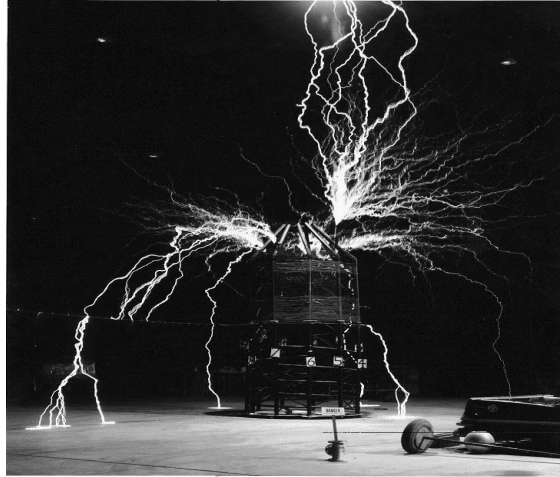


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## **Bio-oxidative therapies: Oxygen, Ozone & H<sub>2</sub>O<sub>2</sub>**

**August 1996**

**edited by**

**M.H.T.Evers**

*Foundation for Alternative Science & Technology (FAST) in cooperation with Ozone Services presents an edited collection of articles downloaded from Internet.*

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Maurice H.T. Evers

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# Table of Contents

- **Ozone: Life-Threatening Pollutant or Powerful Healing Agent?**
- **Oxygen, Ozone and Medicine**
- **AIDS and Cancer Cured by Hyper-Oxygenation**
  - **Using 35% Food Grade Hydrogen Peroxide (H<sub>2</sub>O<sub>2</sub>) - Internal**
- **Ozone - Breath of Life**
- **Oxygen Therapy - The Empire Strikes Back**
- **Ozone is not Smog, Ozone is Good and Natural**
- **What is Ozone Therapy?**
- **Oxygen Radicals: A Commonsense Look at Their Nature and Medical Importance**
- **Pioneers in Ozone Therapy**
- **What you need to know about ozone/oxygen therapy.**
- **A Unique Function for Ascorbate**
- **Generation of H<sub>2</sub>O<sub>2</sub> in Biomembranes**
- **The Wizard of Ozone**
- **Canadian Medical Research Mystery - DOD Positive Ozone / HIV Results Ignored**
- **H<sub>2</sub>O<sub>2</sub> has a role in cellular regulation**
- **Artificial Ionization of the Air**
- **Hyperbaric oxygen therapy**
- **Hyperbaric oxygen: more indications than many doctors realise.**
- **Reactive oxygen species in living systems: source, biochemistry, and role in human disease.**
- **Ozone Applications: An In-Depth Discussion**
- **Physicochemical and Pharmacological Aspects of Ozone Therapy**
- **Negative Ions & Moods/Sleep/Cognitive Ability Etc.**
- **Air Ionization and its Effects on Well Being and Stress and its Biological Effects (The Third Wave).**
- **Ozone in Medicine: Overview and Future Directions**
- **Comparison of effects on tissue oxygenation of hyperbaric oxygen and intravascular hydrogen peroxide**
- **Comparison of Arterial and Tissue Oxygen Measurements in Humans Receiving Regional Hydrogen Peroxide Infusions and Oxygen Inhalation**
- **Regional Arterial and Tissue Oxygen Tensions in Man During Regional Infusion with Hydrogen Peroxide Solutions**
- **Hydrogen Peroxide/Ozone for municipal water supplies?**
- **Hydrogen Peroxide Facts**
- **Indoor Ozone Health Concern: A Statement of the American Lung Associations in Minnesota**
- **Ozone-therapy Today**
- **Ozone in Preventive Medicine**
- **Swimming Pools and Hot Tubs**
- **What is Medical Ozone**
- **Ozone: A Wide-Spectrum Healer**
- **What is Oxidative Therapy?**

- **Growing Demand for Oxygen Therapies**
- **A Dream Come True**
- **Pure Oxygen May Aid Heart Attack Victims Medicine: Preliminary research finds that pressurized chamber used to treat 'the bends' in divers can lessen chest pain and help keep cardiac muscle tissue alive.**
- **Hyperbaric oxygen for treatment of closed head injury.**
- **My experiences with O<sub>2</sub>/O<sub>3</sub>**
- **Chlorine out, ozone in as water purifier**

# **Ozone: Life-Threatening Pollutant or Powerful Healing Agent?**

by Nathaniel Altman  
author of Oxygen Healing Therapies

It's summer in New York City and the National Weather Service has posted another ozone advisory. A grayish haze hangs over the entire metropolitan area, and the air tastes gritty and stale. Young children and adults with lung problems are told to stay indoors, because ozone can aggravate allergies, bronchitis, asthma and other health problems. That's because when combined with carbon dioxide, peroxyacetyl nitrate and other gases (caused by auto exhaust, factories and power plants), ozone becomes a dangerous pollutant. It can not only damage the sensitive surfaces of the respiratory tract and the lungs, but also corrodes buildings and monuments. It can kill the leaves of the trees and also damages crops. In large urban centers like Los Angeles, Sao Paulo and Mexico City, ozone-laden smog has become a major threat to human health. It is no wonder why so many people have negative feelings about it.

Yet at a clinic on West 72nd Street in the heart of Manhattan, the treatment room is filled with patients who are paying up to \$100 to have ozone and oxygen infused into their veins. They believe that ozone will help heal them of cancer, heart disease, candida, HIV-related problems and a host of other diseases. Over ten million people have been treated in Europe with ozone, and many swear by its' safety and effectiveness.

There are few elements that have been as controversial as ozone, and none that have created such a medical paradox: how can a gas be both dangerous to health as a pollutant, yet can also be used to effectively treat some of humanity's most threatening diseases?

## **Ozone: The Basics**

Ozone is an elemental form of oxygen occurring naturally in the Earth's atmosphere, it surrounds the Earth at an altitude of between 50,000 and 100,000 feet.<sup>1</sup> As a pale blue gas that condenses to a deep blue liquid at very low temperatures, it is created in nature when ultraviolet energy causes oxygen atoms to temporarily recombine in groups of three. Ozone is also formed by the action of electrical discharges on oxygen, so it is often created by thunder and lightning. When we go outside after a thunderstorm, the air seems to smell like freshly-mown hay. This is due to the small quantities of ozone generated by the storm. Ozone is also produced commercially in ozone generators, which involve sending an electrical discharge through a specially-built condenser containing oxygen. Because it is made up of three atoms of oxygen, ozone is known chemically as O<sub>3</sub>. The newly-formed molecule is quick to react with other substances.

Then occurring in the upper atmosphere, ozone forms a protective layer that absorbs much of the sun's ultraviolet radiation, which can cause mutation, cancer, sunburn, immunosuppression and other problems. If it were not for the ozone layer, the survival of animal and plant life on this planet would be impossible. The depletion of the ozone layer by the use of

chloroflourocarbons (CFC's), mostly released into the atmosphere by refrigerators, air conditioner and aerosol containers is of grave concern to scientists and physicians the world over. In addition to the health problems just mentioned, ultraviolet radiation has also been cited as a factor in poor crop growth, such as certain species of grains. After many years of study and a considerable degree of procrastination on the part of industry and government, efforts are finally being made to phase out the use of CFC's completely within the next few decades.\*

However, ozone becomes a pollutant in the lower atmosphere when hydrocarbons (like carbon dioxide and nitrogen oxide) from vehicular exhaust and other sources combine with ozone in sunlight, creating photochemical smog. As a result, new and often highly corrosive pollutants are formed. The number of possible chemical reactions that can occur when ozone is combined with these oxides can reach into the hundreds. The effects of ozone-laden smog has been linked to acid rain, a variety of lung-related diseases and the oxidation of buildings and monuments, especially in cities where smog is frequent. Scientific studies in this country have emphasized the negative effects of ozone on breathing. This may be one reason why physicians and others feel that ozone is not only medically useless, but is a dangerous substance to take into the body under any circumstances. However, the value of ozone cannot be dismissed so easily.

### **Properties and Uses**

First "discovered" until 1840 by the German chemist Christian Frederick Schonbein at the University of Basel in Switzerland, ozone gas was used for the first time to disinfect operating rooms in 1856, with the first water treatment plant to use ozone to purify municipal water supplies built in Monaco in 1860. Purifying water with ozone simple: a small amount of ozone is added to oxygen and bubbled through the water. Not only does it kill viruses and bacteria, but it removes the microorganisms that cause bad taste and odor in the water as well.

Ozone is powerful oxidizer that can kill a wide variety of viruses, bacteria and other toxins. It also oxidizes phenolics (a poisonous compound of methanol and benzene), pesticides, detergents, chemical manufacturing wastes and aromatic (smelly) compounds more rapidly and effectively than chlorine, yet without its harmful residues.<sup>2</sup> For this reason, ozone has become the element of choice to disinfect and purify drinking water and wastewater through a wide variety of applications.

#### **1. Municipal water treatment.**

More than a hundred different viruses that are excreted in human feces can be found in contaminated drinking water. Viruses like those associated with hepatitis infect thousands of people a year, and survive for a long period of time in potable water. As a potent virucide, ozone is seen as an effective alternative to chlorine, which (in addition to leaving undesirable tastes and odor) may yield chloroform and other compounds that are potentially carcinogenic.<sup>3</sup> According to The Encyclopedia of Chemical Technology:

"Chlorination as it is practiced in potable-water treatment plants cannot adequately remove viruses to an acceptable level. The complete control of viruses by ozone at low dosage levels is well documented."<sup>4</sup>

As a potent oxidizer, ozone kills bacteria by rupturing the cell wall. Among the harmful microorganisms that ozone can oxidize are *Escherichia coli*, *Streptococcus fecalis*, *Mycobacterium tuberculosis*, *Bacillus megatherium* (spores) and *Endamoeba histolytica*. The Encyclopedia of Chemical Technology reports that:



"Ozone displays an all-or-nothing effect in terms of destroying bacteria. This effect can be attributed to the high oxidation potential of ozone. Ozone is such a strong germicide that only a few micrograms per liter are required to measure germicidal action."<sup>5</sup>

Today more than 2500 municipalities around the world purify their water supplies with ozone, including Los Angeles, Paris, Montreal, Moscow, Kiev, Singapore, Brussels, Florence, Turin, Marseilles, Manchester and Amsterdam.

Ozone has also been used to purify the water in public swimming pools since 1950. During the Olympic Games held in Los Angeles during the summer of 1984, the European teams insisted that the water in the swimming pools be treated with ozone (as opposed to chlorine) or they would not participate in the events.

## **2. Ozone in Industry**

Ozone is used by the bottling industry to disinfect the inside of soda and beer bottles. The ozone later disappears as it decomposes to oxygen. Brewers also use ozone to remove any residual bad taste and odor from the water used in beer production. Ozone is also utilized by the pharmaceutical industry as a disinfectant, and in the manufacture of electrical components to oxidize surface impurities. Ozone concentrations of 1 to 3 parts per million are used to inhibit the growth of molds and bacteria in stored foods like eggs, meat, vegetables and fruits.<sup>6</sup>

## **3. Wastewater Pollution Control**

Ozone can break down industrial wastes like phenol and cyanide so that they become biodegradable. It is often utilized to oxidize mining wastes, wastes from the photographic industry, and the oxidation of harmful compounds like heavy metals, ethanol and acetic acid.<sup>7</sup>

Ozone is also used to disinfect municipal wastewater, and to clean up lakes and streams that have become polluted by sewage and other pollutants. Unlike chlorine, ozone can clean up a lake or stream without killing the resident animal life nor leaving potentially harmful chemical residues in the ecosystem.

## **4. Air and odor treatment**

In the United States, over 100 ozone generators are used by both municipalities and private companies to remove noxious odors from treated sewage. Sewage contains high amounts of foul-smelling chemicals like sulfides, amines and olefins. Ozone gas does not mask their odors: it oxidates these compounds and renders them odor-free.

Ozone is also used to reduce odors in rendering plants, paper mills, compost operations, underground railways, tunnels and mines. The food industry uses minute amounts of ozone to treat odors in dairies, fish processing plants, and slaughterhouses.<sup>6,7</sup>

## **5. Medical Ozone**

After the turn of the century, interest began to focus on the uses of ozone in medical therapy. The Berlin physician Albert Wolff first utilized ozone to treat skin diseases in 1915, and the German Army used ozone extensively during World War I to treat a wide variety of battle wounds and other infections.

However, it was not until 1932 that ozone was seriously studied by the scientific community, when ozonated water was used as a disinfectant by Dr. E.A. Fisch, a German dentist. One of

his patients was the surgeon Erwin Payr, who immediately saw the therapeutic possibilities of ozone in medical therapy. Dr. Payr, along with the French physician P. Aubourg, was the first medical doctor to apply ozone gas through rectal insufflation to treat mucous colitis and fistulae. In 1945, Payr pioneered the method of injecting ozone intravenously for the treatment of circulatory disturbances.

The first physician to treat cancer with ozone was Dr. W. Zable in the late 1950's, followed by Drs. P.G. Seeger, A. Varro, and H. Werkmeister. During the next twenty years, hundreds of German physicians began using ozone in their practice to treat a wide variety of diseases (both alone and as a compliment to traditional medical therapy) through a number of applications, which we will discuss later on. Horst Kief, M.D. is believed to be the first doctor to use ozone therapy to successfully treat patients infected with HIV.

Today some 8000 licensed health practitioners (including medical doctors, homeopathic physicians and naturopaths) in Germany use ozone in their practices, while some 15,000 practitioners use ozone on the European continent, either alone or as a compliment to other therapies. While considered "experimental" by North American scientists, the medical uses of ozone are well-known and well-established outside the United States.

### **Research in Medical Ozone**

Since the end of World War II, literally hundreds of laboratory and clinical studies in the medical uses of ozone have been done, primarily in Europe, and their findings have been published in a variety of scientific and medical journals. Most have been published in German, with the exception of those of findings first reported at international medical conferences sponsored by the International Ozone Association, which were presented in English. At the present time, the bulk of scientific research in the medical uses of ozone are being undertaken in Cuba, Russia and Germany, where researchers receive the cooperation and support of the government and major universities. Research is going on to a far lesser extent in the United States, France, Italy, Mexico and Canada.

However, one recent Canadian study received world-wide attention. Published in the Canadian Medical Association Journal, it showed that ozone kills the human immunodeficiency virus (HIV), the hepatitis and herpes viruses and other agents in the blood used for transfusion. The article's author added: "The systemic use of ozone in the treatment of AIDS could not only reduce the virus load but also possibly revitalize the immune system."<sup>8</sup>

Some of the most exciting research in ozone therapy is taking place in two unlikely countries: Russia and Cuba. It has been approved by the health ministries of both countries and is fast becoming part of the medical mainstream.

Why are the Cubans and Russians so interested in ozone? Citizens of both countries have enjoyed socialized medicine for decades, so private drug manufacturers and private hospitals and clinics have traditionally played a small or nonexistent role in determining the direction of the health care system. As mentioned before, ozone cannot be patented, it is extremely cheap to produce, and can be used effectively in a wide range of therapeutic applications. In countries like the United States, where large drug companies are directly or indirectly involved in all medical research and lobby to influence governmental policy, there is simply no interest in

researching the possibilities of ozone therapy. Yet in countries where the profit motive is absent from health care, physicians, chemists and other researchers traditionally enjoy both government support and funding for their work.

### **Medical Applications**

The applications for ozone in medical therapy were first documented in European medical journals in the mid-1930's. Since that time, over 1000 articles have been published in medical and scientific journals, mostly in German, Russian and Spanish.

Used primarily to kill viruses, destroy bacteria and eliminate fungi, ozone produces a number of important benefits in the human body, including the oxygenation of blood, improved blood circulation, and stimulating the oxygen-producing facility in human tissues. It is also an important immunoregulator. For these reasons, the range of human health problems that can respond favorably to ozone therapy is quite broad. According to Drs. Siegfried Rilling and Renate Viebahn in their book *The Use of Ozone in Medicine*, physicians have used ozone therapy in the areas of angiology (blood vessels), dermatology, (including allergology and proctology), gastroenterology, gerontology, intensive care, gynecology, neurology, odontology (dental medicine), oncology, orthopedics, proctology, radiology, rheumatology, surgery (including vascular surgery) and urology.<sup>9</sup> As the Canadian report cited earlier indicated, ozone has been proven to effectively purify human blood supplies.

According to the Europe-based Medical Society for Ozone<sup>10</sup> (with branches in Germany, Austria, Italy and Switzerland) and the National Center for Scientific Research in Cuba<sup>11, 12, 13</sup> physicians are currently treating the following diseases with different forms of ozone therapy:  
Diseases Treated with Ozone Therapy:<sup>10</sup>

- Abscesses
- Acne
- AIDS
- Allergies (hypersensitivity)
- Anal fissures
- Arthritis<sup>11</sup>
- Arthrosis<sup>12</sup>
- Asthma<sup>13</sup>
- Cancerous tumors
- Cerebral sclerosis
- Circulatory disturbances
- Cirrhosis of the liver
- Climacterium (menopause)
- Constipation
- Corneal ulcers<sup>11</sup>
- Cystitis
  
- Decubitus (bedsores)
- Diarrhea<sup>11</sup>
- Fistulae
- Fungal diseases
- Furunculosis

Gangrene  
 Gastro-doudenal ulcers <sup>11</sup>  
 Gastro-intestinal disorders  
 Giardiasis <sup>11</sup>  
 Glaucoma <sup>11</sup>  
 Hepatitis  
 Herpes (simplex and zoster)  
 Hypercholesterolemia  
 Mucous colitis  
 Mycosis <sup>11</sup>  
 Nerve-related disorders  
 Osteomyelitis  
 Parkinson's disease  
 Polyarthritits  
 Raynaud's disease  
 Retinitis pigmentosa <sup>11</sup>  
 Rheumatoid arthritis <sup>11</sup>  
 Scars (after radiation)  
 Senile dementia <sup>11</sup>  
 Sepsis control <sup>11</sup>  
 Sinusitis <sup>11</sup>  
 Spondylitis  
 Stomatitis  
 Sudeck's disease  
 Thrombophlebitis  
 Ulcus cruris (open leg sores)  
 Vulvovaginitis <sup>11</sup>  
 Wound healing disturbances

### **Ozone in the Dentist's Office**

Since one of the pioneers in ozone therapy was a dentist, it is important to mention that ozone has an important place in dental practice as well. According to the German dentist Fritz Kramer, ozone, such as in the form of ozonated water, can be used in the following ways:\*

1. As a powerful disinfectant.
2. In its ability to control bleeding.
3. In its ability to cleanse wounds in bones and soft tissue
4. By improving the local supply of oxygen to the wound area, ozone can improve healing.
5. Ozonated water can increase temperature in the area of the wound, and this improve the metabolic processes related to healing.

