

Intermittent Hypoxic Therapy/Training (IHT) as etiological and pathogenetic anti-aging treatment

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Oxidative mtDNA damage is a recognized pathogenetic mechanism of aging in mammals. Progressive degradation of mitochondria underlies oxidative stress, which causes accumulative molecular damage, genomic instability, telomeres shortening, metabolic and hormonal decline, accelerates protein glycation and diminishes protein turnover. Continuous rejuvenation of mitochondria in somatic cells can reduce oxidative stress, increase efficiency of oxidative metabolism, slow down aging process, prevent and/or retard development of age-related pathology.

A natural mechanism (mitoptosis) recently discovered in mammals facilitates continuous purification of the mitochondrial pool in an organism from the most ROS-producing mitochondria. Mitoptosis selectively eliminates them, thus providing advantage for proliferation of wild-type (non-mutated) mtDNA. Mitoptosis can be induced by time - and pO₂ tension-controlled cycling of intracellular pO₂ from normoxic to hypoxic state and back in the range between 5 - 1 torr. Such O₂ oscillations can be safely induced by Intermittent Hypoxic Therapy/Training (IHT).

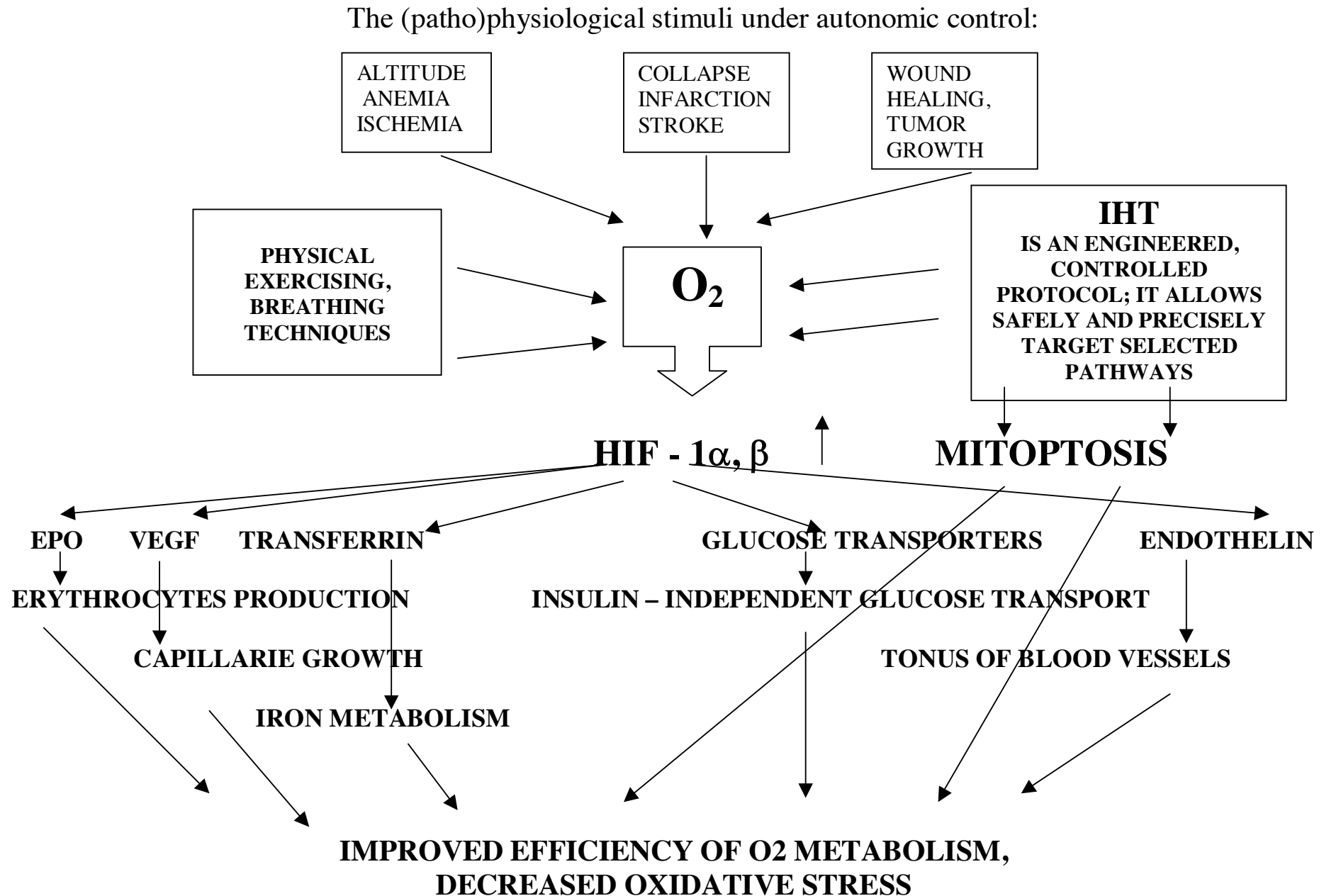
IHT is a novel preventative, therapeutic and rehabilitative treatment that has been developed and refined during the last decades. IHT improves autonomic homeostasis, modulates humoral and cellular immunity and markedly augments non-specific stress-resistance. This brings measurable rejuvenative effects and rapid clinical improvements in numerous diseases, physical and mental conditions. The ability to regulate, adjust and balance metabolism via hypoxic preconditioning that modifies the cellular and mitochondrial life cycle through nitric oxide pathway is the most valuable property of IHT. The cellular and systemic effects of hypoxic preconditioning include: a) rejuvenation of mitochondria via mitoptosis; b) decrease of reactive oxygen species generation; c) increased enzymatic antioxidative defense; d) decreased lipid peroxidation; e) improved oxygen absorption, transportation and utilization; f) improved glucose metabolism and enhanced accumulation of intracellular glycogen; g) increased accumulation of cytoglobins; h) increased erythropoietin and Hsp -70 levels; i) facilitated mesenchymal stem cells-dependent tissue repair.

