.
Serum immunoglobulins
in patients with bronchial
asthma before and after
IHT (M± S.E.M.) g/l.

| Parameters | Before IHT | After IHT |
|------------|------------|-----------|
| IgA | 1.05±0.3 | 1±0.5 |
| IgM | 1±0.3 | 1.71±0.4* |
| IgG | 11±4.6 | 12.50±4.4 |

* - p<0.05

Rheumatoid arthritis

IHT has been used with good clinical results in both adults and children with rheumatoid arthritis. The IHT course reduced the duration of morning stiffness and the number of involved joints and alleviated or abolished arthralgia. Furthermore, IHT positively influenced the general status of patients by improving their mood, sleep patterns, appetite and increasing their level of physical activity. The IHT-induced clinical improvement in patients with rheumatoid arthritis was accompanied by definite immunological changes, in particular, by an increase in the number of mature T-lymphocyte subpopulations, indicating a positive immunomodulating effect of the IHT.

Hypoxic radiotherapy

Hypoxic radiotherapy is the administration of therapeutic radiation to patients while they are breathing a hypoxic gas mixture. It has been used successfully in the treatment of patients with malignant tumors with a variety of localization. This method is based on the observation that having the patient breathe a gas mixture containing 9-10% of oxygen during irradiation of malignant tumors decreased the side effects of radiation exposure.

A study performed on 974 patients has shown that the total number of radiation injuries was decreased to less than half of control levels and that the number of pronounced radiation responses was reduced to less than a third of control levels. In radioresistant tumors (e.g., carcinoma of the stomach and pancreas, retroperitoneal tumors), inhalation of the hypoxic gas mixture by patients during independent and preoperative irradiation allows both single and total focal doses to be increased by 25-50%, which considerably extends the potency of irradiation (Table 4).

Table 4.

Responses in preoperative radiation therapy and hypoxic radiotherapy for cancer of the stomach.

**SFD, Gr (single focal dose)
TFD, Gr (total focal dose)
HGM - hypoxic gas mixture
(10 and 9 are % concentrations of oxygen in HGM).**

| Nature of preoperative irradiation | Number of patients | SFD, Gr | TFD, Gr | General radiation response, number of patients (%) | Of those with pronounced radiation response, number of patients (%) |
|---|--------------------|----------|----------|--|---|
| Control group (Radiation without hypoxia) | 64 | 4 | 20 | 39 (61) | 5 (7.8) |
| Radiation with HGM-10 | 51 | 4.5 | 22.5 | 20 (39.2) | 4 (7.8) |
| Radiation with HGM-9 | 67 | 5 | 25 | 25 (37.3) | 1 (1.5) |
| Radiation with HGM-9 | 66 | 6 | 30 | 30 (45.4) | 4 (5.9) |
| TOTAL | 248 | - | - | 114 (45.9) | 14 (5.6) |

IHT in general health-promoting measures

IHT provides beneficial effects on health and physical conditions of children residing in ecologically unfavorable regions, including radiationally unfavorable environments. These benefits include an activation of neurodynamic processes, a decrease in psychomotor and autonomic correlates of psycho-emotional stress, an improvement in the parameters of bronchial potency, and a decrease in sympathotonic responses. Furthermore, IHT is beneficial for increasing the resistance and adaptive ability of children particularly susceptible to disease and allows them to improve their physical and mental capacities. Thus, the benefits provided by IHT—optimization of autonomic functions, decreased manifestations of psycho-emotional strain, and increased capacity for physical activity—indicate the usefulness of this method both for increasing adaptive potential and for correcting psycho-emotional disturbances. IHT influences the pattern of physiological responses (including those accompanying acute hypoxemia) providing for the optimization of oxygen homeostasis central regulation on both systemic and tissue levels. IHT significantly affects the time course of the decrease in oxygen saturation of blood (Table 5 and Fig. 6).