Dr. Kramer points out that ozonated water can be used in a number of different ways:

1. As a mouth rinse (especially in cases of gingivitis, paradentosis, thrush or stomatitis);
2. as a spray to cleanse the affected area, and to disinfect oral mucosa, cavities and in general dental surgery;
3. As an ozone/water jet to clean cavities of teeth being capped, receiving root canal therapy, and in treating painful gingivitis and stomatitis.<sup>14</sup>

### **How is Ozone Therapy Applied?**

Over the past sixty years, over a dozen methods have been developed in the application of ozone in medical therapy. In most cases, tiny amounts of ozone are added to pure oxygen (usually consisting of 0.05 parts of ozone to 99.95 parts of oxygen for internal use and 5 parts of ozone to 95 parts of oxygen for external applications). The exact amount used is determined on a case by case basis, as physicians have found that not enough ozone can be ineffective, while too much ozone can be immuno-suppressive. At the present time, there are eight simple methods and one highly complex method of ozone therapy that are used in medical practice.

### **1. Direct Intra-arterial and intravenous application**

An ozone/oxygen mixture is slowly injected into an artery or vein with a hypodermic syringe. This method is used primarily for arterial circulatory disorders. According to Gerard V. Sunnen, M.D., "Due to accidents produced by too rapid introduction of the gas mixture into the circulation, this technique is now rarely used".<sup>15</sup>

### **2. Rectal insufflation**

First pioneered by Payr and Aubourg in the 1930's, a mixture of ozone and oxygen is introduced through the rectum and absorbed into the body through the intestine. Used for a wide variety of health problems, this method is considered one of the safest. In a typical treatment for ulcerative colitis, for example, 75 micrograms of ozone per milliliter of oxygen are used (treatment begins with 50ml of oxygen which can be increased slowly to 500 ml per treatment) 16 While administered under medical supervision in Germany, Russia and Cuba, a growing number of private individuals in the United States use this method for self-treatment for cancer, HIV-related problems and other diseases.

### **3. Intramuscular injection**

A small amount of an ozone and oxygen mixture (up to 10 ml) are injected into the patient (usually in the buttocks) like a normal injection would be. This method is commonly used to treat allergies and inflammatory diseases. Intramuscular injections are sometimes utilized as an adjunct to cancer therapies in Europe.

### **4. Major and minor autohemotherapy**

Used since the 1960's, minor autohemotherapy involves removing a small amount (usually 10 ml) of the patient's blood from a vein with a hypodermic syringe. The blood is then treated with ozone and oxygen, and given back to the patient with an intramuscular injection. Thus the blood and ozone becomes a type of auto-vaccine given to the patient that is derived from their own cells, thus forming a unique vaccine that can be very specific and effective in treating the patient's health problem.

Major autohemotherapy calls for the removal of between 50-100 ml of the patient's blood. Ozone and oxygen are then bubbled into the blood for several minutes, and then the ozonated blood is re-introduced into a vein. These methods have been used successfully to treat a wide variety of health problems, including herpes, arthritis, cancer, heart disease and HIV-infection. It is probably the most commonly-used type of ozone therapy today.

### **5. Ozonated water**

This method calls for ozone gas to be bubbled through water, and the water is used externally to bathe wounds, burns and slow-healing skin infections. It is also used as a disinfectant by dentists who perform dental surgery. In Russia, physicians are using ozonated water to irrigate

body cavities during surgery. In both Russia and Cuba, ozonated water is used to treat a wide variety of intestinal and gynecological problems, including ulcerative colitis, duodenal ulcers, gastritis, diarrhea and vulvovaginitis.<sup>17</sup>

### **6. Intra-articular injection**

In this method, ozone gas is bubbled through water and the mixture is injected directly between the joints. It is used primarily by physicians in Germany, Russia and Cuba to treat arthritis, rheumatism and other joint diseases.

### **7. Ozone bagging**

This non-invasive method uses a specially-made plastic bag that is placed around the area to be treated. An ozone/oxygen mixture is pumped into the bag and the mixture is absorbed into the body through the skin. Ozone bagging is primarily recommended for treating leg ulcers, gangrene, fungal infections, burns and slow-healing wounds.

Ozone in a "sauna bag" (which leaves the head uncovered) is now being used to treat more generalized health problems, such as HIV-infection. Typically the patient would take a arm shower and get into the bag. Pure oxygen mixed with small amounts of ozone are then pumped into the bag for a period of twenty to thirty minutes, making contact with all skin surfaces. The skin absorbs the ozone. According to Dr. Sunnen: "Surprisingly, the mixture is able to penetrate far enough into the capillary networks to raise blood oxygen pressure. Presumably then, ozone is able to exert its biochemical influence."<sup>18</sup>

### **8. Ozonated oil**

Used primarily to treat skin problems, ozone gas is added to olive oil and applied as a balm or salve for long-term, low-dose exposure. Other bases (such as sunflower oil) for salves and creams have been developed in Cuba and are applied externally to treat a wide variety of problems including fungal infections (including athlete's foot), fistulae, leg ulcers, bed sores, gingivitis, herpes simplex, hemorrhoids, vulvovaginitis, bee stings, insect bites, acne and other skin-related problems.

The Cubans are also using capsules filled with ozonized oil to treat gastro-duodenal ulcers, gastritis, giardia and peptic ulcers.

### **9. Inhalation of ozone**

The lungs are the organs most sensitive to ozone. Physicians who use medical ozone warn that inhaling ozone into the lungs can bring about alterations in the density of the lung tissue, can damage delicate lung membranes, irritate the epithelium [the surface layer of mucus] in the trachea and bronchi, and can lead to emphysema. They caution users that no ozone should escape into the room in which it is being used. Modern medical ozone generators are specially designed so that the accidental escape of ozone gas cannot take place. Dr. Stephen A. Levine, the co-author of *Antioxidant Adaptation*, cautions people against using commercial air purifiers which generate small amounts of ozone to clean the air, since ozone should not be inhaled.

Having said this, it is important to point out that in Russia, tiny amounts of ozone are being added to oxygen for short-term therapeutic inhalation in certain cases. This has been done with patients suffering from carbon-monoxide poisoning, and doctors have been impressed with the

results. No adverse effects were observed.<sup>19</sup>

Although ozone can be dangerous when mishandled, ozone therapy is safe when administered by a qualified practitioner at established protocols. A 1982 German study of 384,775 patients (5,779,238 treatments) documented only a 0.0007% rate of adverse side effects. However, some physicians believe that direct IV application of ozone is dangerous.

We need to develop a deeper awareness of the importance of ozone, and learn to view it in a broader perspective. On one hand, we must work to reduce the pollutants which combine with ozone in the lower atmosphere by conserving the energy we use at home and at work, buying products that can be repaired instead of replaced, using our cars less, walking and riding bicycles more, and taking public transportation whenever possible will help. At the same time, we must support the use of alternatives to the many dangerous chemicals that destroy the fragile ozone layer which is rapidly being depleted.

At the same time, we can educate ourselves in the therapeutic use of medical ozone. As an inexpensive gas that is readily available, simple to produce, and safe to use, the potential of medical ozone in both preventing and treating disease is enormous. Its use can not only help solve the nation's health care crisis (by providing cheap and safe preventative as well as crisis care), but can help eliminate much of the suffering brought about by the side effects of chemotherapy, surgery and other invasive medical procedures.

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# Oxygen, Ozone and Medicine

by Saul Pressman

As we look around in the world from our vantage point in North America, we see intransigent civil wars and bloody tribal conflicts, economic instability, increasing exploitation of natural resources, mounting population and mounting pollution. There is an epidemic of AIDS and an epidemic of cancer. Tuberculosis is rising again, and new viral infections seem to pop up weekly, as in the native population in the southwest last fall, and the flesh eating staphylococcus.

The situation seems to grow worse daily and the modern doctor has tools of little power to combat these rising health concerns. Antibiotics are losing their effectiveness, prescription drugs kill at least 150,000 people a year in the US, and the chemical/drug companies lobby harder than ever to eliminate the competition--vitamins and natural herbs and the naturopaths that prescribe them. Health care in America costs an estimated two billion dollars each and every day, yet the population grows sicker yet.

Into this gloomy scenario has come a breath of fresh air--an old and proven treatment that American doctors mostly abandoned, but European doctors nurtured and developed. That treatment is medical ozone. It was first used over one hundred years ago and found to be of great value.

In 1896, the electrical genius Nikola Tesla patented an ozone generator and in 1900 founded the Tesla Ozone Co. Many doctors treated patients with Tesla's ozone and got excellent results. However, the corrosiveness of the gas to rubber equipment made ozone treatment unpopular with American physicians, and most had dropped it by the thirties under pressure from the AMA. Tesla developed another type of ozone generator in the twenties, based on a cold plasma principle, but the materials for handling it still did not exist. Also in the twenties, Tesla developed magnesium dioxide and gave it to Dr. Blass, who used it with good results, marketing it as Homozone.

In Germany, during the First World War, a Dr. A. Wolff used ozone on a variety of problems, from gangrene to trench foot to chlorine gas burns to influenza, with great effect. His work and results were written up in German medical journals of the time.

But it was not until the fifties, through the efforts of Dr. Hansler in Germany, that ozone came into its own. With the aid of modern materials including resistant plastics, and with the development of modern ozone generators, it became possible to safely handle and administer medical ozone.

Since that time, over ten million patients have been treated with ozone, with many millions of doses given, by more than 7,000 doctors. It has proven to be the safest medical treatment of all time, with less than ten deaths in fifty years, and with less than 1500 people found to be allergic to ozone in all that time.

Medical ozone has already proven effective against over 100 diseases, and the list grows daily. Since no anaerobic bacteria, virus, protozoa or fungus can live in a high oxygen atmosphere, all diseases caused by these agents are curable with ozone. Patients with cancer, AIDS, tuberculosis, arthritis, heart disease, stroke, etc., are cured by therapeutic applications of ozone almost without exception, and without serious side effects.

These are the facts regarding medical ozone use in Europe. President Reagan received ozone treatment for cancer when he was in Germany in 1986. Members of the FDA have taken their wives to Germany for treatment of breast cancer. NATO has adopted ozone for cleaning the

blood supply, and the Canadian Armed Forces are about to.

Ozone, because of its powerful antiviral / antibacterial / antiprotozoal abilities is the treatment of choice for the water supply in over 3000 municipalities around the world, including almost all the major cities: Paris, Brussels, Moscow, Zurich, Amsterdam, Florence, Singapore, New York, Tampa, Dallas, Los Angeles, etc. It is also employed to treat sewage to such high standards that it is often returned to the input in true recycling. It is becoming the top option for industry to clean its waste, and in the case of pulp mills, mandatory. ozone is replacing chlorine throughout the world, as the carcinogenic dangers of organochlorides are being realized. We are not far away from a worldwide ban on the production of chlorine, which will rid us of a dangerous environmental pollutant. There are over 100 cities using ozone in the U.S. today with many more planned.

But on the medical front, the FDA fights a cynical battle against doctors who are determined that their patients shall not die of AIDS or cancer or ALS or MS or any of the multitude of other diseases that ozone cures, but which no chemical drug touches. But no matter how hard the FDA persecutes these healers, the tide is turning and the outcome is inevitable. Medical ozone treatment will take its rightful place as the leading therapeutic remedy.

Recently, there has been a last-ditch effort by the drug companies to slur ozone as harmful to humans, by promulgating a huge propaganda effort about so-called anti-oxidants. A flood of vitriol has been poured out to make people believe that oxygen is harmful to the system, that it causes cell damage and ageing due to being a free radical. Let us examine these claims.

The human body is composed of nearly 60% oxygen, about the same as the composition of the earth's crust. The human body is about 70% water, also about the same as the surface of the earth. We can survive for about a week without water, and for about a month without food, but we can only live for a few minutes if we are deprived of oxygen. It is our body's most critical need. Oxygen is involved in all the major processes in the body, from respiration to digestion to assimilation to elimination to reproduction. If we have insufficient oxygen in our system, these critical functions will operate poorly, and our health will suffer.

If there is insufficient oxygen for the cell to burn sugar for energy, the carbon in the sugar will be changed into carbon monoxide, instead of carbon dioxide. Carbon monoxide is very difficult for the body to eliminate and so it build up in the body, irritating the organs, and lowering body temperature. The body fights diseases by raising the temperature briefly, which we call fever, in order to "burn out the bug."

Poorly oxygenated cells are good news to an oxygen-shunning anaerobic bacteria or a virus. With less oxygen available than they need, cells are unable to make their defensive enzyme shields strong enough, and viruses can invade and force the cell to replicate viruses. The defensive enzyme shields produced by healthy cells are composed of four major enzymes: super oxide dismutase, reductase, glutathione peroxidase and catalase. As long as the cell maintains this enzyme shield, viruses cannot penetrate them and ozone cannot harm them.

Disease microbes have no enzyme shields. When medical ozone is introduced into the area, it attacks microbes without a coating and diseased cells with deficient cell wall enzymes. It oxidizes them, allowing them to be cleared from the body and replaced with new healthy cells.

Free radicals are atoms with unpaired electrons, a natural occurrence in biochemical reactions. There could be no life without free radicals. The properties of free radicals vary widely: some are toxic to all living cells, others only to the most vulnerable cells. Singlet oxygen,  $O_1$ , is a highly reactive free radical that acts as a scavenger of other free radicals. The oxygen combines with them to render them harmless, thereby protecting cells from damage.

The so-called anti-oxidant enzymes are gaining in popularity as nutritional supplements. They

are not antioxidant at all, but rather are either free radical scavengers, or enzyme enhancers. They have been shown to help protect marginally healthy cells from general free radical damage. Super oxide dismutase in particular has helped reduce a variety of disorders: normally it is among the body's most plentiful enzymes. However, prolonged use of supplements could tend to atrophy the internal biochemical processes that would normally be making these enzymes. In any case, it does not address the cause of the problem: oxygen starvation at the cellular level, which makes the cells too weak to make the enzymes that protect them from disease.

The wide application of ozone in medicine is based on the simple principle that diseased cells cannot exist in the presence of ozone, and that cells cannot become diseased if they are supplied with sufficient oxygen.

In the end, if there were any truth at all to ozone or oxygen therapy being harmful to humans, the evidence would have become clear forty years ago. There is no such evidence, proving the absolute safety of medical ozone. Later generations will look back in amazement at the unbelievable opposition mounted against such a safe and efficacious medical treatment.

Mr. Pressman is President of Ozonifier Industries Inc., producers of the finest quality ozone generators available. The "Ozonifier" series of generators use the PLASMAFIRE (TM) GLASS TUBE technology. The PLASMAFIRE (TM) GLASS TUBE is the perfection of an ozone generator invented by Nikola Tesla in the 1920s. Tesla never patented it, because he was not satisfied with its performance, due to the materials available at the time. With the advent of modern materials, and some ingenious engineering, Ozonifier Industries Inc. was able to perfect this Tesla design. For more information on the "Ozonifier" series of generators, please call 604-532-9596.

# **AIDS AND CANCER CURED BY HYPER-OXYGENATION**

This file is taken from an uncopyrighted newsletter/article called NOW WHAT issue #1 1987. Their address and subscription details are at the end of this file.

The information presented in this article has been suppressed by the medical community for decades due to the repercussions it would have on the pharmaceutical industry. Fortunately some doctors do not feel the same as the general community and are using these processes to cure people. Several dozen AIDS patients have not only reversed their death sentences, but are now back at work, completely free of the disease. They destroyed the virus in their blood by hyper-oxygenation, known in various forms as oxygen therapy, bio-oxidative therapy or autohemotherapy. This is a simple, inexpensive and very broad spectrum process that many feel could force a complete overhaul of the medical industry. The two basic types of oxygen therapy are ozone blood infusion, and absorption of oxygen water (hydrogen peroxide) at very low concentrations. It turns out that the AIDS virus cannot tolerate high oxygen levels in its victims' blood. Not only that, every other disease organism tested so far has the same weakness. Even cancer growths contract and disappear when the oxygen saturation is sufficiently increased in the fluids surrounding them, since they are anaerobic. AIDS, herpes, hepatitis, Epstein Barr, cytomegalovirus and other lipid envelope virus are readily destroyed by hyper-oxygenating the patients blood with ozone. This was demonstrated by among others Dr. Horst Kief in Bad Hersfeld, West Germany. Dr. Kief has already cured a number of AIDS victims by drawing blood, infusing it with ozone and returning it to the patient, at regular intervals until all the virus is gone. (He can be reached through Biozon Ozon-Technik GmbH, An Der Haune #10, Bad Hersfeld, D-6430, Federal Republic of Germany). Dr. S. Rilling of Stuttgart and Dr. Renate Viebahn of Iffezheim are among the growing number of physicians who have obtained similar results with their patients. They are with Arztlich Gesellschaft fur Ozontherapie and JrJ Hansler GmbH, respectively.

