

# Application of The Intermittent Hypoxic- Hyperoxic Therapy (IHHT) in Fertility Medicine

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## Objective:

Current clinical strategies for prevention and therapy of subfertility predominantly rely on pharmacological interventions. Meanwhile, a significant biomodulatory treatments potential, based on physiology of mammalian reproduction remains underused. Here we discuss application of a preventative, curative and rehabilitative intervention, the Intermittent Hypoxic-Hyperoxic Therapy (IHHT), which is based on the physiological intermittent hypoxia/ischemia (hypoxic preconditioning) that governs both the oocyte maturation and embryo development (1), as well as selection of better quality mitochondria (2).

The following mechanisms are modulated by intermittent physiological hypoxia: a) The ability of the cell to store NO as Di-S-nitrosothiol-iron-complexes (DNIC), improvement of the physiological NO-reactivity and downregulation of reactive oxygen (ROS) and nitrogen species (RNS). b) The expression of hypoxia - responsive genes, including those for erythropoietin, VEGF, VEGFR-1 and -2, Endothelin-1, iNOS, HOx-1, glycolysis enzymes, glucose transporters GLUT-1 and -3, iron metabolism, growth factors including TGF- $\beta$ , PGF, PDGF- $\beta$ , HGF, apoptosis regulation factors Bcl-2, Mcl-1, Bax through the activation of hypoxia-inducible-factor-1a (HIF-1a).

On the other hand, hyperoxia upregulates ARE mediated phase-2 detoxifying and antioxidant enzymes, IL8, IGFBP-2, ICAM-1, IL6, ENaC, p21, CCSP. The controlled O<sub>2</sub> partial pressure oscillations at the cellular, even more at the mitochondrial level improve treatment outcome in majority of chronic multi-system fertility pathologies, including preeclampsia, gestational diabetes, chronic foetal hypoxia.

IHT (Intermittent Hypoxic Training) was developed in former USSR and used in fertility medicine in Russia since 1980 and recently has been "upgraded" to IHHT. Application of IHHT results in «training» of gestational and foetal adaptive mechanisms to hypoxia, facilitating correction of multiple metabolic dysfunctions of fertility and augments general resistance of foetus to hypoxia (3).

The IHHT utilizes 10% to 12% O<sub>2</sub> – hypoxic and 40% O<sub>2</sub> - hyperoxic air, intermittently delivered via facemask according to individualized, biofeedback-controlled protocols. The IHHT provides various preventative and therapeutic effects, such as increase in functional reserves of cardio-respiratory system, normalization of acid-base balance, normalization of blood pressure and mobilization of mechanisms of regulation of hypothalamic-pituitary adrenocortical system.

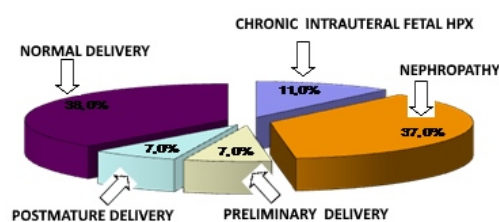
## Methods:

Summary of publications on the use of IHT - IHHT in obstetrics and gynaecology. Own clinical experience.

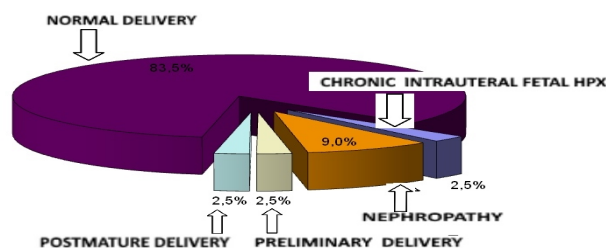
## Results:

The IHHT significantly improves treatment outcome in various fertility disorders.

### Structure of pathology in high-risk pregnancies (anamnesis, 154 cases) before IHT (4)



### Structure of pathology in high-risk pregnancies (same 154 cases) after IHT (4)



## References:

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