Technically, the IHT session consists of 6 - 10 controlled repeated hypoxia-reoxygenation episodes: 2 - 6 min. intervals of hypoxic air inhalation, interspersed with 3 - 5 min. intervals of normoxic or hyperoxic air inhalation. Several times a week training for 2 - 4 weeks gradually induces beneficial clinical effects. The effects of IHT in healthy subjects are moderately expressed, while they are clearly noticeable in patients, suffering from oxidative stress. To achieve better results from IHT the individualized protocols should be used. The efficiency of IHT can be enhanced by intermittent caloric restriction and by synergistic nutraceutical supplementation.

Results of the treatment of 102 patients are discussed. A detailed description and analysis of several clinical cases is provided.

Keywords: Intermittent Hypoxic Therapy, mitochondria, ROS, mitoptosis

Fig. 1. IMPROVEMENT OF OXYGEN METABOLISM VIA HYPOXIC STIMULATION



**Fig. 2. INTERMITTENT CALORIC AND OXYGEN RESTRICTIONS (IOR and ICR)
SELECTIVELY ELIMINATE DAMAGED MtDNA VIA MITOPTOSIS**

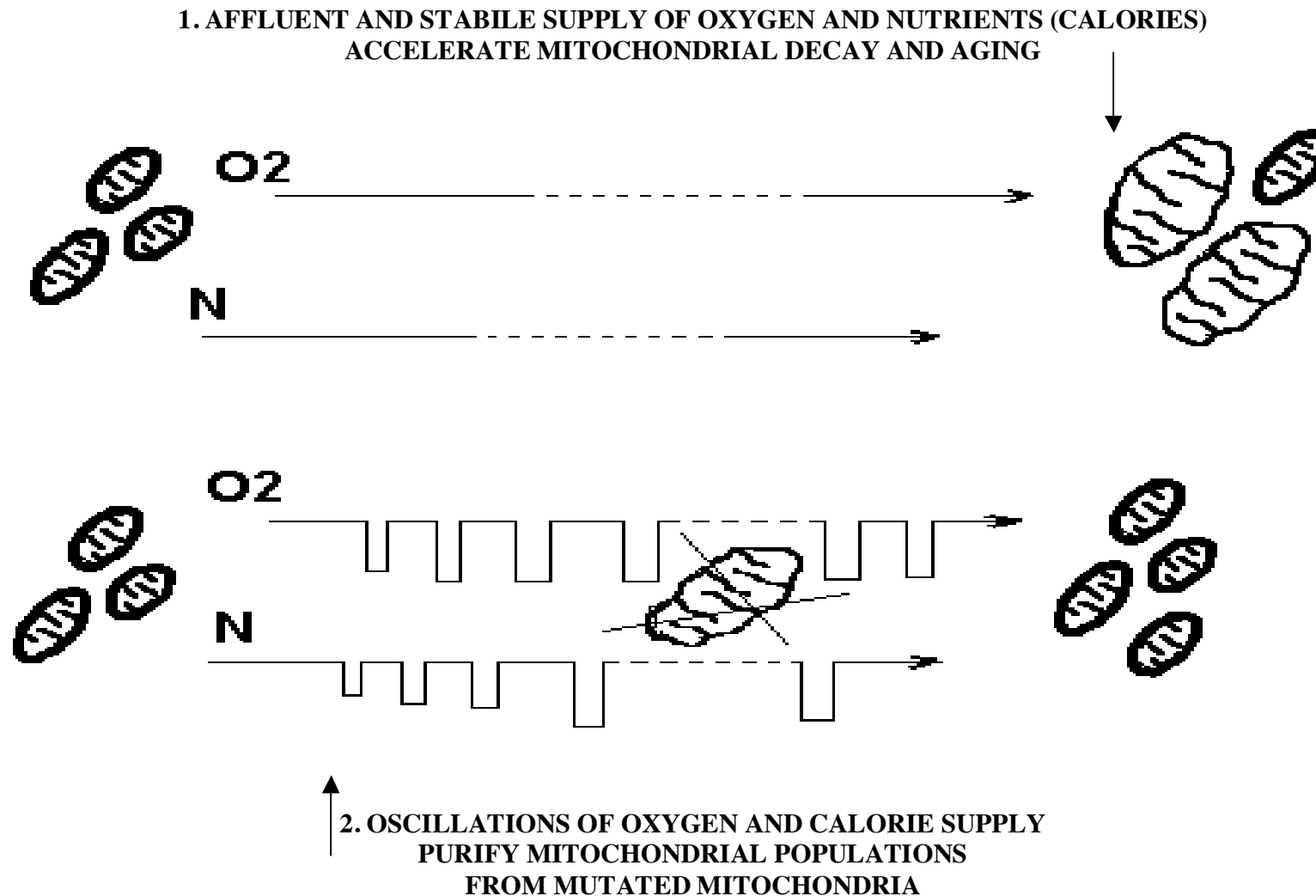


Table 1. The results of treatment of 102 patients in 1998 – 2006

Diseases and conditions		Outcome		
		Improvement or cure	No effect	Worsening
Cardiovascular disease -	8	6	1	1
Arterial hypertension -	12	11	1	0
Type 2 diabetes -	16	15	1	0
Burnout syndrome -	4	4	0	0
Depression -	2	2	0	0
Bronchial asthma –	7	7	0	0
Emphysema -	2	1	1	0
Multiple sclerosis -	3	2	1	0
Neuroborreliosis -	3	2	1	0
Epilepsy -	1	1	0	0
Premenstrual syndrome -	12	10	2	0
Postmenopausal syndrome -	9	9	0	0
Infertility -	4	2	2	0
Hypothyroids -	11	10	1	0
Irritable bowel syndrome -	5	5	0	0
Wound healing -	3	3	0	0
Total	102	90	11	1
	100%	88,2%	10,8%	0,98%

Clinical cases