## **THE BASIS OF BIO-OXIDATIVE THERAPIES**

For many years the health sciences have been seeking to identify the primary physical cause of all diseases, and the cure-all that this basic principal would yield. Now both have been found, but their utter simplicity makes them difficult to accept at first, since it seems like if it's that easy, we should have been using them all along. Our bodies are composed mostly of water, which is eight ninths oxygen. Most nutritional studies tend to get caught up in the small details of biochemistry and overlook our most abundant and essential element, and the fundamental role of its depletion in causing illness. Of all the elements the body needs, only oxygen is in such constant demand that its absence brings death in minutes. The main difference, for healing purposes, between benign microorganisms (including our own cells), and those which cause disease, is that the later require much lower oxygen levels. This is due to their more primitive evolutionary origins, during the ages when free oxygen was far less abundant. Now their descendants can only survive in low oxygen environments such as accompany stagnation and decay. To become a growth medium for such parasites, one has to have allowed the oxygen saturation of the bodies fluids to drop well below the optimum level for healthy cell growth and function. The simplest substances available for restoring one's oxygen balance to a healthy range are ozone ( $O_3$ ), and hydrogen peroxide ( $H_2 O_2$ ), which is much easier to obtain and use.

They are both highly toxic when concentrated, which has tended to obscure their germicidal value except as a skin antiseptic. But when diluted to therapeutic levels (for H<sub>2</sub>O<sub>2</sub>, 1/2 of 1% or less), they are not only non-toxic but uniquely beneficial.

### **OZONE BLOOD TREATMENT**

Ozone overcomes the AIDS virus by a fundamentally different process than usually attempted by drugs. Instead of burdening the liver and immune system with more elaborate toxic substances, ozone simply oxidizes the molecules in the shell of the virus. The treatment is remarkably simple. The ozone is produced by forcing oxygen through a metal tube carrying a 300 volt charge. A pint of blood is drawn from the patient and placed in an infusion bottle. The ozone is then forced into the bottle and mixed in by shaking gently, whereupon the blood turns bright cardinal red. As the ozone molecules dissolve into the blood they give up their third oxygen atom, releasing considerable energy which destroys all lipid-envelope virus, and apparently all other disease organisms as well, while leaving blood cells unharmed. It also oxygenates the blood to a greater degree than is usually reached, what with poor air and sluggish breathing habits. The treated blood is then given back to the patient. This treatment is given from twice a week to twice a day, depending on how advanced the disease is. The strengthened blood confers some of its virucidal properties to the rest of the patient's blood as it disperses. The disease will not return, as long as the patient maintains his blood in an oxygen positive state, through proper breathing, exercise, and clean diet. A Dr. Preuss, in Stuttgart, has written up ten case histories of AIDS patients he has cured by this method. But his and the other physicians' reports are all anecdotal rather than in the form of "controlled studies", since they could not be expected to treat some patients and deny treatment to others just for the purpose of accumulating evidence. Thus their results are not considered "proof" by the US medical community. So the Medizone Company in New York has taken on the task of doing the controlled studies required for the treatment to be approved in the US for general use.

### **MEDIZONE TESTING OZONE BLOOD TREATMENT**

In the summer of 1986 Medizone obtained from the FDA an IND (Investigative New Drug) Approval for ozone, which falls under the heading of drugs even though it isn't. They verified that ozone destroys the AIDS virus in vitro, and completed their animal tests in the fall of 1986. The tests demonstrated no indication of toxicity, at ten times the equivalent amount that is proposed for human treatment. The Medizone Co is at 123 E 54th St. Suite 2B, NY, NY 10022: phone is 212-421-0303. Medizone says that it has obtained the rights to US patent #4,632,980, on "ozonation of blood and blood products", from the company "Immunologics", in exchange for Medizone stock shares. The patent pertains specifically to inactivating lipid-envelope virus. In humans, this includes AIDS, herpes, hepatitis, Epstein Barr virus, and cytomegalovirus, among others. Medizone obtained tentative FDA approval in April 1987 to begin human testing, but for a variety of "bureaucratic reasons" the FDA has postponed the actual start of the tests eight times now, with requests for further data, some of which had already been given to them. Twenty months now have passed [as of December 1988], along with several thousand AIDS victims, since the first announced starting date was postponed. The Medizone staff is hoping to finally begin in the spring of 1989, but are no longer announcing expected starting dates with much confidence. "There are no technical problems, but this is the FDA we're dealing with, after all." As the Company's future hangs on their decision, no one at Medizone wants to risk antagonizing the FDA, by speculating about their actual motives for stalling such a broad-spectrum cure. All this can be done with virtually no

publicity. The official reason for is that the accepted procedure for publishing medical breakthroughs is to complete all the tests first, even though victims may die waiting for the cautious, methodical testing procedure to run its course. No one in the industry wants to raise false hopes, let alone repeat the medical disasters that have resulted in the past, from rushing approval on new treatments. On the other hand, the enormously expensive and dubiously effective drug AZT was widely publicized and many months before it was approved in the US, as is ongoing research into possible AIDS vaccines. In fact, FDA Commissioner Frank Young has even announced a proposal to make experimental drugs available to AIDS victims as swiftly as possible, without waiting for full FDA approval procedure to be completed. So there appears to be a sever double standard involved here. It seems that highly profitable "treatments" with serious side effects can be promoted through massive news coverage, while an actual cure, repeatedly demonstrated in Europe, with minimal cost and no apparent harmful effects, must be delayed and kept quiet while panic and deaths mount. Surely at this stage the benefits of unauthorized publicity will outweigh the risks.

### **SAFE PURIFICATION OF BLOOD FOR TRANSFUSIONS**

Ozone infusion also provides a simple method of purifying stored blood and blood components, eliminating any possibility of disease being transmitted by transfusion. It also pre-oxygenates blood to be transfused, greatly reducing the burden on the body receiving the blood. This application alone, of the Medizone process has enormous profit potential, and the treatment will have vast international demand as the news spreads. This has not gone unnoticed by various investment analysts. "Confidential: report from Zurich", "Penny Stock Insider" and "Low-Priced Stock Edition", among others, are urging their readers to get in on Medizone now, comparing the opportunity to getting in on Xerox, IBM, or Polaroid when they were still unknown. Various physicians have independently discovered ozone to be also effective against cancer, leukemia, arthritis, coronary heart disease, arterial circulation disorders. colitis, gum diseases, and assorted childrens' diseases. Some of these findings have now been collected and published in the volume, "Medical Applications of Ozone", available from the International Ozone Association, 83 Oakwood Terrace, Norwalk, Ct 06850. Some of the medical uses of ozone have been appreciated for years in Europe, Brazil, and elsewhere, as well as its advantages over chlorine for water treatment (no toxic residues, 5000 times more rapid disinfection) but its still relatively unknown in the US.

### **OXYGEN WATER**

A much simpler type of Oxygen Therapy uses hydrogen peroxide ( $H_2O_2$ ) which is what ozone ( $O_3$ ) forms on contact with water. It can be taken orally if diluted with water to 1/200 or less, absorbed through the skin by bathing in it (anywhere from 1-8 pints of 3%  $H_2O_2$  in a standard size bathtub half full), or in severe cases it can be injected (250 cc of .075% to .15% or roughly 1/1300 to 1/650). Injections obviously require a physicians assistance, but self treatment is possible with oral and skin applications. The principle is the same as with ozone blood treatment. All hostile micro-organisms prefer lower oxygen levels than the bodies cells require to remain healthy. Boosting the oxygen level revitalizes normal cells while killing virus and other pathogens. The domestic sales of hydrogen peroxide are rising at 15% per year, as the news of this option spreads at the grass roots level. The rapid expansion of the peroxide movement is especially remarkable considering there has been almost no media coverage, and in fact the FDA, American Cancer Society and other enforcers of established medicine have tried hard to discourage the practice. Hydrogen peroxide is the only germicidal agent

composed only of water and oxygen. Like ozone, it kills disease organisms by oxidation as it spreads through the patient's tissues. This also destroys cancerous growths which are anaerobic. Nobel prize winner Dr. Otto Warburg demonstrated over 50 years ago the basic difference between normal cells and cancer cells. Both derive energy from glucose, but the normal cell requires oxygen to combine with the glucose, while cancer cells break down glucose without oxygen, yielding only 1/15 the energy per glucose molecule that a normal cell produces. This is why cancer cells have such a huge appetite for sugar, and also why people who consume excessive quantities of sugar tend to get cancer more often. The anaerobic breakdown of glucose by cancer cells forms large amounts of lactic acid as a waste product, the same substance formed by fermentation of lactose, as in spoiled milk. The liver converts some of this back into glucose, in an attempt to salvage a food source from a toxic waste. In doing this the liver uses 1/5 the energy per glucose molecule than a normal cell can derive from it, but that's three times the energy a cancer cell will get from it. The more the weak, deranged cancer cell multiply, the more energy is lost to the normal cells. Thus we find that low levels of both oxygen and energy tend to occur where cancer is present, and vice versa. This wasteful metabolism becomes self-sustaining and dominant unless the oxygen and/or energy levels are sharply increased, or the cancer's food source is eliminated.

### **HEART TRANSPLANT PIONEER RECOMMENDS OXYGEN WATER**

Dr. Christian Bernard, who performed the first heart transplant, said in march 1986 that he was taking peroxide and water himself, several times daily to reduce arthritis and aging, and he recommended it highly at the time. Since then he has come under heavy attack by the medical establishment for this position, and now states that he "is not involved" with the peroxide movement. But he does not retract his original endorsement, nor deny that he still uses it personally. Over a hundreds physicians are already curing a broad assortment of "incurables" with this natural anti-microbial agent. This includes some forty or more in the US. A principal liaison to these free-thinking physicians is DR. Charles H. Farr, who wrote "The Therapeutic Use of Intravenous Hydrogen Peroxide". He directs the International Bio-Oxidative Medicine Foundation, and publishes the "IBOM Newsletter" which contains procedural updates and technical refinements for physicians using intravenous H<sub>2</sub>O<sub>2</sub> therapy on their patients. By classifying the treatments as experimental they can get around the FDA's archaic restrictions for now, until massive public demand and/or media exposure force official approval. Dr. Farr summarizes the beneficial effects of H<sub>2</sub>O<sub>2</sub> in "IBOM" issue #2; these include killing bacteria, protozoa, yeast, and virus, oxidizing lipids from arterial walls, increasing oxygen tension intracellularly, stimulating oxidative enzymes, returning elasticity to arterial walls, dilating coronary vessels, and regulating membrane transport. IBOM is at PO Box 61767, Dallas/Ft. Worth, TX 75261; 817-481-9772. Dr. Farr is at 1130 North May Ave, Oklahoma City, OK 73120; 405-752-0070 and 799-8781.

### **H<sub>2</sub>O<sub>2</sub> CAN BE SELF ADMINISTERED**

The oral and skin applications offer the option of home treatment, as no blood needs to be drawn, and hydrogen peroxide is cheap and plentiful. Keep it diluted though; in high concentrations it can irritate sensitive skin and induce vomiting when ingested. (Veterinarians routinely give common 3% H<sub>2</sub>O<sub>2</sub> to animals that have swallowed poison, to make them throw it up.) The starting dosage is one ounce of .5% (1/200) H<sub>2</sub>O<sub>2</sub> in water, and some find they need to start with less. As the peroxide contacts pathogens in the stomach it liberates free oxygen,

so those with high levels of virus and streptococcus in their stomachs may feel slight nausea while the reaction is occurring. The dosage is increased by an ounce per day, up to five ounces on the fifth day, then finally up to five ounces three times daily for a week (or until disease is no longer present). Then the dosage is tapered back down over a five week period. Food-grade or Re-agent (these are 35%, dangerous if undiluted) is better for internal use, since the common USP 3% H<sub>2</sub>O<sub>2</sub> contains small amounts of chemical stabilizers and other impurities. It can still be used if food-grade is unavailable; it just isn't as pure. An alternate dosage regimen uses three drops of 35% H<sub>2</sub>O<sub>2</sub> in a glass of water three times a day, which is then increased by a drop per dose, per day, up to 25 drops per dose in extreme cases. Candidiasis victims should start at one drop per dose, and build their tolerance gradually. Some find the taste rather blechy and unpleasant, and may wish to chase it with plain water. It can also be mixed with fruit juice, and citrus juices in particular cover the taste pretty well. Adding seven drops of 35% H<sub>2</sub>O<sub>2</sub> to a gallon of drinking water and shaking well purifies it and gives it a pleasant waterfall-like flavor. For more dosage details and extensive references on H<sub>2</sub>O<sub>2</sub> taken internally, contact Walter Grotz, box 126, Delano, MN 55328; 612-972-2144. His progress report, "ECHO", costs \$1. He provided much of the material regarding H<sub>2</sub>O<sub>2</sub> in this article. Another source is father Richard Wilhelm, Box 18, Union Rd, California KY 41007; 606-635-9297. These gentlemen have continued the research initiated by Dr. Edward Carl Rosenow (1875-1966). They have located over 4000 peer-reviewed medical articles on the applications of hydrogen peroxide, some dating back to the 1800's. They received the National Health Federation's Pioneer Award in Medicine this year, for this ongoing research. Walter Grotz, in particular, has been touring and lecturing extensively on the benefits of self-administered H<sub>2</sub>O<sub>2</sub>, literally saving lives wherever he goes, and bringing hope to people who have been told their causes were hopeless. Dr. Kurt W. Donsbach at the Bio-Genesis Institute in Rosarita Beach, Baja Mexico (714-964-1535), has achieved a remission rate exceeding 70% in over 300 patients, at last count, most of whom had been previously told they were beyond hope, and had "tried everything else". Bio-oxidative therapies are now applied to all cases that arrive at this clinic, and all respond except for those who arrive already very close to death. The Guadalajara Medical School, Mexico's largest, is initiating their own tests this summer, and will add it to their curriculum upon verification. **As Dr. Donsbach has pointed out, no US clinic or institution has ever tested intravenous H<sub>2</sub> O<sub>2</sub> as a treatment for cancer, so any claim that it is not effective is not based on clinical trial, and amounts to willful disinformation.** The Gerson Institute and La Gloria Clinic in Mexico are also using Hydrogen Peroxide therapies on their patients, after the staff tested it on themselves and found it beneficial.



The document by Walter Grotz for the self-administration of Hydrogen Peroxide is included below. It is intended for informational purposes only. It is not intended as medical advice (m.e.).

## **Protocol for the self-administration of Hydrogen Peroxid** by Walter Grotz

### **USING 35% FOOD GRADE HYDROGEN PEROXIDE (H<sub>2</sub>O<sub>2</sub>) - INTERNAL**

Use the dosages listed in the chart with 5 ounces of distilled or purified water. When reaching higher dosages, more water may be used.

Take on an empty stomach, 1 hour before a meal and at least 3 hours after a meal. If your stomach gets upset at any level, stay at that level, or go back one level.

NOTE: Candida victims may need to start at 1 drop 3 times per day.

#### **Dosage Schedule for undiluted 35% H2O2**

1st day, use 9 drops ( 3 drops, 3 times/day)	2nd day, use 12 drops ( 4 drops, 3 times/day)
3rd day, use 15 drops ( 5 drops, 3 times/day)	4th day, use 18 drops ( 6 drops, 3 times/day)
5th day, use 21 drops ( 7 drops, 3 times/day)	6th day, use 24 drops ( 8 drops, 3 times/day)
7th day, use 27 drops ( 9 drops, 3 times/day)	8th day, use 30 drops (10 drops, 3 times/day)
9th day, use 36 drops (12 drops, 3 times/day)	10th day, use 42 drops (14 drops, 3 times/day)
11th day, use 48 drops (16 drops, 3 times/day)	12th day, use 54 drops (18 drops, 3 times/day)
13th day, use 60 drops (20 drops, 3 times/day)	14th day, use 66 drops (22 drops, 3 times/day)
15th day, use 72 drops (24 drops, 3 times/day)	16th day, use 75 drops (25 drops, 3 times/day)

For more serious complaints stay at 25 drops, 3 times per day for 1 - 3 weeks. Next graduate down to 25 drops, 2 times per day until the problem is taken care of. This may take from 6 months. Don't give up!

When free of complaints, you may taper off by taking:

- 25 drops once every other day, 4 times
- 25 drops once every third day for 2 weeks
- 25 drops once every fourth day for 3 weeks

A good maintenance would be 5 - 15 drops per week, depending on the amount of cooked and processed foods you are eating.

#### **Possible Reactions to Hydrogen Peroxide**

Skin eruptions, nausea, sleepiness, unusual fatigue, diarrhea, colds (in head or chest), ear infections, boils, or any other method that the body uses to emit toxins from the body (the toxins have been rooted out by the use of hydrogen peroxide).

This is the natural way for the body to cleanse and the natural cleansing will be of short duration, as you continue to maintain your program. Above all, even if you must decrease the dosage, continue the program, don't give up.

If you get a cleansing reaction, you may want to increase the dosage to hasten the cleansing. A cleansing is the effect on the body of bacteria dying off, or various forms of poisons being released through the eliminative organs of the body, i.e. skin, lungs, kidneys and bowels.

Remember: When hydrogen peroxide comes in contact with virus and streptococcus, it will liberate free oxygen (O<sub>2</sub>).

This may be happening in your stomach. If your stomach feels uneasy, it is only the hydrogen peroxide seeking out the virus and streptococcus to destroy.

**CAUTION:** If you spill 35% hydrogen peroxide on your skin, immediately rinse under tap water. It will burn and turn the skin white. Avoid spillage.

## **ADDITIONAL USES FOR HYDROGEN PEROXIDE**

To make 3% Solution, mix 1 ounce of 35%  $H_2O_2$  with 11 ounces of purified or distilled water.

### **In the Kitchen**

Vegetable Soak: (In place of Clorox). Add 1/4 cup 3%  $H_2O_2$  to a gallon of cold water. Soak light vegetables (lettuce, etc.) 20 minutes, thicker skinned vegetables (like cucumbers) for 30 minutes. Drain and dry, (they keep longer too). If time is a problem, you can spray the vegetables with straight 3%  $H_2O_2$ , let stand for a couple of minutes, rinse and dry.

