

## MIRACLE OF OZONE THERAPY AS AN ALTERNATIVE MEDICINE

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### ABSTRACT

Ozone (O<sub>3</sub>) is a molecule consisting of three atoms of oxygen in a dynamically unstable structure due to the presence of mesomeric states. Although ozone has dangerous effects, yet researchers believed that it may have therapeutic effects. Thus ozone therapy has been thoroughly studied for more than a century in various countries. Its effects were proved to be consistent, safe, with minimal and preventable side effects. Medical ozone was then used to disinfect and treat diseases. Medical ozone generators were used to evaluate some mechanism of action and possible toxicity. Mechanism of actions which were found is inactivation of bacteria, viruses, fungi, yeast and protozoa; stimulation of oxygen metabolism; activation of the immune system; etc. Ozone therapy acts as a form of oxygen therapy that stimulates mitochondria and gives them bath of fresh air. Diseases treated using ozone therapy is infected wounds, circulatory disorders, geriatric conditions, macular degeneration, viral diseases, rheumatism/arthritis, cancer, skin healing and AIDS. Medication forms in a gaseous state are somewhat unusual and it is for this reason that special application techniques had to be developed for the safe use of ozone. This review summarizes biological effects, defines any possible damage by ozone and their preventive measures.

**Keywords:** Autohemotherapy. Interleukin-2. Ozone. Peroxidation. Red blood cells.

### INTRODUCTION

Ozone therapy acts as a form of oxygen therapy that stimulates mitochondria and gives them bath of fresh air. Oxygen is the most vital element required for human life and it is the key to good health. The best way to optimize health is to oxygenate every cell in our body. The more oxygen we have in our system, the more energy we produce and more efficiently we can eliminate wastes. Ozone is oxygen with an extra molecule added. It should be introduced in large quantities into the body so that the singlet oxygen molecule that is unattached and freely circulating will attack all immature, sick and deformed cells, which are foreign to the body, like viruses, bacteria, fungi etc. Thus, it increases the

stability of normal good healthy cells. It is the treatment of choice for a wide variety of diseases and has proven to be the safest medical therapy. Ozone also stimulates production of superoxide dismutase, catalase and glutathione peroxidase, which are the enzymes in our cell walls that protect our cells from free radical damage. A good normal cell is protected by anti oxidants. Ozone stimulates the production of anti oxidants and thus prevents the cells which are being attacked by the free radicals<sup>1</sup>. Because of the various applications of ozone, medical literature began to show serious interest in this topic.

## History

Ozone therapy has been in use since the 1800s and in 1896 the genius Nikola Tesla patented the first ozone generator in the US, later forming the 'Tesla Ozone Company'. After that the Institute for Oxygen Therapy-Healing was formed in Berlin and the man credited with founding naturopathy, Dr. Benedict Lust, began practicing in New York, and wrote many articles on ozone. This form of treatment is highly popular in Germany and in 1959; an ozone machine called "Ozonosan" was patented by Dr. Joachim Hansler which formed the basis of the expansion in German ozone therapy<sup>2-6</sup>.

## Definition

Oxygen/ozone therapy is a term that describes a number of different practices in which oxygen, ozone or hydrogen peroxide are administered via gas or water to kill disease microorganisms, improve cellular function and promote the healing of damaged tissues<sup>2</sup>.

## Ozone in nature

Ozone is a molecule consisting of three atoms of oxygen in a dynamically unstable structure due to the presence of mesomeric states<sup>7</sup>. It has a half-life of 40 min at 20°C and about 140 min at 0°C<sup>8</sup>. Ozone is produced by lightening in nature and by pulsing high currents of electricity through medical grade oxygen<sup>3</sup>. In nature it is abundant only in the stratosphere (20,000-30,000 m) where their concentration is about 16-20 mg/m<sup>9</sup>. In this layer, it is produced by the action of ultraviolet solar radiation and in turn, protects the earth from ultraviolet solar radiation. In recent decades, photochemical pollution of the lower atmosphere, caused by degradation of petroleum gas and volatile combustion products of oil, coal etc. has led to much higher ozone levels, especially in cities. In the stratosphere, chlorofluorocarbons in liquid refrigerants and spray cans have destroyed part of the protective layer, causing a "hole" at the South Pole. These events are widely reported in the mass media<sup>8,9</sup>.