1. Mrs. Elena N. (born in 1947) suffered from epilepsy since the age of 14th. In July 2004 her attacks became more frequent (2-3 times a week). She took a long time coming round after each seizure and experienced a noise in the ears, headache, dizziness and felt as if she had just had an electric shock; often she suffered numbness in the extremities and a partial loss of coordination. Her doctor recommended increasing the main medicine for epilepsy, but this only made her feel much worse.

She was prescribed IHT, vitamins and microelements for two months. She has been doing IHT regularly for 40 minutes every day (one 25-day course in 3-4 months with occasional additional sessions, if her condition worsened). After even 20 minutes of IHT usually her headache and the numbness gradually passed. Her condition significantly improved, she reduced medication to minimum.

2. Mrs. Francoise P. (born in 1940) consulted on 25 March 2004. She complained of a severe allergic reaction to sun-bathing four-five days earlier. Symptoms included intensive shaking, heart palpitations, swelling and redness of skin all over the body, pale blue phalanges and nails, unbearable skin itching, slightly reduced only by cold showers. BP 180/100. Pulse 110.

There was no evidence of earlier food allergies. On 24 March she had cortisol injection and took pain killers (in relation to pain in her right hip), and for the previous three days had been taking anti-histamine tablets, after which the allergic reaction intensified.

She was treated with intermittent hypoxia therapy (90 minutes), homeopathy and acupuncture. After treatment BP 155/90. Pulse 84. Her skin color returned to normal in 2 hours, marked relaxation was established. Treatment was repeated on 26 March (IHT for 60 minutes, homeopathy and acupuncture). Allergic reactions resolved, BP 145/85.