Leftover Tossed Salad Put 1 Tbsp. 3%  $H_2O_2$  in 1/2 cup of water and spray the top of the salad with the solution before covering and refrigerating.

To Freshen Kitchen Keep a spray bottle of 3% (straight) in the kitchen. Use it to wipe off counter tops and appliances. It disinfects and gives the kitchen a fresh smell. Works great inside the refrigerator and on Formica desk tops.

Washing/Laundry Add 8 ounces of 3% to your wash in place of bleaches with fumes.

Marinade: Place chicken or beef in a casserole (avoid use of aluminum pans), and cover with 3% hydrogen peroxide. It may take several pints depending on amount of meat/chicken. Place, loosely covered, in refrigerator overnight. The next day, rinse and cook.

In the Dishwasher: Add 2 oz. of 3% hydrogen peroxide to your regular washing formula. Your glasses will really sparkle!

Sprouting Seeds: Add 1 ounce 3% hydrogen peroxide to 1 pint of water and soak the seeds overnight. Add the same amount of hydrogen peroxide each time you rinse the seeds. Some people have reported 3/4 inch sprouts in 24 hours.

Plants & Flowers Put 1 oz 3% hydrogen peroxide in 1 quart of water. Water or mist plants with this solution.

Insecticide Spray Put 8 ounces white sugar, and 4 8 ounces 3% hydrogen peroxide in 1 gallon of water.

Humidifiers/Steamers Use 1 pint 3% hydrogen peroxide to 1 gallon of water. (Helps keep them clean too).

### **In the Bathroom**

Keep a spray bottle of 3% hydrogen peroxide in the shower. Spray your body after washing to replace the acid mantle on your skin that soap removes.

Spray toilet paper with 3% hydrogen peroxide before using.

Use 3% on a cotton ball as a facial freshener after washing.

Add 1/2 to 1 pint 35% hydrogen peroxide to a full bathtub for a detoxifying bath. Note: try not to use this after 6-7 p.m. as the increased absorbed oxygen may keep you awake.

Athlete's Foot Soak feet nightly in 3% hydrogen peroxide.

Mouthwash Use 3% hydrogen peroxide. Add a dash of liquid chlorophyll for flavouring if desired.

Toothpaste: Use baking soda and add enough 3% hydrogen peroxide to make a paste. Or, just dip your brush in 3% hydrogen peroxide and brush.

Douche: Equal parts of 3% hydrogen peroxide and water is the MAXIMUM dosage. Start with 3 tablespoons and gradually increase the amount.

Colonic: 1 pint 3% hydrogen peroxide to five gallons of water is the MAXIMUM dosage. Start with 1/2 pint and gradually increase the dosage.

## **HYDROGEN PEROXIDE IN NATURE**

Hydrogen peroxide occurs naturally in rain and snow, from atmospheric ozone, and in mountain streams where rushing water is continuously aerated. Most of us learned at an early age to drink only from a stream only where the water is running white, because that is where it gets cleansed of germs. The reason is that  $H_2O_2$  is forming there due to its rapid agitation, and that's what kills any harmful microbes present. By just shaking a bottle of water vigorously for

a while you can tuck enough extra oxygen into it to form detectable amounts of  $H_2O_2$ , improving its purity, flavor and vitality. It turns out that the spring waters at Lourdes, France, long recognized for their remarkable healing properties, are very high in natural hydrogen peroxide. The spring is fed by high altitude snow melt, so the snow apparently absorbs unusually large quantities of ozone on its way from the upper atmosphere. Other less-known high altitude springs are said to be likewise effective. Similar benefits can be obtained in a swimming pool or hot tub, by discarding the chlorination system and simply pouring in  $H_2O_2$ , or by bubbling ozone through the water. One simple method of making pool-grade ozone is to pump air past an enclosed ultraviolet lamp. Raw, uncooked vegetables and fruits can contain natural hydrogen peroxide. Cooking drives off the extra oxygen. Fresh fruit juices are well known for their blood cleansing and revitalizing capabilities, particularly when they are not combined with other foods; this is largely due to the  $H_2O_2$  they contain. Reconstituted frozen juices have much less and are no longer "alive", thus they are not nearly as effective.

### **$H_2O_2$ IS THE HEART OF THE IMMUNE SYSTEM**

Mother's milk contains a high amount of  $H_2O_2$ , especially colostrum, the first milk secreted after birth, which activates the newborns immune systems, and key to many other metabolic processes. Under conditions of optimum health,  $H_2O_2$  is produced by the body's immune system in whatever amounts are needed to quickly destroy any invading hostile organisms. It is made by combining water in the body with the free oxygen that is supposed to be available. When the body is oxygen-starved, it can't produce enough  $H_2O_2$  to wipe out invading pathogens, which can then get the upper hand and cause visible disease.

### **OXYGEN BOOST IS KEY TO OTHER HEALING METHODS**

When penicillin is effective against infection, it is largely due to the formation of bacterial amounts of  $H_2O_2$ , when glucose is oxidized by  $O_2$  in the presence of penicillin notatin. (General Biochemistry, Fruton & Simmonds 577.1 F944 p. 339) Much has been made about the healing properties of interferon, but it is unbelievably expensive. However, much of its effectiveness is apparently due to the fact that it stimulates the production of  $H_2O_2$  and other oxygen intermediates, which are a key factor in reactivating the immune system. (Journal of Interferon Research Vol 3, #2, 1983 p. 143-151.) Thus Interferon may turn out to be simply a very elaborate way to accomplish essentially the same thing as  $H_2O_2$  regimen. Vitamin C (ascorbic acid) has long been recognized as essential to the proper use of oxygen by the cells. Dr. Linus Pauling has demonstrated that large doses of vitamin C are effective against cancer. The mainstream medical community still has not acknowledged this discovery, let alone put it to use, despite Dr. Pauling's previous credentials. As it turns out, vitamin C actually creates extra  $H_2O_2$  in the body. Organic Germanium (bis-carboxyethyl germanium sesquioxide) is gaining increasing recognition as a potent healing substance, primarily through the work of Dr. Kasuhiko Asai. This compound directly increases the body's oxygen supply, as it contains a great deal of oxygen in a form that can be easily assimilated. (See "Miracle Cure: Organic Germanium" by Dr. Paul Asai, Japan Publications, Inc., Tokyo and New York.) Taheebo (aka Pau D'Arco or Lapacho Colorado) is a tree that grows in the Andes and fixes high concentrations of oxygen in crystalline form in its inner bark. The bark has been used for centuries by the native peoples of the area to prevent and reverse illness, and it is one reason, why they do not get cancer. In recent years it has become popular in the US, and it gets by the FDA as an "herbal tea" whose distributors wisely make no medical claims for it. Again, much of its effectiveness is apparently due to its high oxygen content, released in solution when

brewed as a tea.

### **CAUSES OF OXYGEN DEPLETION**

There are several common practices that drop a person's oxygen level far below what it should really be. At sea level, 20% of the atmosphere is supposed to be oxygen, but city air gets down as low as 10%, due to smog and removal of trees. Air that tastes bad induces a tendency to breathe shallowly, getting even less oxygen to the blood. So does lack of exercise. The carbon monoxide (CO) in smog does not normally occur in nature in much quantity since it's formed by incomplete combustion of carbon compounds. It is electrically unbalanced, so it seeks to bond with any available oxygen to form the more stable carbon dioxide (CO<sub>2</sub>). Those who breathe too much carbon monoxide tend to die, fast or slow depending on the concentration. It strips oxygen molecules from the blood to form CO<sub>2</sub>, which the body can't use and must exhale, at least until its oxygen runs out. The fact that the body considers CO<sub>2</sub> a waste product, by the way, doesn't say much for carbonated beverages. Tap water is very low in oxygen, having no opportunity to be aerated during its journey through the pipes, and being loaded down with chlorine and various contaminants. Since cooking drives the extra oxygen out of vegetables, if one diet is mostly cooked or processed foods, there's yet another oxygen source lost.

### **EATING, FASTING AND OXYGEN BALANCE**

Overeating is so common in the US it's considered "normal". One cause is the widespread use of oral antibiotics. While destroying the target germs, these drugs also kill off one's intestinal flora, which are needed for healthy digestion. With these friendly bacteria gone, digestive efficiency plummets. As a result, the sensation of hunger comes more often and lasts longer, as the body tries to compensate for ineffective digestion by increasing the amounts consumed. Even just eating daily, without ever giving the gastro-intestinal tract a rest, loads down the blood with toxins and impurities, especially uric acid crystals. Under a microscope these resemble tiny coffin lids, interestingly enough, another clue to our Creator's whimsical sense of humor. When the waste products exceed the cleansing capacity of the kidney's, the blood ends up just having to haul it around the body and stash it wherever possible. These toxins literally take up so much room in the blood cells that the cells can't take on enough oxygen when they pass through the lungs. The blood's primary function of picking up and distributing oxygen gets blocked by overuse of garbage-hauling function. Fasting restores health by giving the overloaded blood cells a chance to dump the toxins and inert matter through normal organs of elimination at a rate they can handle, instead of through the skin, as in acne, or other inappropriate places. If the fast is long enough, accumulated residues in the body are also scoured out and expelled, giving a considerable spiritual resurgence once all the backlog is cleared away. While the debris is flushed out, various toxic reactions may come and go. Once the blood is cleansed the red corpuscles have a lot more room for oxygen molecules, the oxygen saturation of the molecules is high, and health and energy are boosted considerably. Each breath now gives more life than it was able to in the blood's earlier state. Most long-lived native peoples, who are not affected by our more common diseases, either include fasting as a regular part of their yearly food cycles, or eat much less overall, than industrialized peoples. Today many Americans are existing at such high levels of toxicity, that their toxic reactions when attempting to fast can seem intense enough to make them start eating again before any serious cleansing can be accomplished. Fortunately one can partially bypass the lungs and get the blood level back up, by taking oxygenated water internally and through the skin. Several

weeks of detoxification of this regimen will also make it much easier to fast without discomfort, if one chooses. It reduces appetite, logically enough, to a level more in line with the body's actual needs. The bacteria that aid digestion are not killed by oral use of H<sub>2</sub>O<sub>2</sub>, as long as it's diluted properly.

### **OXYWATER MAY EVEN CURE STUPIDITY**

Perhaps the greatest potential benefit is the reversal of the slight brain damage caused by long-term oxygen depletion, which can be observed in the "average" human, and is not always all that slight. It's well known that after about nine minutes of no oxygen, from drowning or whatever, you can kiss your brain good-bye. By the implications of constant gradual oxygen starvation in our cities somehow escape notice, despite the tiredness, depression, irritability, poor judgement and health problems affecting so many citizens. Increasing the oxygen supply to the brain and nervous system will reverse these conditions. The oxywater regimen improves alertness, reflexes, memory and apparently intelligence, and may offer the elderly a new weapon against senility and related disorders. Alzheimer's and Parkinson's are reported to be responding to it. Alcoholics who start taking H<sub>2</sub>O<sub>2</sub> soon loose interest in alcohol, and the thirst does not come back. Look up what alcohol does to your blood oxygen and your ability to use it, and you'll see why. One possible spin-off of a coming major increase in the blood oxygen supply to human brains is that various short-sighted and oxygen-depleting activities such as deforestation, and other intelligent practices, should fade from the scene. Americans especially, will have an opportunity to outgrow many stupid things. It's strange that the common drug aspirin "stops pain" by interfering with the nervous systems ability to use oxygen, in the electrochemical reactions needed to transmit impulses. Though maybe it's not that strange, considering that the Bayer Company which originated it was a subsidiary of IG Farben, the German chemical conglomerate that is famous for, among other things, developing and mass-producing the lethal gas Zyklon-B specifically for the exterminations at nazi death camps.

### **ECONOMIC INERTIA**

DR Terry McGrath, the CEO at Medizone, confirmed that Hydrogen peroxide would in principle act much like ozone in destroying AIDS virus, but pointed out that it's never likely to be tested and proven in the laboratory. There's simply no economic incentive, since it's an unpatentable process and offers no commercial returns than most other natural remedies. So it's completely up to individual patients and concerned citizens to push these options out into the open, immediately, before various companies get too financially committed to the assumption that AIDS (or any other disease) will continue to spread and be incurable. This is a good place as any for the FDA-required disclaimer: "Information given here is for research and educational purposes only and is not intended to prescribe treatment."

### **VETERINARY AND AGRICULTURAL APPLICATIONS**

Human's aren't the only life form to benefit from compensation for their oxygen deficient air, water and/or lifestyle. H<sub>2</sub>O<sub>2</sub> in animals' drinking water, not enough to taste unpleasant, knocks out a growing list of illnesses. Locally, cats have gotten rid of their feline leukemia and chlamydia, and are back to their old energetic slapstick selves. Distemper in dogs has been reversed with H<sub>2</sub>O<sub>2</sub>, and a growing number of farmers are applying it to their livestock to cut losses from disease and infected wounds. Plants grow better with an ounce of 3% H<sub>2</sub>O<sub>2</sub> per quart of water they're given. Spray the solution on their leaves as well. Seeds germinate faster, with bigger sprouts, when they are first soaked in 1 ounce of 3% H<sub>2</sub>O<sub>2</sub> to a pint of water.

Instead of cutting trees that are diseased or otherwise struggling, spray them with  $H_2O_2$  and water (1 part 3% to 32 parts water).

### **WHY ISN'T IT ALREADY IN USE ?**

The obvious question is, if hyper-oxygenation is so simple and effective, why has it taken so long to discover it? Ozone is hardly new and hydrogen peroxide has been on the market for over a century. Why aren't all doctors already using it ? How come this story isn't all over the major news outlets? Turning the question around helps clarify the problem. Just exactly what would happen if a cure was discovered that was completely effective against the vast majority of diseases, ridiculously cheap and plentiful, and in most cases could be self-administered without a physician? Would the current medical establishment welcome a breakthrough that could render 98% of all drugs, testing and disease related surgery obsolete? What would the response be of the pharmaceutical industrialists, hospital chain owners, health insurance moguls, AMA, and FDA? Would you expect to read or hear such an announcement from any medical journal or media outlet owned by people financially committed to the medical status quo, which is practically all of them? How many want to make their own occupation unnecessary? And if the cure had already been suppressed once, wouldn't the possible blame for allowing people to die without it provide even more incentive continue keeping the whole thing quiet? All right then. This precisely the situation that exists, and the cure has indeed been around for ages. It has been independently reported effective against virtually every disease at one time or another, in thousands of public-domain medical articles, which had never been collected or correlated until recently. And it is so simple and basic that concealing it from physicians and the general public has required a tremendous smoke screen of artificial complications, narrow specializations, symptomatic classifications and user hostile treatments. If this is so, it follows that the more profit-fixed elements of the medical establishment will not be too thrilled about the recent surge in interest in oxygen therapies. The drug industry has expanded enormously since WWII, while America's level of health has dropped from the world's highest to the lowest among the industrialized nations. It does look as if the bottom line has been money and not health, for a long time. The battle for the future of medicine, between Nature's truth and lucrative lies, is about to really heat up. We can expect to see disinformation articles and newscasts with persuasive medical experts, some of whom will even believe what they're saying, warning of the dangers of hydrogen peroxide, ozone and even regular oxygen. These reports will attempt to blur the distinction between using therapeutic dosages at safe dilutions, and the harmful effects of excessive concentrations. Plenty of grizzly examples are available, of what happens when various tissues are over-oxidized. Anti-oxygenation propaganda pieces will probably not mention that over the years the FDA has approved  $H_2O_2$  as a skin antiseptic at full 3% strength, as a hair bleaching agent at 6%, and for internal use as an additive for milk and in antiseptic long-shelf-life packaging. Nor are they likely to acknowledge that many European countries use ozone and  $H_2O_2$  in their cities' water supply, and that they enjoy much better health than in the US. And they will be unable to truthfully cite any examples of people who were harmed by using  $H_2O_2$  in the current demonstrated therapeutic concentrations. If not enough public move quickly to help spread the news of this alternative, those who fear it could reduce their economic power may go so far as to try to knock off someone who promotes it, while trying to make it look like "too much oxygen" is the cause. Also, product tampering has thus far mostly targeted Bayer Aspirin's competitors, in case you hadn't noticed, but drugstore hydrogen peroxide would not be immune to such tactics. One approach might be to plant a contaminated batch in a town where

oral use is catching on and the medical establishment is losing ground, so someone gets hurt and the story gets nationwide coverage. It is vital for Americans to realize that current economic dynamics don't allow the businessmen in charge of health and industry any incentive at all, to make people permanently healthy and lose them as customers. It's the same reason why the energy conglomerates do not encourage citizens to become energy-self-sufficient, the Pentagon has no incentive to stop wars, and the American Psychiatric Association sees no advantage to ending mental illness. Fortunately the majority of physicians really do want to see their patients get well. They also wouldn't mind gaining the respect and admiration with which physicians were once widely regarded. When it comes down to choice between saving lives and protecting profits, most will be brave enough to overhaul their medical belief systems, discard obsolete methodologies, and basically tell the pharmaceutical conglomerates to go shove it. The rest will simply get left behind.