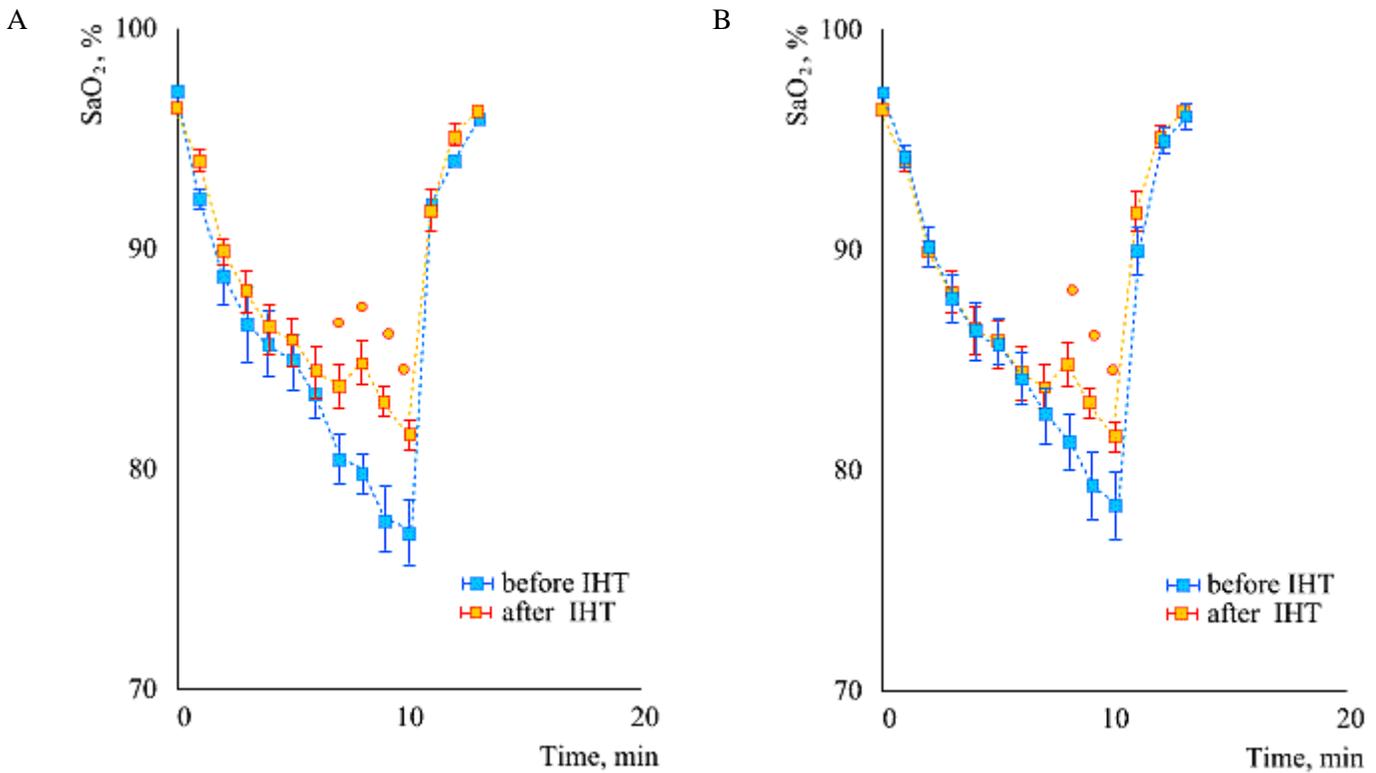
Figure 6

Changes in SaO₂ during hypoxic test (inhaling 11% O₂ during 10 min., then inhaling atmospheric air) in healthy men:

A - before and after IHT,

B - after IHT and after placebo course;

*** - p<0.05**



IHT can be used for stimulation of adaptive and compensatory mechanisms in premature aging and in elderly people undergoing health-building measures.

Table 5.
Changes of SaO₂, heart rate (HR) and minute expiratory volume (VE) during hypoxic test (11% O₂) before and after IHT (M ± S.E.M.)

| Parameters | Before IHT | After IHT |
|-----------------------|--------------------|-------------------|
| SaO ₂ , % | 16.0 ± 1.6 (80%) | 12.5 ± 1.3 (84%)* |
| VE, l/min | 0.76 ± 0.20 (109%) | 2.2 ± 0.5 (123%)* |
| HR, min ⁻¹ | 12.8 ± 1.3 (113%) | 8.4 ± 1.3 (108%)* |

Differences of respective parameters during hypoxic test are presented (in parentheses - percent of the initial value); * - p < 0.05 comparing with the values before IHT.

The effect of IHT on the efficiency of sport training

IHT improves the functional and psycho-physiological state of athletes and increases both their general and special physical capacity (in rowers, swimmers, bicyclists, skiers, volleyball players, track and field athletes, etc.) (Figs. 7, 8). The efficiency of IHT in enhancing conditioning and performance is similar to those that follow high-altitude training, which makes the IHT an excellent substitute for altitude training for world-class athletes.

In summary, IHT is a promising trend in treatment, rehabilitation, and prophylaxis of a wide variety of diseases and physical conditions.

These results were obtained in collaboration with the Hypoxia Medical Academy Clinical Research Laboratory.