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## ХРОНИЧЕСКИЕ ВОСПАЛИТЕЛЬНЫЕ ПРОЦЕССЫ И ИСПОЛЬЗОВАНИЕ НИЗКИХ ДОЗ ОЗОНА В СООТВЕТСТВИИ С МЕЖДУНАРОДНЫМ ПОЛОЖЕНИЕМ О ПРИМЕНЕНИИ МЕДИЦИНСКОГО ОЗОНА: СИГНАЛЬНАЯ ТРАНСДУКЦИЯ И БИОРЕГУЛЯЦИЯ С ПОМОЩЬЮ ПЕРОКСИДОВ ОЗОНА В КАЧЕСТВЕ ВТОРИЧНЫХ МЕССЕНДЖЕРОВ

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## CHRONIC INFLAMMATORY PROCESSES AND THE LOW-DOSE OZONE CONCEPT BASED ON THE INTERNATIONAL GUIDELINES OF MEDICAL OZONE: SIGNAL TRANSDUCTION AND BIOREGULATION THROUGH OZONE PEROXIDES AS SECOND MESSENGER MOLECULES

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Inflammatory processes as the classical indications for systemically administered medical ozone have one general phenomenon in common: oxidative dys-stress, mostly chronic oxidative dys-stress (chronic vascular inflammation, diabetes, pain syndrome, rheumatoid arthritis, age related diseases, and - last but not least - cancer), initiated and maintained by an excess of oxygen radicals (superoxide radicals  $\cdot\text{O}-\text{O}^-$ , hydrogenperoxide  $\text{H}_2\text{O}_2$ ,  $\cdot\text{OH}$ -radicals.).

As one of the consequences, the downregulated and/or insufficient cellular antioxidant system (superoxide dismutase (SOD), catalase (CAT) and others) supports chronic inflammations.

Ozone, being a strong oxidant itself, interrupts this vicious circle via formation of «ozone peroxides», reduction by cysteine

residues and/or glutathion (GSH), -bypassing SOD and CAT consumption- signal transduction and regulation through Nrf2 (antioxidants) and NFkB (immunoregulation). These seem to be the central mechanisms to understand pharmacological and therapeutical effects of ozone.

As a consequence pathological concentrations of stress-relevant parameters ( $\text{H}_2\text{O}_2$ , MDA malone dialdehyde, TH total hydroperoxide...) decrease significantly following systemic ozone treatment (low-dose concept), cellular antioxidants are regulated as well as the cytokin production (such as IL-1, IL-6, TNF- $\alpha$  ...) in chronic inflammatory processes.

**Key words:** Inflammation, «ozone, peroxides», oxygen radicals, oxidative stress, Nrf2, antioxidant regulation, NFkB, immunomodulation.