### **SOURCES FOR FOOD-GRADE HYDROGEN PEROXIDE**

Most pharmacists have never heard of it, so it's usually a waste of time to ask them. A number of chemical supply houses have 35%  $H_2O_2$  available; check your local directories and call a few. Under FDA pressure, DuPont and possibly other major chemical companies have recently issued warnings to their distributors, not to sell hydrogen peroxide to people who want it for healing purposes. So when you inquire, if they ask what you want it for, it will unfortunately be necessary to lie. If you say you want it as a cleaning agent, that's at least pretty close to the truth. Several physicians quietly sell it through the mail, but they aren't the same ones promoting its health properties, for obvious FDA-related reasons. A good source in California, though he can ship it anywhere, is Dr A J McDonald, at PO Box 775, Lodi, CA 95240; 209-368-8681; 12\$/pint. Your best move would be to share this information with owners of health food stores in your area. Call them and ask if they have food-grade  $H_2O_2$  (some already do) and tell them you want it and how it works. Encourage them to carry it and give them Dr McDonald's address if they don't seem inclined to track down a local source. **Cleanroom-grade 30%  $H_2O_2$**  (used for cleaning in computer rooms it is a powerful disinfectant and leaves no residue when it evaporates) is reported to be just as pure as food grade and much cheaper. Check with labs that make "water fabrication" chemicals, or contact the manufacturers of silicon chips and other computer parts, and the data processing complexes that might use it in their cleanrooms, and ask where they buy it. The more sources become known, the harder it will be for anyone to make it unavailable.

### **GET THE WORD OUT**

Write your elected officials, send copies of this information, and point out what will happen to a politician whose constituents learn he knew of a cure for cancer and AIDS but didn't tell them about it. Call in on a radio talk show and share the good news, or send copies to their reporters and program directors, especially at listener-supported stations as these are less likely to suppress it. Don't assume your local papers have already heard of this; write letters to editors, and/or send copies of this report. Tack it on every bulletin board you see, and post it on all relevant computer bulletin boards. If you know teachers, physicians, or health officials who can still think for themselves, tell them about this and give them the references. Notify your local police officials that hyper-oxygenation gives them a way of making sure they'll be safe from infection due to contact with AIDS carriers. If you really feel bold, walk into the local hospital cancer's wards and give a copy of this to anyone who can still read, and slip out the back door before the doctors walk in. Share it with anyone you know who has a health

problem, even a minor one; H<sub>2</sub>O<sub>2</sub> apparently works on everything from acne to warts. Above all, stop buying the idea that cancer, AIDS, and other "terminal" illnesses are automatic death sentences. When you hear some celebrity is sick or dying from this or that, look up their mailing address in Who's Who or whatever, and mail them this information. If the address is for an agent, which are notorious for blocking attempted communications to their client, you might include a cover letter to the agent, stating that the enclosed vital news is also being sent to their clients family members, and that if he or she learns through them that there was life saving information sent but held up at the agent's, that agent will be out of a job. Act like you have the clout it takes to make a difference, and you soon will. Major scientific breakthroughs go through three stages: first they are ridiculed, then violently opposed, and finally they are accepted for being self-evident all along. Let's see if we can short cut those first 2 stages a bit, OK?

#### **FURTHER INFORMATION SOURCES:**

"ECHO", a newsletter on Oxygen Therapy, is available from Walter Grotz, Box 126, Delano, MN 55328, (1\$, 8p); 612-635-9297) have extensive references and case histories of successful treatments.

"The Peroxide Story" George L Borell, 3035 Rome Ave, Anaheim, CA 92804; 60 pp, \$4.95 plus \$1 postage.

The International Bio-Oxidative Medicine Foundation (IBOM) Newsletter contains technical updates for physicians using H<sub>2</sub>O<sub>2</sub> therapies on their patients. PO Box 61767, Dallas/Ft. Worth, TX 75261; 817-481-9772.

Rex Research (PO Box 1258, Berkely, CA 94701) has five folios on Ozone Therapy; #4 (\$2, 10 pp) is specifically on ozone treatment of AIDS; see also #1, ozone vs a wide variety of conditions (6\$, 55pp); #2, ozone vs herpes, hepatitis, rheumatic diseases, also dental use (\$4, 29pp); #3, cardiovascular, ozone enrichment of blood prior to transfusion (4\$, 23 pp) and Ozone vs Cancer (\$6, 55pp).

The International Ozone Association, 83 Oakwood Ave, Norwalk, CT 06850; (203-847-8169) has available "Medical Applications of Ozone" the largest single volume on the subject, for 50\$.

"Self-Treatment for AIDS: Oxygen Therapy" (\$12.95, 100pp), and home remedies for Candida" (\$8.95, 112pp) consist mostly of article reprints, compiled by Betsy Manning, 1600 Larkin #104, S.F. CA 94109.

"Search for Health", APW, PO Box 3052, Iowa City, Iowa 52244. Tom Valentine, Editor. Includes info on other oxygenating compounds for internal use, including AEROX, which they sell, and which is reported to give the same benefits as H<sub>2</sub>O<sub>2</sub>, but tastes better and is more stable, though more expensive. (We have not yet obtained a sample for testing.) APW also is a source for full-spectrum health-enhancing KIVA lights.

Some of the formal medical articles on H<sub>2</sub>O<sub>2</sub> include: "Hydrogen peroxide mediated killing of bacteria", D P Clifford and J E Repine, (Molecular and Cellular Biochemistry 49, 143-149, 1982); Generation of H<sub>2</sub>O<sub>2</sub> in Biomembranes", T Ramasarma, (Biochemica et Biophysica Acta,



694, 1982, 69-93); "Removal of Cholesterol and Other Lipids from Experimental Animal and Human Atheromatous Arteries by Dilute Hydrogen Peroxide", James W Finney, Bruce E Jay, et al, (Baylor University Medical Center, Dallas, Texas); also a series on the role of H<sub>2</sub>O<sub>2</sub> in immunity to malaria, in The Lancet, 12/25/82 p 1431-1433, 1/29/83 p 234, and 2/12/83 p 359-360.

Medizone International, 123 East 54th St, Suite 2B, NY, NY 10022; 212-421-0303; issues shareholder reports updating the stateside verification of ozone blood treatment. Hansler ozone generators will also be available to licensed physicians through Medizone.

Biozon Technik Co, in Bad Hersfeld, Federal Republic of Germany, also makes ozone generators for medical use.

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# OZONE - BREATH OF LIFE

by Robert Willner, M.D.

OZONE (O<sub>3</sub>) "Breath of God" (Ancient Hebrew)

NOTE: THE USE OF OZONE THERAPY IN THE TREATMENT OF CANCER OR ANY OTHER DISEASE IS UNPROVEN AND NOT RECOGNIZED BY THE FDA OR THE MEDICAL PROFESSION IN THE UNITED STATES. THIS ARTICLE PRESENTS INFORMATION ABOUT ITS HISTORY AND HOW IT IS BEING USED BY THOUSANDS OF PRACTITIONERS THROUGHOUT THE WORLD. ONLY 34 CASES OF SIDE EFFECTS OUT OF 5,500,000 PATIENTS HAVE BEEN REPORTED.

## ABOUT OZONE

The discovery and naming of ozone is attributed to Christian Friedrich Schonbein in 1840. Its value in medicine was debated for many decades and references to its use were sporadic. Dr. Albert Wolf, a German physician wrote in 1915. "As regards the medical usability of ozone, the viewpoint of experimental science may be considered as being in direct opposition to the practical experiences gained by industry." He used ozone successfully in the treatment of decubitus ulcers. During the First World War (1915) ozone gas was used to purify the drinking water of major cities since 1901. The first was Vienna and the most recent was Los Angeles. It does not give water the disagreeable taste that chlorine does. Although many authorities refer to it as poisonous and a hazard to life, like anything else on this planet, if used properly it is beneficial - in fact life would become extinct without ozone in our atmosphere. The breathing of inappropriate concentrations is indeed harmful to the lungs, but in proper concentrations it purifies the air we breath. Home and industrial ozonators are used throughout the world (including the United States, to purify the air), and yet, comments are being made publicly by authoritative figures that ozone is poisonous and a hazard to life. This is indeed true if, as in the case of any substance on this earth, it is used in unsafe amounts. Statements of this nature are unjustified and fraudulent when they are intended to misinform or alarm the public in a way that would indicate that ozone is unsafe under any circumstances. Ozone is created by the action of ultraviolet light or a strong electrical field on oxygen atoms. The result if the forcing together of 3 atoms into unstable groups (O<sub>3</sub>) that rather quickly break down into the usual oxygen molecule (O<sub>2</sub>). Ozone is lethal to almost all viruses, bacteria, fungus and cancer cells. The scientific literature is replete with articles proving these facts. Ozone is formed in our atmosphere naturally by the effect of lightning on oxygen. It is that wonderful sweet smell that you can detect after a summer storm. It is nature's method of cleansing our atmosphere of contamination. The poisonous ozone levels reported effecting our cities differs dramatically in that it represents the combining of the extensive overwhelming pollution with ozone insufficient to do the job. If you wonder why cancer rates have tripled in the last 20 years, consider this startling fact: The oxygen level of the air we breathed 200 years ago is much higher than it is today. (From the work of LaVosier - the discoverer of oxygen and current figures. In 1931, Dr. Otto Warburg was awarded the Nobel Prize in biochemistry. Dr. Warburg demonstrated that the metabolism of a cancer cell was like that of a plant cell, which thrives on carbon dioxide and gives off oxygen as its waste product. It actually represents the process of fermentation. We are composed of animal cells and oxygen is essential for our assimilation of nutrients and the detoxification and elimination of waste products. When ozone is introduced into the bloodstream, it is converted into oxygen, hydroxyperoxides and other beneficial free radical scavengers which actually seek out and destroy diseased cells. Nearly 50 years later, the prestigious journal SCIENCE, VOL. 209, 22

AUGUST 1980, published a paper entitled: OZONE SELECTIVELY INHIBITS GROWTH OF HUMAN CANCER CELLS. This paper dealt with the exposure of human lung, breast, and uterine cancer tissue to ozone at concentrations of 0.3 to 0.8 parts per million, well within the non-toxic limits tolerated safely during the average ten minute period that medically administered ozone takes and concentrations far less than that are used. In the experiments, normal human cells were not effected at these levels. The modern development of ozone application in medicine gained impetus in the 1950's in Europe, and its use gradually spread throughout Europe to Australia, Israel, and Brazil.

INTRA-VEIN OZONE GAS is extremely safe and effective against all infections. The earliest evidence that I could locate of ozone's recommendation as therapy in the United States, appeared in an 1885 issue of the Journal of the Dade County Medical Association. In spite of this and many other references prior to 1920, the FDA has illegally raided and confiscated ozone generators from the offices of advanced (alternative) physicians. Ozone is classified as a toxic gas if inhaled in large quantities. However, it is not toxic when injected slowly into the body by intra-arterial injections, I.V., intramuscularly, subcutaneously or by vaginal or rectal insufflation. Ozone has no side effects when administered, using these methods, in the proper quantities and concentrations. It does not effect healthy cells of any type adversely under those conditions. It is obvious why it is lethal to cancer cells. The cancer (plant) cell is being given toxic waste product, while our normal cells are being given their essential for life. Individuals receiving ozone for the first time are usually apprehensive. It is scary to have "air" injected into their veins. They have images of dying from an air embolus. Almost everyone seems to recollect a murder mystery in which the villain killed his victim that way in the hopes of committing the perfect crime. It will never happen in real life because:

1. Nitrogen would have to be present in order to cause a toxic reaction and therapeutically only pure medical grade oxygen is used.
2. It would take at least 50 cc of gas given within 2 to 3 seconds. That cannot even be accomplished with a very large bore 18 gauge needle. The procedure is done with a fine 25 gauge needle. Death could only occur intentionally, never accidentally.

Specific therapeutic applications of ozone include the treatment of circulatory problems, decubitus ulcers, some forms of cancer (still under investigation as to how many), AIDS, viral diseases, wounds, scars, burns, gangrene and liver disease including hepatitis. Ozone is the only substance known which is virucidal, bactericidal, fungicidal, protozoacidal and cancericidal. Over 1,000 medical papers exist in the world medical literature attesting to its efficacy in the treatment of disease in many tens of thousands of patients. Typically it has been ignored in America because it cannot be patented. Therefore, it is not profitable for the pharmaceutical industry to spend the millions of dollars necessary to prove its effectiveness by FDA standards. It would reap scorn and outrage of incredible proportions if the truth were known. The pharmaceutical industry and the FDA confuse and distort the role of ozone in our ecosystem and suppress its use therapeutically (even though, under law, it should be "grandfathered in"). In addition to the many articles on the use of ozone in medicine, there are medical texts such as "THE USE OF OZONE IN MEDICINE" by Prof. Siegfried Rilling, M.D. and Renate Viebahn, Ph.D., and medical organizations in the major industrial nations of the world dedicated to the education and instruction of its use.

A WORLD OZONE CONFERENCE has been held frequently since the early 1970's, the most recent was held in San Francisco (1993), and was attended by hundreds of doctors from many countries. Russia sent seven scientists to present papers on their discoveries of its application.

In no other science does acceptance take as long as it does in medicine. The use of deep freezing techniques took over 80 years and television over 30 years, but in medicine, where human life is at stake, it can take 150 years and maybe never if there is no profit to be made. Fortunately for mankind, there are still countries where investigation into non-drug, non-patentable, non-toxic and inexpensive therapies are still being carried out.

### **SUBSTANTIAL EVIDENCE**

The PROCEEDINGS OF THE WORLD OZONE CONFERENCES have documented and published the techniques and dosages of ozone for its beneficial use in the following conditions. Cancer (Carcinoma), Spastic Colon, Arterial Thrombosis, Osteomyelitis, Acne, Proctitis Bladder Fistula, Wounds, Ulcers, Varicosities, Radiation burns, Phlebitises, Parkinson's, Ulcerative Colitis, Mucous Colitis, Chronic Cystitis Colitis, Chronic Cystitis, Coli Infections, Chronic Hepatitis, Hemorrhoids, Anal Eczema, Arthritis.

Intrarectal insufflation is excellent for diarrhea and candidiasis (in women intravaginal insufflation is also effective), and it is applied in this manner when intravenous administration is impractical or unavailable. As long as the lobbyists and influence peddlers for the pharmaceutical industry and the AMA are able to convince our representatives that anything outside of the mainstream of medicine is either useless, fraudulent or dangerous, many safe, non toxic and effective therapies will be denied to the public. Our representatives must be made aware that although the safety is not usually the problem, proof of efficacy by the double-blind standard is economically prohibitive. In those instances where such proof has been offered, fraudulent tactics by the opposition have resulted in blocking the use of some incredible therapies. If you want to know what benefits ozone bestows in disease, ask the doctors and patients who have used it - but, of course, that's anecdotal!!!

### **THE IMPORTANCE OF OXYGEN**

Virtually every patient's room in a modern hospital is equipped for the administration of oxygen. Certainly, an emergency room cannot be without one because it is required by law. Deep breathing exercises are prescribed for patients with lung problems and for individuals recovering from surgery. The narrow use of these techniques are indeed unfortunate, they should be routine for all patients. The local gymnasiums and health spas routinely employ the proper use of deep breathing exercises. The average person takes their respiration for granted. There are large religious cults who incorporate consciousness of breathing as an important ritual of their beliefs. Indians refer to breathing as an important ritual of their beliefs. Indians refer to "Prana" as a wonderful substance that God has provided for a healthy life. Certainly, Prana is oxygen, or possibly even ozone. Both aptly fit their description. Obviously, chronic and gradual oxygen deprivation on metabolism is devastating and leads to an inadequate processing of the toxic wastes that our bodies are constantly producing. One of the consequences of lowered oxygen concentration is the elevation of uric acid in the body. This one compound alone, is implicated in a wide variety of metabolic problems. The most common disease associated with uric acid disorder is gout and it is primarily due to an inability to process meat protein. However, the far reaching effects on almost every system of the body gives us an indication of the widespread effect that a low-grade increase can have. The formation of a stone in the kidneys and gallbladder, the blocking of circulation and the destruction of joints by the formation of crystals are just a few of the problems that arise. There are literally hundreds of known biochemical reactions in the body that utilize oxygen. There are probably many thousands more waiting to be discovered. Acute deprivation of

oxygen leads to a rapid death. We are getting there more quickly than we should. The importance of oxidative processes is discussed more fully elsewhere, but the relationship with the development and progress of cancer is no longer in doubt. The use of ozone appears to go beyond the benefit of oxygen in the treatment of disease. The production of electromagnetic energy at the molecular level, as the ozone molecule disassociates into oxygen, undoubtedly plays a role in its usefulness in therapy. Permit me to list just a few of the proven effects of ozone.

### **OZONE ACTIONS**

1. Ozone activates the enzymes involved in peroxide or oxygen "free radical" destruction i.e. glutathione, catalase, s.o.d.
2. Accelerates glycolysis (breakdown of glycogen) in RGSs, thus it:
  - a. Increases the release of O<sub>2</sub> from the hemoglobin in the blood to the tissues.
  - b. Enhances formation of acetyl coenzyme-a, which is vital in metabolic detoxification.
  - c. Influences the mitochondrial transport system which enhances the metabolism of all cells and safeguards against mutagenic changes.
  - d. Increases red blood cell pliability, blood fluidity and arterial PO<sub>2</sub> (oxygen content) and a decrease in rouleaux formation (clumping) which interferes with the normal functioning of red blood cell metabolism.
3. Increases leukocytosis (production of the white blood cells) and phagocytosis (the manner in which certain white blood cells destroy foreign matter). Both processes are part of the immune defense system.
4. Stimulates the reticulo-endothelial system, the rebuilding of tissue.
5. Strong germicide - inactivates enteroviruses, coliform bacteria, saphylococcus aureus and aeromona hydrophilia.
6. Disrupts the cell envelope of many pathogenic organisms which are composed of phospholipids, peptidoglycans and polysaccharides.
7. Opens the circular plasmid DNA which lessens bacterial proliferation.
8. Fungicidal, inhibits candida cell growth.
9. Low doses stimulate the immune system.
10. High doses inhibit the immune system.
11. Limit dose to 3,000 ug.