## Industrial production of ozone

The most widely used process for the production of ozone is based on the following reaction:



For production of ozone, oxygen flows across an electric arc having a potential difference of about 10,000 Volt in an ozone generator. All components of which must resist oxidation, because ozone is one of the strongest oxidizing agents known and attacks most plastics (except polyethylene, polypropylene, silicone and teflon) and most ferrous materials (except stainless steel 316 and titanium). An ozone generator requires a photometer to monitor the ozone concentrations produced. They must also have a system for destroying unused ozone, which cannot be released into the atmosphere<sup>7-9</sup>.

Generators use several technologies to produce ozone:

- UV lamp – makes small amounts of ozone and is unreliable in making accurate concentrations. They burn out easily.
- Corona discharge – dual dielectric sealed systems produce ozone but also produce lots of heat which is both destructive to ozone and to the machine.
- Cold plasma generators – which produce ozone using low level current passed in 2 tubes of a noble gas between which an electrostatic plasma field is formed that ionizes the oxygen<sup>10</sup>.

## Mechanisms of action of ozone

### 1. Inactivation of bacteria, fungi, virus, yeast and protozoa

Ozone therapy disrupts the integrity of the bacterial cell envelope through oxidation of phospholipids and lipoproteins. In fungi ozone inhibits cell growth at certain stages. In viruses, ozone damages the viral capsid and upsets the reproductive cycle by disrupting the virus to cell contact with peroxidation. The weak enzyme coating on the cells which make them vulnerable to invasion by viruses and make them susceptible to oxidation and

elimination from the body, which then replaces them with healthy cells<sup>11,12</sup>.

## 2. Stimulation of oxygen metabolism:

Ozone therapy causes an increase in red blood cell glycolysis rate. This leads to stimulation of 2, 3 diphosphoglycerate which leads to an increase in amount of oxygen released to the tissues. Ozone stimulates the Krebs's cycle by enhancing the oxidative carboxylation of pyruvate and stimulating the production of ATP. It also causes a significant reduction in NADH and oxidizes cytochrome C. There is a stimulation of production of enzymes

which act as a free radical scavengers and cell wall protectors: glutathione peroxidase, catalase and superoxide dismutase. Production of prostacyline a vasodilator is also induced by ozone<sup>11,13</sup>.

## 3. Activation of immune system

Ozone administered at a concentration of 30 to 55  $\mu\text{g}/\text{cc}$  causes the greatest increase in the production of interferon and greatest output of tumor necrosis factor and interleukin-2. The production of interleukin-2 launches an entire cascade of subsequent immunological responses<sup>11,14</sup>.