3. Mrs. Katharine B. (born 1959) in March 15, 2002 the post-viral infection syndrome and arterial hypertension was diagnosed. For several weeks before she had been under observation by her GP for extreme exhaustion and increasing bouts of depression. She was prescribed anti-depressant drugs, which she refused. After the first IHT treatment (March 2002) she began to feel better. She had a 12-treatment course after which she enjoyed a steady improvement to the present day (2007) when she reported that she felt better than she had done in years. Her blood pressure normalized from 170/90 to 130/80.

4. Mr. Ata A. (born 1940) suffered his first asthma attack (mild), at the age of thirteen. At the age of 40 his condition grew worse, resulting in his move from Iran to England. He progressively increased doses of Ventolin, Becotide, Becloforte, etc. A six-week course (May - June 2000) of IHT completely cured his condition; currently he doesn't use medication, although carries it with him for safety.

5. Adam L. (born 1989) suffered from asthma since the age of 6. Four years before consultation he had been prescribed Bricayl (3,200 mg daily) and Pulmicort (1,600 mg daily). During the IHT treatment his breath-holding ability increased from 4 sec to 40 sec. After IHT treatment (continued for 17 days and included morning fasting and diet control) he was able to abandon all medication. Has been under observation since then and there have been no incidences of relapse (2007).

6. Mrs. Jennie W. (born 1961) consulted regarding her depression, which she suffered during all her life. She was already using anti-depressants as a teenager. At the age 31 she went into treatment for addiction to alcohol, drug abuse and eating disorders.

In the spring of 2003 she had IHT for the first time. After a few weeks of IHT she felt totally free of depression and described it as being "like seeing life in color for the first time". She no longer suffered from depression and felt physically fit (she mastered advance hatha yoga).

In August 2003 she began IHT course again and within 3-4 days was considered to be a normal and happy woman. She commented: "It makes perfect sense to me that we need to heal ourselves at ALL levels, spiritual, emotional and physical and that they all relate and correspond in ways that we are only just beginning to understand."

7. Mr. John M. (born 1950), is suffering from metabolic syndrome, cardiovascular disease. For 7 years noted progression of neuropathy (loss of sensitivity) in both feet. Patient smokes since teenage years up to 2 packs cigarettes a day, has high nicotine – dependence, attempted numerous unsuccessful smoke-cessation cures; but consumes no alcohol. Craves for carbohydrates and sweets. Suffers severe mood swings. BP 160/100, HR 85. In June 2003 embarked on IHT program. He started using modified IHT protocol (a combination of short bursts of treadmill exercise with

hypoxic air inhalations) for wellness and weight reduction. After 2 weeks of 45 min. daily training, on the background of significantly improved exercise tolerance and continuous weight reduction the patient noticed a gradual return of sensitivity in both his feet (sensitivity was lost completely 4 years ago and didn't respond to medication). In 4 weeks of training sensitivity in his feet returned near 60% of normal. The patient reduced smoking to 1 pack a day. After 2 weeks of IHT patient added to the therapeutic protocol one fasting day a week and vitamin-nutraceutical supplementation program. After 6 weeks of treatment the sensitivity in both feet returned to near 85% of normal. Weight loss 5.8 kg. Patient noted complete elimination of carbohydrate craving, a dramatic improvement in emotional stability, and notable increase in physical and mental performance. BP 135/80, HR 68. Smokes less than pack a day.

Table 2. The results of IHT treatment in the prophylaxis clinic “Tamara”, Murmansk, Russia. (from: Kononenko et al, 1997)

(the number of complaints in % to overall 687 patients)

	Complaints	Before IHT treatment	After IHT treatment	P
1	Headache	39,2 ± 1,5	7,1 ± 0,8	<0,001
2	Heart aches	36,3 ± 1,5	4,4 ± 0,6	<0,001
3	Breathlessness	24,7 ± 1,3	13,7 ± 1,0	<0,001
4	Suffocation fits	4,1 ± 0,6	07, ± 0,3	<0,001
5	Cough	20,1 ± 1,2	4,6 ± 0,6	<0,001
6	Insomnia	33,3 ± 1,4	3,3 ± 0,5	<0,001
7	Irritation	37,5 ± 1,5	6,6, ± 0,8	<0,001
8	Fatigue	72,2 ± 1,4	17,2 ± 1,1	<0,001
9	Impaired work capacity	58,0 ± 1,5	5,7 ± 0,7	<0,001
10	Unpleasant sensations	70,8 ± 1,4	7,8 ± 0,8	<0,001
11	Joint aches	37,0 ± 1,5	15,4 ± 1,1	<0,001
12	Depressed mood	37,6 ± 1,5	9,3 ± 0,9	<0,001

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