### **References:**

The information for this article is culled from the hundreds of papers presented at the World Conferences on Ozone. The scarcity of information available in the major medical journals is testimony to the power of the Pharmaceutical industry. With good reason, they have established a wall of silence and welcome the dissemination of falsehoods about the effects of

ozone. They have an entire market of antibiotics that are at odds with ozone therapy. My conversations with practitioners in several countries, including the United States, confirms the remarkable results that I observed first-hand in my own practice. Reprinted with kind permission from: The Family News 9845 N.E. 2nd Avenue Miami Shores, Fl. 33138  
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## Oxygen Therapy - The Empire Strikes Back

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Edited by Ruth Parnell from the transcript of a taped radio interview conducted in mid-1993 by Gary Null of WBAI, a public supported radio station in New York. 505 Eighth Avenue, 19th Floor, New York, NY, USA. Ph: (212) 279-0707

The Australian media recently spearheaded the international assault on ozone therapy. Utilising a range of Orwellian tape-editing tricks mixed with half-truths, the media down-under have ensured that AIDS patients will continue to die in ever increasing numbers! Meanwhile, those who have experienced ozone treatments for cancer and AIDS are lobbying to continue ozone therapy -- as the treatment of their choice!\*"Basil Wainwright has categorically invented a process to purify whole donor blood in the bag, and his invention of polyatomic apheresis ozone technology has created the most significant break-through in the treatment of AIDS and degenerative diseases found anywhere in the world to date." (Richard Bernard - Polyatomic Apheresis Inc.)

GN = Gary Null

SAT = Sue Ann Taylor

BW = Basil Wainwright

GN: This programme is Natural Living, and I'm Gary Null of WBAI, a public-supported radio station. Tonight I'll be talking to Sue Ann Taylor, an investigative journalist, and Basil Wainwright, a scientist and inventor of a particular ozone machine. Why is he in the Metropolitan Correction Center in Miami--the jail? Why hasn't he had a trial in three years? Why does the government not want his story to get out? More on that later. Is HIV the cause of AIDS? HIV has never been found in any scientific studies anywhere in the world to be the sole cause of AIDS. No one can prove it. It is speculation. It is political and economic. The man who said in 1984 that HIV was the probable cause of AIDS (instantly it became dogma that it was)--did he also inform the public he was the primary beneficiary of a test for HIV, that he owns the patent and that millions of dollars have gone to him and his associates? No. Did the press vigorously explore all the allegations of fraud and corruption? No. The alternative press did. We're the ones that brought you that information. They tell you don't challenge orthodoxy. We challenge you not to believe that but rather to believe the experience of those who are the ultimate authorities: the patients who are alive and well, having had the opportunity to intelligently review the best of both and see what works, and that's what we bring you.

You've heard previously from patients successfully treated using non-toxic therapies, you've heard from the physicians who've treated them. Now today, in this segment, Sue Ann Taylor, investigative journalist, welcome to our programme.

SAT: Hello!

GN: Sue, you recently returned from the Philippines where you observed and recorded the

effects of ozone treatment and a polyatomic apheresis therapy on a group of HIV-positive and AIDS patients. Would you give us the background of this and why it is so important that the people hear this story?

SAT: Well, I was researching for a documentary that I had been working on, called Living Proof--People Walking Away From AIDS Healthy, because I was finding more and more evidence that there were things that were in fact working for some AIDS cases and/or HIV-positive cases. In doing that research I came upon ozone therapy, and I also came upon all the controversy that surrounds it. So when I was offered the opportunity to actually watch a trial happen first hand, in the Philippines, I jumped at the chance. I went to the Philippines and I was stunned with what I saw, because I was expecting the entire thing to take place in a sort of wing of a hospital, or something that looked a little bit more like what I expected medicine to look like. It was actually a clinic that was set up rather ad hoc to provide space to do justice to this trial, so I started out a little on the sceptical side, not knowing what I was getting into. There were 19 HIV-positive people there, five of whom had full-blown AIDS. Over the course of about three weeks I watched the patients, or participants as they preferred to be called--six of whom were in pretty bad shape--I watched them go through some pretty remarkable transformations and I saw it happen before my very own eyes. There's no amount of journalists or medical people who can tell me that what I saw I didn't see. I saw people who were unable to walk, be able to walk again. I saw people who were very, very ill just get considerably better, and all of the treatment was cut short by a raid by the government. The Philippines government came in and shut down the entire operation, and only about one-third of the prescribed amount of treatment had been accomplished. It was a trial, so remember there wasn't an absolute number on how much treatment they were going to need--that was part of what they were there to establish--but one-third of what they were expecting would be close to the magic number of hours on the machine, had been accomplished, and in that period of time remarkable reversals in these people's conditions were evident.

GN: Alright, describe the clinic.

SAT: The [Cebu] clinic itself was an upscale home in the Philippines. An upscale home in the Philippines looks kind of like an upscale home in America. It was a very large home, two storey, fairly large lot, and behind the home they had built grass hut kind of things, but it wasn't as crude as that makes it sound; it really had a vacation resort feel to it. It was not really unacceptable--and by Philippines standards it was just fine. I had an opportunity to go to one of the Philippines hospitals, and our cleanliness within the clinic beat the cleanliness of the Philippines hospitals that I visited. So, what I had to do was readjust my western benchmarks to a third world's benchmarks, and I learnt a lot in the process, educating all the Filipino staff who were excellent--I would pit their training against any training of any nursing staff anywhere in the world; their knowledge was excellent. But some of the things we take for granted, like refrigeration and insect control, they just have really come to learn to live with those things, so we had to educate those people as to what western standards would be. The clinic was, by our own standards, crude but it was, you know, acceptable also. The materials were all new; it's just, again, it didn't meet my preliminary expectations.

GN: Who was working there?

SAT: Working there were three parties, actually. There was a group from Australia--the clinic was actually owned by a couple named Bob and Rosanna Graham. The second group was PAI, the polyatomic apheresis unit group, and all they did was supply the equipment and people to



train the Philippine staff to use the equipment; and the third group was the Philippine staff which consisted of two Philippine doctors and 11 nurses.

GN: And who were the patients?

SAT: The patients were 20 Australians, 19 with HIV, one with multiple cancers.

GN: Is it illegal to enter the Philippines if you are an HIV-positive person?

SAT: My understanding is that it is illegal to go in HIV-positive, but Immigration does not question you; there is no testing and I don't know that the patients realised that it was illegal.

GN: Could you tell us some of the success stories of the patients?

SAT: The most dramatic success story was a man named Paul. Paul is 42 years old, he has been HIV-positive since 1984, has full-blown AIDS and Kaposi's sarcoma. The lesions, the Kaposi's sarcoma lesions on the bottom of his feet were so great when he left for the Philippines that he couldn't walk. He was in slippers for over a year. He could not wear shoes. He gingerly walked on the outsides of his feet and it was very difficult for him to get around at all. After 11 hours of treatment on the machine, Paul's lesions went away. He was able to wear leather shoes and, most importantly to Paul, he was off morphine for the first time in four years. Prior to his going to the Philippines, the cancer hospital had told him that he had reached the maximum amount of radiation that he could receive safely, and he would have to simply continue to increase his morphine to deal with his increasing pain. And Paul believed that he experienced just miraculous treatment, that in 11 hours of that treatment the lesions on his feet went away and he could wear shoes and walk normally again.

GN: Let's now describe what the treatment consisted of.

SAT: Certainly. The polyatomic apheresis looks like the following: a patient sits in a chair that looks a little like a dentist's chair. It's a comfortable chair. There are needles, intravenous needles inserted in both of their arms. The blood coming out of the left arm is pulled through a pump that is somehow in synch with the heart rate, and a circuit of blood is created between the left arm coming out and the right arm coming in. The blood goes through a series of tubes, goes down through a cascade tube where it is met with ozone under pressure, and at that point that's where the viral kill happens. The blood continues down through an escape tube, through a filter, back into their right arm. What you see visually is the blood exiting the left arm is a very black colour; it is **BLACK**. It goes down through this cascade tube, which is a wide-bore cascade tube, about an inch in diameter, and it goes back into the arm, the right arm, a bright cherry-red colour. It comes out looking alarmingly different--this is with the HIV patients--alarmingly different than you would expect. Now, the first patient I saw on the machine was a person without HIV. She was a normal person who had an infected foot, and her blood came out looking like yours and mine would, and went back in only slightly differently than it came out; so what I witnessed was that the HIV patients' blood was considerably blacker than a normal person's and went back considerably lighter. That's, in a nutshell, what it is.

GN: Alright, now, what other parts of the therapy were included with this ozone treatment, and how does this ozone treatment differ from, let's say, one which would be done in New York where you pull out about, oh, a half a pint of blood, ozonate it and put it back in the arm over about a 15 to 20 minute period?

SAT: Okay, I've never witnessed any of the other treatments that you're talking about. The only two ozone treatments that I've seen actually operate are the polyatomic apheresis and, using the same equipment, a process called rectal insufflation where the ozone gas is put in through a catheter into the rectum, which becomes an ozone enema, so to speak. Those two were used at the clinic and in conjunction with one another. Some of the participants in the study had experienced that treatment that you are talking about and had some success with it. What they believe from their own experience, what they told me, is that it was the difference between a Volkswagen and a Rolls Royce, from what they felt with the treatment you're talking about getting in New York versus what they got in the Philippines.

GN: So, far more productive in the Philippines?

SAT: Correct.

GN: Now, what happened to these 20 patients? Where are they at now and have there been any additional protocols for these people to follow?

SAT: Okay. The turning point of everything was on March 19. The youngest participant was a 23-year-old woman named Jodi, and she had full-blown AIDS. It was a real tragedy because she really kind of represented all of our daughters, and her courage was phenomenal. She died in the clinic and that's when things started to tumble very quickly. She died from a series of complications. I'm not a medical expert but I believe she received two insufflations too close together and her body had trouble coping with the amount of ozone that she had taken in. She also received those against doctors' orders, so I guess it would have to be chalked up to human error rather than anything to do with the equipment. She received the ozone via the rectal insufflation.

GN: You mean the Philippine doctors had suggested she not take those?

SAT: Actually, it was the American doctor, the expert on the ozone, who had said this girl shouldn't have another until she recovers a little bit. She had remarkable success on the equipment, though. When I first arrived I was afraid Jodi was not going to make it until the equipment arrived. There were all kinds of customs hang-ups that prevented the equipment from getting into the country and getting set up on time. So the patients arrived ahead of the equipment, which was a real management error because it just added too much stress to the patients.

GN: By the way, who raided the clinic?

SAT: It was raided by the Department of Immigration.

GM: Was there any evidence the FDA had been involved in the raid?

SAT: There was not any evidence that the FDA had been involved; but what I was told was that the story really got underway when Australia's version of A Current Affair did a scathing story on the clinic and what the patients were about to experience, just as they were getting on the plane. I was told by another journalist in Australia who I trust, that ACA is the one who went in to the Department of Immigration and tipped them off; so I believe that there was something operating there. I was also told that the producers were directed by their upper management to do a 'chuck job' on the ozone therapy. An no matter what they were told, no matter how much positive information they were given, it never aired; and I watched this happen time after time.

GN: So, in other words, there was a gross bias in the media, from your interpretation, to

prevent positive stories about the success of ozone from getting back to the general population?

SAT: It's not even a question of interpretation. I watched it happen; I watched the participants give interviews; I gave interviews myself. We would turn on the TV and we would be shocked at what actually would show up. Paul, whom I was telling you about, would tell his entire story; he would show his feet, all of those things; and he made a comment in one of the television interviews where he said, After I got going I could just feel in my heart that this was working.

That little snippet is the only thing that they would use, and then they would cut to the doctor saying, Well, you know, there's a certain amount of mind over matter, and all that kind of stuff. So they were completely dismissing the science of it and trying to make it sound like their improvements were all in their own minds; but 15 patients had improved T-cell counts, one as high as a 70% increase.

GN: We are talking with Sue Ann Taylor about one particular type of therapy and one clinical experience that was interrupted in the Philippines. A group of 19 individuals with AIDS and ARC underwent a particular type of ozone treatment. As you have heard Sue Ann Taylor say, remarkable results were shown in the majority of patients. Unfortunately, the clinic was raided and closed down and the participants went back to Australia. I would like to shift gears, however, and bring in another individual to share a different perspective on this, and one that we haven't talked about in the past. Basil Wainwright, welcome to our programme.

BW: Thank you very much, Gary. I must congratulate you on running a super programme and a very courageous one too.

GN: Basil, you are now incarcerated in Florida?

BW: That's right, so if any of your listeners hear any background effects, I must apologise for that. I am currently incarcerated down here in Miami.

GN: From what I understand, you are a scientist and you are the inventor of this polyatomic machine, this ozone machine, and that you have been incarcerated without trial for three years. Is that correct?

BW: Yes, I'm now well into my third year without trial and some seven violations of my basic human rights.

GN: What are those violations?

BW: Well, there's the 4th amendment and the 5th amendment, the 6th amendment has been violated, and the 8th, and 14th. So...

GN: What has happened to your attorney filing proper motions to get a fair and speedy trial? That's one of the constitutional provisions for people who are incarcerated. I haven't heard of people waiting three years except this particular political detainee who was here in New York, the IRA supporter who was held for some seven years.

BW: That is absolutely right. Well, it all started that--really, I suppose I should give you and your listeners a brief synopsis. I was working with Dr. Viebahn in Germany and I was brought into this project along with Medizone, and then got very much involved in the process. And I was somewhat intrigued to find that nobody had really done any specific testing, i.e., looking at

the cytotoxic levels or, that is, the concentration of ozone, looking at the specific atomic structures of that, and also the contacting time; so there were an awful lot of areas that particularly interested me. I worked with the University of Medicine and Dentistry and also the Mt. Sinai Hospital with Dr. Weinburg and with Dr. Michael Carpendale, and started to get very, very involved in the course. It was very evident there were some phenomenal results being seen in the AIDS area and I started to look at it more in-depth. There were several controversies going on as to whether it was a function of free radical reaction or oxidation--but of course both of those functions occur extensively--and also this ionisation; and I wanted to determine the specific parameters of that, because when people refer to ozone you might just as well refer to a vehicle being involved in a collision because you're not really defining the atomic structure of ozone which can be multifold. There can be many aggregate combinations of molecules which can have very specifically different responses, and I wanted to determine this.

GN: Since 1985 you have been working with some German doctors including Dr. Viebahn that you talked about. Now, you had a way of determining that the ozone being used back then was not as effective as the way you could create a better ozone; they were using  $O_2$  but you also saw  $O_3$  and  $O_4$ .

BW: Yes.

GN: And you also were looking at two major factors: the concentration in relationship to agglomerate measurements, and oxidation; and then you were looking at the viral inactivation?

BW: Yes.

GN: Now tell us about what you found with what you created concerning viral inactivation.

BW: Well, of course, I think it's very important for your listeners to know that the reason scientists refer to retroviruses' inactivation as opposed to being killed is because normal micro-organisms have metabolic mechanisms, whereas a retrovirus could almost be considered a piece of genetic material drifting around in the bloodstream. And, so, it's rather difficult to kill a non-living thing, hence scientists refer to inactivation. We looked at these various techniques and procedures and I suppose what really kicked it off was our study which we did with Biotest down here in Miami, where--having determined that the German process worked but indeed wouldn't be dramatically effective because they were not treating high enough volumes of blood--they'd also determined that once someone had been taken back to negative using polyatomic oxygen or ozone, they indeed remained negative. I think there is only one case of Horst Kief's that actually went back to positive, so that was rather unique because all the doctors were saying, Okay, so what? You get somebody to negative, but in a couple of months' time they're going to go back to positive. Well, that fact was proven not to be the case, which I think even surprised the Germans. And it might well be that the immune system kicks back in, and when we say negative we're looking a nucleic acid response or PCR work to determine that; but certainly the patients were not going back to positive--that was very interesting. So we thought, okay, if these patients are going to use autohemotherapy which you referred to earlier, Gary, where you take out half a pint of blood, treat it with ozone, and then reinfuse it back into the patient, that was taking typically 11 months, of course combined with a very rigid nutritional control as well. But using that process it was very evident that it's like chipping away at a mountain with an ice pick when you're looking at the view of the pandemic facing mankind; and it became very apparent in 1987 that the best way to go was with dialysis

or a dialysis-type procedure. So I worked with Cobe and other dialysis equipment and in fact filed my first dialysis patients using ozone in 1988. But, however, using ordinary dialysis equipment which is a hollow fibre membrane, we discovered there was too much homolysis occurring as a result of that; also, the thing that we refer to as mechanical shear. The very fact of pumping the blood round outside the body can cause all sorts of trauma to cells--there are thermal reactions, there are pressure zones, the pumping head itself can actually crush cells--so we had to look at a number of factors. And then, when we did more research, we found that  $O_4$  in particular had some very unique responses. It has a phenomenal amount of electrons; as a matter of interest in  $O_4$  you have 40 electrons, and that makes it a very powerful negative ionising platform drifting around in your

bloodstream. It also was far more stable than  $O_3$  which again was completely the reverse of what everyone was projecting. It was very evident that  $O_3$  had a better oxidative effect, and that was very effective in eliminating infected cells, but  $O_4$  had the ability because of its ionisation to break down, we believe, the RNA, and of course uracil, which is a very important sugar combination--the 5-carbon sugar in the virus RNA--was actually being broken down. Well, when we actually achieved this, we did our first study down at Biotest Laboratories here in Miami--hence my incarceration down here. We did this study and as far as I know, for the first time in history, using apheresis we successfully converted HIV-positive to negative, and we could do this time and time again using PCR. That's the reason we came here, actually, because Biotest Laboratories in conjunction with Miami University had this latest state-of-the-art equipment; and from that very moment the FDA which hunt started. We tried to keep a relatively low profile but of course the word soon got around the system, and then one night I came home and the SWAT team descended, guns drawn, and eight of them sort of crashed in the front door. I was arrested and charged with practising medicine without a licence, which of course is complete nonsense. But the SWAT team, instead of looking for anything that might indeed have been relevant to my practising medicine without a licence, all they did was dig out all my patent specifications, technical data and intellectual property rights. So they came with a very specific directive from the FDA, to seize all my intellectual property rights. From there I was sort of thrown in a state prison; mechanisms graunched on. Eventually I had charges from the FDA which boil down to sending and selling ozone generators from interstate-interstate trading laws, etc. Unfortunately, a couple of months after I was in prison, I detected a very severe heart condition. In fact, if this radio show had been yesterday I doubt very much if I could have done it. But nonetheless they detected I had a very severe heart condition, and it's progressed to a point now where I'm collapsing and having blackouts and stuff, but still hanging in there. I've just recently done a technical paper. Well, from that episode this series of things went on, and as you quite rightly say--and I certainly won't bore your listeners with the phenomenal list of violations against me--I'm now into my third year; come October I'll be commencing my fourth year without any trial. I've just recently been appointed some new attorney who is hopeful of trying to get me bond. In fact, Dr. Michael Carpendale and other doctors very courageously were flying into Florida for a major hearing in front of the judge. Everything was scheduled but at the very last moment the FDA stepped in again and the hearing was cancelled, and my research team had to frantically phone around and cancel everyone coming in. I did get bond, much to the amazement of the FDA, which was really a administrative error, and I was out for a few months. During that time we managed to get a number of apheresis systems put together and out into studies. Most of the studies which were conducted in and around the United States of course have already had the FDA SWAT teams descend on them, close them down and seize equipment. And we've had things reported

like seven p24 antigen negatives, a couple of PCR negatives, but at no time have we ever been able to get into the real completion of a study. In every case, I think the doctors would tell you they've seen absolutely dramatic results, and that's not from me because this information has been fed back to us. They of course are very concerned that they're not in a position to pursue this, and the process does really show some pretty dramatic potential--that's exactly what Dr. Carpendale is saying--and the only way we are ever going to get this out there is if the AIDS groups get up and demand polyatomic apheresis so that we can get these studies up and running. We've got a group working with two very, very prominent stars that are hopeful of applying the sufficient pressure to be able to get this achieved. During our studies we managed to determine that protein aspects in the blood, in other words, high protein levels would have an inhibiting effect. The normal procedure that has been adopted by the Germans, i.e., introducing antioxidants--which is very popular over here too--was negating the effects of ozone. Everyone in the United States can enjoy the wonderful efficacy of ozone; there is nothing against the law that you can't use it, and there are several ways of applying it. In our protocols, prior to treatment the patients will be receiving no antioxidants so that we get the maximum oxidative effect from the O<sub>3</sub> component which we use 2% by weight, and 6% by weight of O<sub>4</sub>; and we have a pretty rigid nutritional programme too.