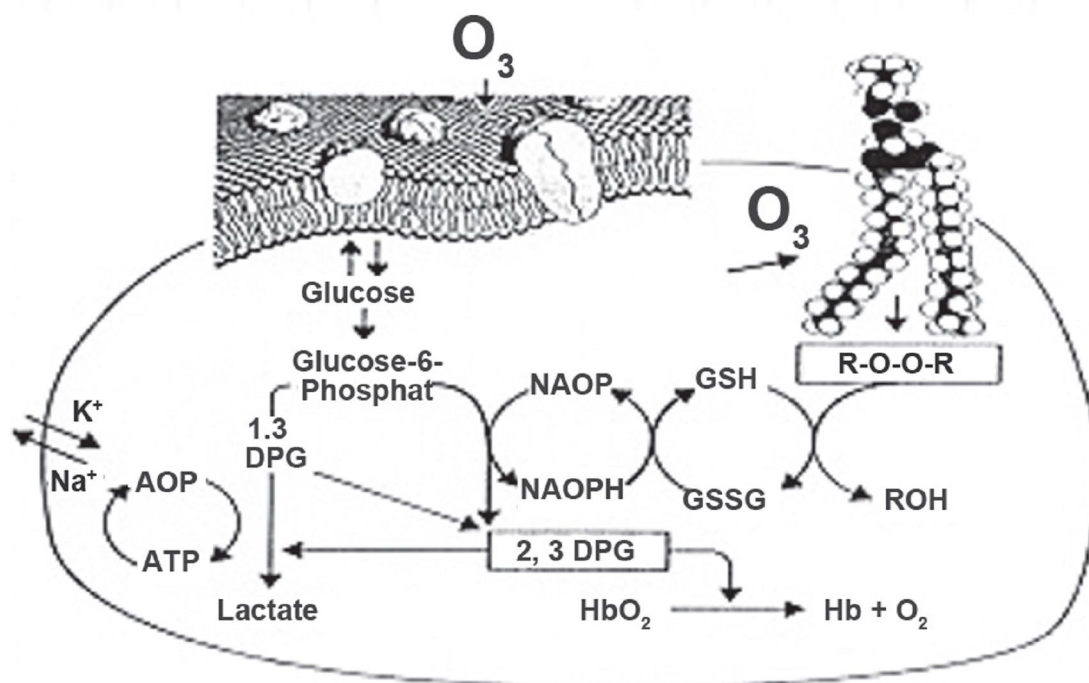


Fig. 1: Action of ozone on RBC Metabolism

### Method of administration

Administration can be through any route with modifications:

- Major auto-hemotherapy – Anticoagulated blood is mixed with ozone and is infused into a blood vessel. (It requires 200-250 mL of blood)
- Direct IV infusion – Ozone slowly administered into a major vessel.
- Rectal/vaginal insufflations – Humidified ozone is administered by catheter.
- Minor autohemotherapy – Blood mixed with ozone is injected intramuscularly. (It requires 5-10 mL of blood)
- Limb or body bagging – Body or parts are bathed in humidified ozone.

- Ozonated water – Dissolves easily in water to be used topically or consumed.
- Ozone in Saline – Can be used topically or given IV or SQ.
- Intra-articular administration – For joint healing and prolotherapy.
- Prolo/Sclerotherapy – Very good, less painful than other agents.
- Acupuncture – With ozone, more effective than B<sub>12</sub>.
- Ozonated olive oil – Ozone is bubbled through oil until the oil is thickened. This will produce ozonides that are not irritating and thus is applied topically even to eyes.
- Inhalation – Ozone that has been bubbled through olive oil and humidified will not irritate respiratory epithelium.
- Subconjunctival injection – For ulcers and keratitis sicca.
- Gingival and tooth apex injection – Can eliminate infection.
- Urinary bladder insufflation – For chronic inflammation.
- Disc protrusions – Prolotherapy, which can be injected at interspinous space and around facets, stabilize joints and accelerate healing.
- Auricular – Can be direct, humidified, or bagged with a homemade device made from IV bags and tubing<sup>10</sup>.

### Concomitant treatment

Anticoagulants such as heparin can be used to reduce the possibility of clotting during autohemotherapy<sup>15-17</sup>. Heat and ultraviolet irradiation can also be in autohemotherapy or intramuscular ozonated blood injections, presumably to enhance the antimicrobial activity of ozone<sup>18-20</sup>. The study on retinitis pigmentosa also used electrical stimulation, ocular surgery, vasodilators, B-carotene and multivitamins in conjunction with ozone<sup>21</sup>. For e.g. if ozone administration causes any respiratory irritation from out-gassing through the lungs, a bolus dose of 1 to 5 grams of vitamin C can be given and will eliminate any coughing instantly<sup>6,11</sup>.

### Monitoring of ozone therapy

It is technically impossible to measure ozone directly in the blood or assay ROS in ozonated plasma because of their very brief half-life (fractions of a second)<sup>7</sup>. However, there are indirect methods of monitoring the oxidizing action of ozone in the body through terminal products or biochemical modifications of the plasma antioxidant system. Indeed, it is possible to measure lipid peroxidation, antioxidant capacity and markers typical of oxidative status and enzyme activities in plasma. Many of these parameters are cumbersome to measure (for example, assay of isoprostanes and 8-hydroxyguanosine as markers of oxidative status) or time-consuming (enzyme activities) or without commercially available kits (2-3 diphosphoglyceric acid)<sup>22, 23</sup>. In this case two parameters of lipid peroxidation are used that are relatively easy to measure and give reproducible results:

#### 1. Assay of thiobarbituric acid reactive substances (TBARS)<sup>7</sup>:

Ozone in plasma reacts with unsaturated fatty acids to produce a vast range of aldehydes, including malonyldialdehyde (MDA). Determination of MDA gives an indication of the degree of peroxidation. The method, described by Buege & Aust, is a colorimetric determination based on reaction with thiobarbituric acid (TBA). This determination is useful in clinical practice, providing an indication of the degree of peroxidation of treated blood. Greater the peroxidation, greater is the concentration of TBARS<sup>24</sup>.

