Ozone improves the delivery of oxygen to hypoxic tissues, as well as reactivating the oxygen metabolism of cells. The mechanisms of these systemic actions involve both direct and indirect processes.

Ozone directly changes the electric charges of the erythrocyte membrane, increasing the flexibility and plasticity of the erythrocytes, thus enhancing the flow properties of the blood and the transport of oxygen to the cells and tissues. This is especially applicable in arterial occlusion disease whereby “pile of coins” erythrocyte formation (rouleaux) is typical. The indirect mechanism consists of ozonolysis, i.e., the ionizing reaction of ozone with the unsaturated fatty acids in the cellular membrane producing peroxides. It must be pointed out that ozone behaves as an ion, not a free radical, under normal physiological blood pH, and therefore no radical chain reaction occurs to cause oxidative damages. The reaction activates the enzyme 2,3-Diphosphoglycerate (2,3-DPG) in hemoglobin to release oxygen. This is of particular importance to diabetics in which 2,3-DGP is depressed.

**Ozone Induces Specific Enzymes**

Ozone induces the formation of short-lived peroxides at the membrane which are injected into the cell and are removed by the enzyme glutathione peroxidase. Therefore, it is recommended to supplement with vitamin E, N-acetyl-cysteine, and selenium during ozone therapy to support the glutathione detoxification system. In addition, the enhancement of the glycolysis enzymatic pathway results in an increase in adenosine triphosphate production (energy currency of the cell). This is significant in the management of stroke and burns. The elevation of adenosine triphosphate synthesis will decrease perifocal edema formed in the injured site, minimizing tissue necrosis and subsequent scarring. But this is effective only when ozone is administered within the first 24 to 48 hours. In Germany, many ambulances are equipped with ozone and it is injected intravenously in patients who have just suffered stroke.

**Ozone Activates Immune System**

It is well documented that ozone can activate monocytes and lymphocytes, and induce the production of an array of cytokines such as interleukin, interferon, and tumor-necrosis factor (The Journal of International Medical Research 1994). Its ability to elicit endogenous production of cytokines and its lack of toxicity make ozone an indispensable therapeutic modality since today’s most devastating diseases are characterized by immunodepression such as chronic viral diseases, cancer, and AIDS. Of course, restoration of the immune system depends on a total approach of detoxification, lifestyle modification, and supportive therapies.