GN: So let me see if I can put this into perspective. Basil Wainwright is now in a jail in Florida for developing a special form of ozone machine that puts an O<sub>4</sub> into the body. There are a number of patients, estimated as high as 200, who have undergone this polyatomic apheresis treatment so far. These have included HIV, environmental and degenerative diseases, approximately 30 persons with AIDS. Of those 30 people, all show dramatic improvement, seven are p24 antigen negative, and two are PCR negative, meaning there is no HIV viral DNA found in their bodies, and the p24 means there is no active replication--all replication of the HIV is done. For the effort, you have been put in prison without trial. When the doctors did come to testify on your behalf, the FDA saw that the hearings were postponed. On a technical glitch, you were allowed out, and then, when they found out the technical glitch they put you back in; and you have been in violation of several due processes including a speedy trial. Why weren't the other doctors put on trial or arrested? Why were you the only person involved in this?

BW: Well, because I was the primary motivating force and the one that indeed held the patents in the United States office for polyatomic apheresis, which is quite unique. The only reason that I can think of is that I enjoyed the energy in working in the process. We have a wonderful team, they're all terribly dedicated to helping people, and we would like to think we are motivated in attempting to do God's work. Sue Ann and everyone else who have been involved have expressed love and compassion to all these patients, so it's been more than just a research project for me. I thoroughly enjoyed working with the patients. Of course, the pharmaceutical companies cannot file a patent on ozone, and you can only file patents on the intellectual property rights or the designs of the delivery mechanisms to the patient; and being as we have those, I suppose the best thing they could do and their only reaction was to throw me in prison, hoping that it would completely bring everything to a halt. It hasn't done that. There's been a dedicated bunch of people out there; they definitely need more support. We would certainly provide equipment for AIDS groups in the United States if they would only get up and demand polyatomic apheresis and demand studies which they could do. We would be only too pleased to provide the equipment and, indeed, a number of very top doctors are prepared to come along and offer their services and monitor and support these test studies. You undoubtedly

know that Ed McCabe has been doing some tremendous work in trying to open people's horizons on these issues, and Ed of course has been very supportive and he's become very supportive because he's been seeing the successes. Unfortunately, a lot of the doctors that have been involved in the research have had terrible pressure applied to them; in fact, their very jobs and livelihoods have been threatened by the FDA, which is very, very sad. I must admit when I first came to the States in 1987 on this particular project, the people told me this sort of thing existed in the United States and I thought it was all James Bond stuff, but of course I soon learnt to the contrary that indeed it was fact, and here I am. All I want to do in fact is get out here and research and work for the betterment of mankind and just simply conduct God's work. In fact, I've just finished two scientific papers whilst I've been incarcerated, and I've been working very, very hard. A lot of good things: we've got a Middle East project which has been confirmed which will be up and running very soon; the Canadian government with NATO of course, as you've probably read, indicated great interest. Well, they've actually approached us and we've had talks with them about structuring a very special process which we've developed. It's from the blood bag to the patient, so for the armed forces, if they get injured out in the field and they're having delivery or transfusion of a unit of blood, there's this process we've developed which goes in series or in line with the IV to the patient, which actually purifies the blood with polyatomic structures before it goes into the wounded soldier. So, despite my various bouts of illnesses and I must admit it's been a bit touch and go at times, I've certainly been keeping myself active, Gary, and as I said I've certainly been following your programme with intent and your work with intent, and I hope your listeners out there realise what a super person you are and how you're projecting this work and making this awareness to the people out there.

GN: Thank you Basil Wainwright, and let's hope for the best and that justice will be served by being fair and by seeing that your machine is tested. I want to thank you also for being on today, Sue Ann Taylor. Any closing thought for us?

SAT: Well, the closing thought that I have is, after the raid the mayor of the city gave the Department of Health the opportunity that if they wanted the study to continue, he would make space available in a hospital and make the patients the guests of the city. For them to turn down that offer and shut it down without looking at the patient's records, of which the blood tests all showed improvements, or watching a demonstration--that's when I started to believe that there was some level of a conspiracy happening right before my eyes, because they had made up their minds in the face of an offer from the mayor and said let's finish it right here. The only other point that I wanted to make, that I found alarming, is that people who have the ability to make those decisions were that closed-minded about the patients' pleas that this could save our lives, that they shut the door in their faces.

GN: Sue Ann Taylor, you learned a good lesson, and that lesson unfortunately is a bitter one: not always do the patients count when there is a political or economic agenda ahead of their interest. Thank you very much. I am Gary Null; the programme is Natural Living.

#### **NEWS UPDATE -- 29TH OCTOBER 1993**

-Under a new agreement between the USA and Mexico, the FBI has been conducting armed raids of ozone clinics inside Mexico.

-NEXUS has learned that Basil Wainwright is being held in a 20-man cell currently holding 41

people. He has had 2 heart attacks plus 4 major blackouts in the last 6 weeks, and has been hospitalised 19 times since his incarceration. It was discovered two months ago that his medication for Parkinson's disease had been altered so that he was receiving the maximum, and often lethal, dosage of the drug Simatrol and its generic, Amantadine.

-In both Australia and New Zealand, as well as the USA, the health authorities have been conducting crackdowns and closures of businesses involved with oxygen therapies.

-NEXUS has been contacted by scores of readers who have reported excellent results from their experience with oxygen therapy.

For more information on the Polyatomic Apheresis unit:

POLYATOMIC APHERESIS INC.

6278 North Federal Highway, Suite 410

For Lauderdale, FL 33308, USA.

Phone (305) 942-8976; Fax: (305) 942-8482

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From Nexus Letters to the editor...

Nexus February - March 1984

Volume 2, Number 18.

Re: Ozone Therapy vs AIDS

Dear Duncan

The report in your last edition in regard to Sue Ann Taylor and Basil Wainwright was reasonably accurate. There are a couple of corrections, one being that Jodi did not die because of human error; she died of AIDS and the side-effects of that disease. Jodi was taken to my in-laws' place

for the cremation arrangements. In regard to the financial problems that we had when A Current Affair ran their story, the bank closed our accounts, including a \$50,000 line of credit, and posted a cheque to us made out to Cebu Ozone Treatment Centre. The cheque could not be cashed because we could not open an account at any other bank. We finally got the cheque re-written and payable to one of the directors. As for the \$50,000 line of credit, a caveat was enacted on the property and it is only next month that we will be able to go to court to have it removed. My wife flew home on the same plane with the patients. What the press stated was a lie--that my wife and myself fled the Philippines long before these events happened. We stated this during my TV interview, but it was never shown and the press never printed it. We have the Polyatomic Apheresis unit ready in Australia. We offer it on loan to any group or individual doctors who will

operate this on clinical trial basis to save lives. What we have seen with this equipment indicates that it may be the answer for AIDS victims and cancer sufferers, but we will never know unless trials are conducted and completed. Many great forces are at work to make sure that this technology will ever serve mankind.

Robert Graham

PO Box 61

Carlton North, Vic 3054

Fax: (03) 336-4467



Nexus Magazine is available by subscription by calling 815-253-6464. (\$25 per year USA within USA - 6 issues, or \$30 USA for Canadian subscribers.)

# OZONE IS NOT SMOG, OZONE IS GOOD AND NATURAL

by Ed McCabe

Adapted from Ed McCabe's "Oxygen Therapies"  
Copyright 1990 by Ed McCabe

Ozone is one of the most beneficial substances on this planet, and the BAD science you hear quoted on the news every night is causing you to subconsciously be afraid of nature, and therefore, a part of life itself. They tell you that somehow hydrogen plus nitrogen or sulfur equals ozone.  $H + N + S = O_3$ ? Not on this planet it doesn't!

What is ozone? Simply, oxygen. Three atoms of nature's oxygen. It exists in a very active form for about 30 minutes before breaking down into two atoms of regular oxygen - by giving up one atom of singlet oxygen.

Where does ozone come from? Nature. And nature is efficient. The new growth in the forests, the trees, the grass on your front lawn, and the plankton in the ocean are continually creating oxygen. As you read this, this oxygen is rising up into the atmosphere to where the ozone layer is. In the region of the ozone layer, our rising oxygen is bombarded by the sun's photo chemical energy in the form of ultraviolet (UV rays). The UV energy bombardment changes the oxygen from  $O_2$  - two atoms of stable oxygen, into  $O_3$  - three atoms of unstable active oxygen. We call this pure form of oxygen "ozone." The using up of the UV rays to create ozone is how the ozone layer shields us from their harmful effects. This is all part of the natural process of life on this living biosphere called earth. The chemical formula for this is  $3O_2 > UV > 2O_3$ . Being heavier than the oxygen in the atmosphere, this newly created ozone falls back to earth, eventually giving us one atom of oxygen, it changes back to  $O_2$ , and is immediately replaced by more rising oxygen which is also soon changed into ozone by the sun. The ozone falls to earth and is all around us purifying our water and air, decomposing bacteria, molds and fungi. It is the fresh smell of laundry dried outdoors in the country. It is the fresh air at a clean seashore, and the sweet smell of the air after a lightning storm. Lightning, also possessing photo chemical and electrical energy, creates ozone as well. At least this is how our world was operating until man started ruining it.

Ozone has always been with us in nature, and the fact that ozone gives off that single oxygen atom is a significant factor in life, in medicine, and in toxic waste cleanup technology. Thousands of physicians in Europe have been using ozone as medical treatment for over 50 years, and the use of Ozone in medicine is starting to finally catch on here in the U.S.

How is it used in medicine? This  $O_3$  Ozone is not as stable as regular  $O_2$  oxygen because it has that extra atom of  $O_1$  attached to it. Ozone will readily give up this extra atom of  $O_1$  and revert it back to stable oxygen again. This giving off of the  $O_1$  is the reason why ozone has been used in medicine. It has been proven extensively that  $O_3$  will kill bacteria, viruses, fungi and molds by attaching to them and oxidizing and eliminating them, oxidizing means to burn without giving off light or heat. These bacteria, etcetera, are lower life form organisms, and are mostly anaerobic. That means they can't live around activated oxygen/ozone. Doctors using the proper concentrations and correct medical protocols have achieved substantial positive clinical results with ozone.

Far from being a poison, ozone, when used properly, has been shown repeatedly to kill

pathogens - yet not harm nominal cells. This is because disease causing pathogens do not have any strong enzyme coatings to protect them - as do all the higher life forms like us for example, pure ozone is available to purify all our county's stored blood supplies. There is no reason why people have had to come home from the hospital with AIDS or hepatitis from blood transfusions. European doctors and respected NY University researchers all state that ozone has been used to eliminate AIDS in humans, animals and blood tests. Without any side effects. Why don't we see this on TV? Why isn't it being used?

Breathing ozonated air or drinking ozonated water (at the safe legal concentrations that are already conservatively laid out by the government) are two of the ways of getting activated oxygen into your body. Did you ever drink clean water just downstream from a waterfall and feel invigorated? That was because the water had tumbled over the rocks, thinned out, and absorbed oxygen/ozone from the air. Other methods being explored medically in the US are rectal ozone insulation, ozone autohemotherapy and intravenous ozone infusions. All these methods require the use of pure medical grade ozone. Being blatantly non toxic, these methods of killing viruses and bacteria in humans have been in use in European medicine for over 50 years.

Most European and several major US cities have been purifying water, sewage and toxic dump sites with ozone, some for over 70 years. Ozone based systems can even break down PCB's and all other industrial chemical wastes both organic and inorganic. This is possible because ozone based systems are able to create enough of these singlet oxygen atoms to oxidize anything unnatural found in our air, water, sewage, and sediment. Ozone can do this yet is so safe that it is used on humans and animals as the water purifier at Marine World and in the Olympic swimming pools.

#### **Why do they call Ozone "smog?"**

Bad science and bad reporting. A political misrepresentation. It's also dangerous to promote this concept. A Los Angeles nurse I met told me she actually treated a patient who got sick from going around breathing bus fumes deeply: The poor man had heard that ozone kills the AIDS virus and because of TV had thought ozone was the same as smog!

By calling nature's oxygen "poison," and diverting your attention away from the real polluters, no one has to clean up the environment. Did you know that your automobile emits its own weight in pollutants into the air every year? Television tries to position itself as "concerned" and wastes your time arguing over what type of shopping bag you should lobby for at the local supermarket. Meanwhile, the factory next door continues its deadly course of spewing tons of poisonous pollutants into your breathing air and drinking water. While you are constantly made to feel guilty about every day living, they won't give any significant air time to cover the far more dangerous industrial polluters that are too cheap to put scrubbers on their smokestacks. Why? Because the corporations might be "offended."

Go into a city, look up, and taste the dirty air you're breathing. Try and tell me that the brown / gray / yellow colour is ozone. I doubt that I'll believe you. All of this can be cleaned up with colorless, clear ozone

Ozone based systems are able to purify 99% of every liquid, or gas or toxic substance coming out of any industrial operation. The engineers even tell me we can include radiation in the list since the radiation is carried by something. Why aren't the ozone systems being used?

Nature constantly works through the balancing out of different electrical, magnetic, and chemical charges. When man dumps pollutants into the air, nature tries to clean it up by in effect, "sending" ozone into the affected areas to oxidize and clean up the pollution. What got us into this mess was the old idea that the earth and water and air magically combined into one

giant "sponge," where we could just "toss it out" and it would all disappear. Well our sponge is full now, and although nature still tries, the ocean polluters and rainforest clear cutters have significantly choked off nature's means of cleanup - the ozone.

That is why Ozone is always found as a very tiny component of air pollution. Here we find out why the newscasters and scientists try to blame your respiratory problems on your friend ozone and call her names like "smog." You can almost hear them thinking..."Well boss, here's 5 000 pounds of toxic hydrocarbons and nitric compounds coming from our factory, and those pesky environmentalists are starting to notice it and make noise...Let's see...There's less than .12 parts per million (or only 12 millionths of a pound) of ozone in the area...I've got it J.R.! We'll blame the teensy weensy little air ozone molecule - so the sheep won notice our toxic soup, the real cause of their dead trees and lung, eye and throat irritation!" "Smithers, that's brilliant! Let's do lunch at the club. By the way, how's your daughters rash?"

By blaming nature, the huge polluters are never forced to take responsibility for the current dirty engine designs and factories, and never have to incorporate any of the already invented clean energy sources. What they call "ozone smog" is a toxic soup of compounds. Why they don't tell you is that Nature's ozone is trying to clean it up, and is a very tiny portion of the smog they report. **THE MORE CHEMICALS DUMPED IN THE AIR, THE HARDER NATURE TRIES TO CLEAN IT UP, THEREFORE THE REPORTED OZONE LEVELS WILL BE HIGHER.** They also don't admit that ozone is strictly, always, only O<sub>2</sub>+O<sub>1</sub> pure oxygen, and never anything else.

The ray of hope here is that the media professionals and federal, state, and corporate decision makers and their families are themselves coming down with all manner of new mutant diseases. Their vacation hideaways are spoiled. It is no longer an "us" versus "them" class struggle. We are all in this earth boat. This is quickly forcing change in business as usual.

As to their claims that ozone is a poison, I can refer detractors to internally clean people who work in very high concentrations of pure ozone all day long without ill effect. In fact, they commonly report a healthy invigoration. Where these scare stories come from is the following typical scenario. When a typical smoker, or junk food or drug addict - a person whose body cells are loaded with toxins finally gets near enough to an activated oxygen (ozone) source, his or her body starts to oxidize the toxins within it, in an effort to finally remove them. The pathways out of the body become filled with cellular debris, swollen, irritated, and fluid filled. Often this is uncomfortable, but only for a few days, while, and until, the oxidized toxins leave the body. The health professionals skilled in medical ozone usage call this a typical cleansing reaction.