#### 2. Assay of protein thiol groups (PTG)<sup>25</sup>:

Plasma protein sulphhydryl groups are the first line of defense against oxidants. PTG are released in the reaction and can be detected by the Ellman reagent which produces a colored compound, measured by spectrophotometry. Ozone causes a decrease in PTG in plasma. The patterns of TBARS and PTG provide sufficient indication of peroxidation

status induced by ozone in clinical practice<sup>7,8</sup>.

### Dosage

The dosage of ozone used therapeutically in these studies was mainly reported in gammas. The conversion for gammas to more familiar units is as follows:

$1 \mu\text{g/ml} = 1 \text{ mg/l} = 1 \text{ g/m}^3 = 1 \text{ gamma}$

The dosage range reported in these studies varied from .00001 gammas (lonozone therapy)<sup>26, 27</sup> to 100 gammas (autohemotherapy)<sup>28</sup>.

**Table 1: Ozone doses used in autohaemotherapy**

Pathology	Ozone doses ( $\mu\text{g/ml}$ per gram of blood)	
	Initial	Final
Vascular disease	20	40
Degenerative disease	20	40
Infectious disease	25	70
Respiratory disease	20	40
Autoimmune disease	20	40
Metastatic cancer	25	80

### Case Studies

#### A. HIV/AIDS:

1. A cohort study of 9 patients with intermediate HIV as determined by CD4 lymphocyte count. These patients were treated with 4-8 weeks of intramuscular ozone injection treatment. This method of ozone administration reported no significant difference in lymphocyte count pre and post-treatment; HIV p24 antigen titer did not change significantly.
2. A cohort study of 4 patients with phase 2 AIDS treated with daily ozone autohemotherapy for 5-10 days reported an average increase in immunological response to all 3 mutagens examined. In addition, all symptomatic patients experienced clinical improvement and there were clinical trends that the patient's antibody mediated immunity was shifting back to a normal cellular mediated immunity. This was a promising outcome that may indicate a reversal of the AIDS related downward spiral of the

immune system. These results need to be verified with a larger controlled trial of patients from both phases.

3. A cohort study of 5 patients with AIDS-related intractable diarrhea were treated with 21-28 daily colonic ozone insufflation treatments reported that at the 6-month follow-up, 3 patients experienced complete resolution of diarrhea, 1 improved. The fifth patient, whose diarrhea was due to *Cryptosporidium*, experienced no change. There was no change in CD4/CD8 ratio pre- and post-treatment.

#### B. Skin healing:

1. A cohort study of 35 patients with gunshot wound-related skin grafts treated with ozone bagging techniques every other day for 10 days reported that 75% of skin grafts were successful with ozone, compared with only 40% of skin grafts without ozone<sup>21</sup>.
2. A cohort study of 200 patients with open wounds, ulcers, and pressure sores treated with lonozone therapy 2-7 times/week reported that 168 patients were healed, 19 had considerable improvement, 8 had some improvement, and 5 had no response<sup>29</sup>.
3. A cohort study of 10 patients with retinitis pigmentosa treated with ozone autohemotherapy, electrical stimulation, ocular surgery, vasodilators,  $\beta$  carotene, and multivitamins reported no significant change in visual acuity after 6-8 months<sup>21, 27</sup>.

#### Adverse events

As with other non-conventional therapies, safety is a primary concern. Adverse reactions of ozone that were revealed from the human studies are erythrocyte damage, hemolysis reduced glutathione concentration, reduced leukocyte viability, cytokine production and pancytopenia<sup>20, 30, 31</sup>.

### Major effects of ozone therapies

1. Ozone Therapy stimulates the production of white blood cells. These cells protect the body from viruses, bacteria, fungi and cancer. If, deprived of oxygen, these cells malfunction. They fail to eliminate invaders and even turn against normal, healthy cells (allergic reactions). Ozone significantly raises the oxygen levels in the blood for long periods after ozone administration; as a result, allergies have a tendency to become desensitized.
2. Interferon levels are significantly increased. Interferons are globular proteins. Interferon inhibits viral replication.
3. Ozone Therapy stimulates the production of Tumor Necrosis Factor. TNF is produced by the body when a tumor is growing. Ozone stimulates the secretion of Interleukin-2 (IL-2). IL-2 is one of the cornerstones of the immune system. It is secreted by T-helpers. T-helper causes it to produce more IL-2. Ozone's main duty is to induce Lymphocytes to differentiate and proliferate, yielding more T-helpers, T-suppressors, cytotoxic T's, T-delayed's and T-memory cells.
4. Ozone Therapy kills most bacteria at low concentrations.
5. Ozone is effective against all types of fungi. This includes systemic *Candida albicans*, athlete's foot, molds, mildews, yeasts, and even mushrooms.
6. Ozone fights viruses in a variety of ways. As discussed above, ozone also goes after the viral particles directly.
7. Ozone is antineoplastic. This means that ozone inhibits the growth of new tissue because rapidly dividing cells shift their priorities away from producing the enzymes needed to protect themselves from the ozone. Cancer cells are rapidly-dividing cells and are inhibited by ozone.
8. Ozone oxidizes arterial plaque. It breaks down the plaque involved in both Arteriosclerosis and Arthrosclerosis.
9. This means ozone has a tendency to clear blockages of large and even smaller vessels. This allows for better tissue oxygenation in deficient organs.
10. Ozone increases the flexibility and elasticity of red blood cells.
11. Ozone accelerates the Citric Acid Cycle. Also known as the Krebs cycle or TCA Cycle, this is a very important step in the glycolysis of carbohydrates for energy.
12. Ozone makes the antioxidant enzyme system more efficient.
13. Ozone degrades petrochemicals. These chemicals have a potential to place a great burden on the immune system<sup>7, 15-17</sup>.
14. Ozonized water is particularly used in dental medicine in a form of spray or compress.

### Merits of ozone therapies

Ozone therapies are thought to benefit patients in the following ways:

- It improves circulation, oxygenates hemoglobin, kills parasites, corrects dizziness, neutralizes acid and overcomes weakness
- It acts as cell energizer, vitality booster, immune enhancer, skin purifier, liver cleanser, blood purifier
- It kills viruses (ozone and hydrogen peroxide)
- It improves the delivery of oxygen from the blood stream to the tissues of the body
- It speeds up the breakdown of petrochemicals
- It increases the production of interferon and tumor necrosis factor, thus helping the body to fight infections and cancers
- It increases the efficiency of antioxidant enzymes
- It increases the flexibility and efficiency of the membranes of red blood cells

- It speeds up the citric acid cycle, which in turn stimulates the body's basic metabolism<sup>3,32</sup>.

### Demerits of ozone therapy

An array of ill effects are observed owing to the reactivity of ozone via oxidation, peroxidation or generation of free radicals and giving rise to cascade of reaction like peroxidation of lipids leading to changes in permeability<sup>33</sup>, lipid ozonation products (LOP) act as signal transducer molecules<sup>34</sup>. The main reason for this being presence of unsaturated fatty acids in both both lung lining fluid and pulmonary cell bilayers, ozone react with unsaturated fatty acids to give their specific products i.e. LOP, which activate the lipases triggering the release of endogenous mediators of inflammation<sup>35</sup>. The loss of functional groups in enzymes leads to enzyme inactivation. These reactions further results in cell injury or eventual cell death combination of ozone and NO<sub>2</sub> occur in photochemical smog have hazardous effects on lung alveoli and act additively or synergistically. Dietary antioxidants or free radical scavenger like Vitamin E, C, etc. can prevent aforementioned effects of ozone<sup>36-38</sup>.

### Recent development

1. Ozone is effectively used as an antibacterial agent to treat oral infections caused by *Actinomyces naeslundii*, *Lactobacilli casei* and *Streptococcus mutans*. Exposure of about 60 seconds exhibited 99.9% killing efficiency but exposure for such a long period showed degradation of saliva proteins. So exposure of 10 seconds to 30 seconds was proved effective to kill significant number of bacteria<sup>38</sup>.
2. A single subcutaneous injection of ozone in mouse with spared nerve injury of the sciatic nerve was found to decrease the neuropathic pain-type behaviour<sup>39</sup>.

### CONCLUSION

Considered an alternative therapy, Ozone therapy has been increasingly used in recent decades and has been found useful in various diseases: It activates the immune

system in infectious diseases; it improves utilization of oxygen and stimulates release of growth factors that reduce ischemia in vascular disease; it activates the immune system and may kill cancer cells but ozone must be used with utmost care that is too small may be useless and too much can be harmful. Thus researches should focus on this topic so as to find detailed mechanism of action of ozone increase its applications.

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