Most air ozone "studies" are halted at the point of detoxification discomfort, and not after the full cleansing has occurred. Therefore "damage" is erroneously reported in the Scientific literature. In contrast, any properly conducted experiments are allowed to continue past this point - and report how the body replaces the weak, old, diseased, dying, feeble cells with new and very healthy oxidative stress resistant ones.

At times, an isolated and questionable report will surface in the scientific literature, telling of animals exposed to ozone who developed lung scarring. These studies were usually done at super high concentrations way beyond the typical medical protocols, and relate to impure ozone made from high amperage electricity and air, which is 80% Nitrogen, not pure Oxygen. Nitrogen plus heat plus moisture plus ozone equals nitric acid. Acid will definitely cause lung scarring. Again, this is not nature's pure natural ozone.

I've actually cornered a few scientists and reporters and asked if they knew that they were not being scientifically accurate when in the press they equate ozone with the toxic soup of smog.

The admitted (in private) that they knew they weren't, but keep up the charade "because everyone else does!"

What about the holes in the ozone layer? Consider the gluttonous "clear cutting" of the oxygen producing rain forests and the disappearance of our own oxygen producing national forests. Where is our oxygen going to come from? Then add the constant selfish polluting of the oceans and the greedy discharge of industrial pollutants, nuclear radiation and electrical energy into the atmosphere. These electrical, electronic, and radioactive discharges further scramble the elements in nature's air. At home, chlorine gas comes out of your water faucet and rises up into the sky. More and more, our oxygen is either missing or bound up in toxins. What we're experiencing is an increasing shortage of atmospheric oxygen that's available to be turned into ozone in the first place! That's why there is an ozone hole at both poles, and the rest of the ozone layer is starting to look like Swiss cheese. Greed, not ozone is the problem.

The ozone layer is constantly changing, almost a living boundary, paper thin, and missing at night. When the oxygen is all bound up with toxins, then there will be no ozone layer. Without available oxygen, the sun's ultraviolet light passes right on through without being absorbed in creating ozone, and we are seeing increased cataracts, skin cancer, blindness, and burning of vegetation. So our bodies and our food supply - therefore our very existence - is in danger, unless you personally do something about turning back the rampant greed that is destroying us. What can you do to help preserve and re-supply the missing oxygen in your life? Stop those unevolved people who think "We're all going to die anyway so I'm gonna get all I can now" from cutting down all the trees. Convince the factory managers to install existing devices like ozone based smokestack scrubbers, factory discharge point ozone based purifiers, and to fund existing ignored clean energy sources. Plant lots of trees. Don't sell aerosols. Stop polluting the clean.

Industrially, ozone air purifiers have been in use for decades. There have been no problems associated with their use, as long as they are used in average sized rooms, at the levels just below where someone feels discomfort. Enlightened hospital operating rooms commonly use ozone air purifiers to keep everything sterile. The doctors and nurses aren't falling over dead with scarred lungs are they?

Ozone air sterilizer/purifiers/deodorizers are commonly used: by hotel chains to remove odors; by used car dealers to give old cars that "new car smell"; by morgues to get rid of formaldehyde odors; by schools when they refinish a floor, so they don't have to close the school because of the dangerous refinishing chemical odors; in bars, comedy clubs, and restaurants - so the majority non-smokers can patronize them again and go home without stinking like an ashtray; in fitness/exercise clubs and gymnasiums where patrons don't smell body odor, they only smell fresh air and report increased endurance and strength; by grain storage building owners who report an end to mold and rot.

Owners of animal excretion soiled stable, barns, veterinary kennels, and professional dog and horse racing paddocks love them. If the animals could talk, they would probably echo this sentiment, and describe the air as fresh as a day in the country.

Entrepreneurs even buy - at a discount - sick cattle who are worn out from antibiotics and drugs, ozonate their air and water, and then sell them as healthy, disease free animals a year later at a profit. Plus, the consumer eats chemical free meat. Do you have any smoke damaged goods? Fire damaged furniture? Stick it in a room with an ozone air purifier running full tilt, and in a few days the useless items are restored. The applications are endless, wherever stale, polluted and toxic odors are encountered.

Factory and closed-up-tight office workers could ask management to install ozone air purifiers.

Management would benefit at the bottom line, because happy oxygenated workers are more efficient workers, cheerier to customers, and don't need as many sick days. In the fifties, ozone air lamps were placed in schools, and absenteeism dropped. Commercial clothes dryers came with UV ozone lamps in them. The federal government required their use in all government restrooms. If your home or work air stinks, think of ozone solutions.

If some sat only inches from an ozone generator and breathed deeply for a long time, they might have cell lysis (destruction) problems. But no one is advocating that, and product warning labels could handle the liabilities. No one deeply inhales oven cleaners, paint thinners or other common toxic household chemicals, and they are available everywhere without restriction. Why should ozone be any different? Jumping on the media hype- created bandwagon, some government agencies want to regulate the amount of ozone emitted from an ozone generator. That's not the point, and way off the mark. The output can't be regulated, because we never know the size room it will be used in, or the toxic cellular level of its occupants.

### **ED McCABE'S CONSUMER SAFETY GUIDELINES FOR OZONE GENERATORS.**

1. Is it a "cold process" ozone generator - the kind that doesn't create lots of nitric acid out of air nitrogen and moisture?
2. What is the ozone output concentration compared to the size of the room it is used in?
3. Does the generator have instructive labeling saying: "Operate only at a level where no discomfort is experienced?"
4. Is the generator a quality design, using safe components?

"Ozone is bad" is a great, quick, one liner for the media to hype, but it is far from reality. This instant journalism created a hysteria is so bad that the "Earth Day" environmental organizations even emblem their signs with well meaning but uninformed slogans. In a twisted way, people subconsciously are made to fear the very act of breathing, so that every breath taken on a hot summer day in the city is tainted with a fear of life itself.

At the home level, many thousands of people are now exploring the many medical oxygen therapies and pollution control devices I wrote about in my book "Oxygen Therapies." One of the simplest methods of using ozone at home is by installing a home ozone air or water purifier. Home purification units aren't manufactured for medical or industrial purposes. They generally use air as the incoming gas, and not pure pharmaceutical quality "green bottle" oxygen - as is required in the medical ozone generators. However, they do a fine job for what they were designed for, general air and water purification. There are several brands on the market, and I use them at home with pleasant results.

Many readers of my "Oxygen Therapies" book have even called and written to me of their own personal experiences. After installing air ozonators, they claimed "their house mold went away," "the odors stopped," their "emphysema became less," or their "lupus got better," and one fellow actually told me "the tartar fell off his teeth!" Sounds fantastic, but hearing these stories first hand has been my experience.

Of course no one is making illegal medical claims for these devices, but the anecdotal evidence in this area continues to amaze us as it piles up steadily. Since anaerobic (most) disease organisms simply cannot exist in oxygen, then oxygen is the first line of defense in your immune system. It's also necessary for the removal of every single bit of toxic waste in your body. Every waste product that comes out of you is oxygen combined with hydrogen, nitrogen, sulfur, or carbon. If the toxins in you don't have any available oxygen to combine

with, they pile up inside you and they can't leave.

Dr. William F. Koch, MD., was a brilliant free radical chemist and former professor of chemistry at Wayne State University. He wrote that ALL disease originates from toxins in the body. Now think about the fact that we were genetically designed during a time when the atmosphere was 38 to 50 percent richer in oxygen than you now live in - especially if you live in a city. We are living way below our optimum efficiency. If your car has dirt in it's oil, has half its air supply cut off, and has never had an air or gas or oil filter changed, it will die after sputtering along for a while. Our bodies are vehicles for Soul.

Your liver and kidney and lymph system are the vehicle filters. You die too soon, and full of dirt as well. The Bible dates some in the old Testament as being over 900 years old. How did dinosaurs get to be 5 stories tall? You can guess why so many are sick so often in our "modern" society.

I am convinced that what we've presently experiencing in our society is the rise of the age of toxins, diseases, and plagues all corresponding to the fall of our planetary and body oxygen levels. Fueled by greed and self imposed ignorance, the phenomenon is sad indeed, and unless abated, will drastically change or even eliminate life on this orb.

Some, including doctors, have added up the numbers, and concluded that half of the world's population will possibly be dead from AIDS, alone, in the next 10 to 20 years. I have seen slides brought back from Africa by Dr. William Douglas, the book author. Slides of whole villages that are now empty, and roads lined with burial mounds where the victims fell. Not a fantasy, it's real, it's right now, it's your problem. Pay attention to the warnings.

Take heart my friend, if you're reading this, it's not over yet.

We can change above dire predictions, if YOU get involved at some level. Plenty of evidence exists proving that an increase of planetary and cellular oxygen levels will solve most of our life threatening industrial and medical problems. Ozone is our friend. We should get to know it better.

**"Oxygen Therapies" by Ed McCabe**, is published by Energy Publications and is distributed by over 30 distributors to health food stores, select clinics, and booksellers worldwide.

Further info, publications, tapes, subscriptions, and past issues are available from

"The Family News" 9845 N.E. Second Ave. Miami Shores, FL 33138. United States of America Telephone: 305/759-8710

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At the urging of many in our oxygen family, The Not For Profit "Foundation For The Advancement of Oxygen Therapies" has finally been formed. Our stated purpose: We are bringing our case to the public by educating them that oxygen supplements, therapies and related activities are historically inexpensive, safe, and proven effective when used as directed by competently trained healthcare professionals. We are using education, the media, and soon, with your help, aggressive research as proof to silence whomever postures against oxygen, your very right to life itself.

While America dies of AIDS, Tuberculosis and a host of other diseases, and the FDA stands before Congress and declares as truth that "there is no evidence that ozone has any medical benefit," and Congressmen say we should "imprison anyone who promotes or uses ozone for 25 years as a felon," and doctors curing diseases are railroaded into prison, and homes are broken into by government agents seizing ozone machines, things have gone way too far. They are referring to us. You and me and our friends. Won't you please become a contributing member by joining the foundation today? Donations will be in a segregated account and only

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2. If no charitable deduction tax receipt is needed, just send directly to:  
The Foundation For The Advancement of Oxygen Therapies, Ed McCabe, Executive Director Non-Domestic c/o P.O. Box 654 Cazenovia, New York State Postal District 13035

Thanks, and Happy Oxygen!



# **WHAT IS OZONE THERAPY?**

## **(For Hartford AIDS Project)**

by Ed McCabe  
**Author of The classic bestseller "Oxygen Therapies"**  
**And the new hit "O<sub>3</sub> vs. AIDS"**

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It's so simple it befuddles the great minds. Unlike healthy human cells that love oxygen, the disease causing viruses, bacteria, fungi, and parasites - including HIV and others - are like most primitive lower life forms. They are almost all anaerobic.

That means these microbes cannot live in oxygen. Therefore, what would happen to these anaerobic viruses and bacteria if they were to be completely surrounded with a very energetic form of pure oxygen for a long time? What if enough of this special form of oxygen/ozone was to be slowly and harmlessly introduced into the body daily, over the course of a few months, by bypassing the lungs, and yet eventually saturating all the bodily fluids and every cell with it? The disease causing microbes that can't live in oxygen would cease to exist.

All 30 or so oxygen therapies, including ozone, work because they flood the body with Nature's single oxygen atoms. Singlet oxygen and its by-products are very energetic oxidizers - they "burn up" waste products, pollution, and microbes which can't protect themselves because they are either inert, or lower life forms. Normal body cells protect themselves from the oxidizing effects of oxygen by naturally producing their own protective antioxidant coatings.

We are 66% water. Most European and many American cities purify their municipal drinking water by bubbling ozone through it to kill all the bacteria and viruses, etc. See Inactivation Kinetics of Viruses and Bacteria by use of Ozone, by E. Katzenelson, et. al., American Water Works Society, 1974. Most bottled water in the U.S. goes through the same ozone purification methods. Since your body is two-thirds water (we are internally permeated with fluids), the same purification principals would directly apply to us. Ozone is simply infused into your personal body liquids to sterilize and purify them. This method has been successfully applied to the human body by knowledgeable doctors treating diseased persons for over 100 years. It's simple. Our natural intake of oxygen from food, air, & water is the way Nature intended us to keep healthy and clean by oxidizing away the microbes and toxins.

Unfortunately, due to human ego and greed, mankind has polluted the eco-system, cut down the rainforests, and ruined the oceans. This is where the oxygen all comes from. So because we are all oxygen deficient, our bodies can no longer take out (oxidize) the trash. Even the ozone layer above us that protects us from ultraviolet rays is born when the rainforests make the oxygen that eventually turns into ozone. The removal of our planet's oxygen generating forests and atomic bomb testing rendering the natural oxygen isotopic and unable to turn into ozone is directly relating to the "mysterious" holes in the ozone layer.

I have witnessed hundreds of AIDS and other patients receiving ozone infusion therapy. When they start out their blood is filthy, diseased, and so empty of oxygen that it is almost black in color. Keep putting the ozone into them for a while, and the blood turns back to a bright cherry red color, full of life giving oxygen and clean. Human ego is presently preventing us from exploring ozone's use in US medicine without great difficulty. For example, In New York

City it is illegal to say any therapy helps AIDS. This law has been used as an excuse to shut down experimental ozone clinical trials in progress before they could produce the documentation. There is plenty of documentation already around in major journals. See Ed McCabe's "O<sub>3</sub> vs. AIDS" for proof.

### **50+ years of Ozone application methods**

IV slow injections of the O<sub>3</sub> gas - no air, just pure oxygen forms.

Autohemotherapy - withdrawing 600 ml of blood and re-infusing it after putting ozone into it.

Ozone bagging - every body part except the head in a bag full of O<sub>3</sub> for up to two hours.

Ozone rectal insufflation - average 1 1/2 liters of 27mcg/ml O<sub>3</sub> gas into colon.

Ozone vaginal insufflation - average 5 minutes of insufflating body cavity.

Ozone ear insufflation - average 5 minutes of letting O<sub>3</sub> fall into ear cavities.

Ozone air purification - low levels of ozone sterilize and rejuvenate the room air.

Ozone charged drinking water - must be imbibed immediately while O<sub>3</sub> still in glass.

There are over 3,000 medical references in the German literature showing ozone's use in over 50 years of application to humans by way of millions of dosages. The International Ozone Association and the machine manufacturers report over 7,000 M.D.'s in Europe using medical ozone safely and effectively, some for more than 40 years, yet for the past 5 years, the FDA has prevented formal human testing or any ozone generating device approvals.

I have seen people sero-convert to HIV negative, and even more importantly, lose all secondary infections from being on ozone. BUT they stuck to a full protocol - getting it daily, IV, the right dosage, and the right concentrations, and combining it with other significant modalities. People who have never tried it, or only just "dabbled" in it, end up being the only nay sayers. Go ahead and ask anyone who is dissing ozone - Ask them, did you work up to least 150cc (not the starting dosage) of 27-42 mcg/ml concentration strength of only pure medical ozone gas? Was it once or twice a day, every single day, for four to six weeks? Was the ozone delivered IV or better? If they say it's dangerous, or ineffective, they're doing it wrong! 99% of the many successful people that I have interviewed - and written or spoken about - have received ozone only this proper way. And none were hurt. - see below on the 5 1/2 million dosage German study showing ozone to be completely safe. Those that use ozone continue to come back for more because they live the benefits within their own bodies.

The German Medical Society has published that 384,775 patients were treated with ozone with a minimum of 5,579,238 applications and the side effect rate observed was only .000005 per application! The report also stated "The majority of adverse effects were caused by ignorance about ozone therapy (operator error)." The University of Innsbruck's Forensic Institute published Dr. Zacob's dissertation quoting this in The Empirical Medical Acts of Germany. This paper is a part of a much larger chronology found in Ed McCabe's new oxygen/ozone report "Ozone vs. AIDS." His first work, the self published best seller "Oxygen Therapies: A New Way Of Approaching Disease" has sold over 100,000 copies by word of mouth. Over the past seven years, Ed McCabe has appeared on over 1,075 radio, TV and speaking platforms. Books and audio/video tapes of proof and testimonials are available from "The Family News" 9845 N.E. 2nd Ave., Miami Shores, FL 33138. 800/284-6261 or 305/759-8710, M-F 9-5 EST. Free sample newsletter.

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At the urging of many in our oxygen family, The Not For Profit "Foundation For The Advancement of Oxygen Therapies" has finally been formed.

Our stated purpose: We are bringing our case to the public by educating them that oxygen supplements, therapies and related activities are historically inexpensive, safe, and proven effective when used as directed by competently trained healthcare professionals. We are using education, the media, and soon, with your help, aggressive research as proof to silence whomever postures against oxygen, your very right to life itself.

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Thanks, and Happy Oxygen!

# Oxygen Radicals: A Commonsense Look at Their Nature and Medical Importance

by B. Halliwell

From the Department of Biochemistry,  
University of London King's College,  
London, U.K.

Medical Biology 62:71-77, 1984

## Introduction

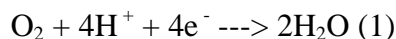
"Oxygen radicals" are now popular subjects for research papers; several hundred are published each year. Many of these pass rapidly into oblivion, joining the great mass of unread scientific literature that clogs library shelves and dilutes important research findings to an increasingly great extent. The basic chemistry of oxygen-derived species was established years ago by radiation chemists (1,6), but "superoxide" is still endowed with miraculous properties by the uninitiated. Demonstration that the action of a disease or toxin *in vivo* produces increased lipid peroxidation (a currently-popular scientific activity) means nothing more than the fact that its action produces increased lipid peroxidation: it does not automatically follow that the lipid peroxidation causes the damaging effects of the drug or disease.

The purpose of this paper is to explain: i) what oxygen radicals are ii) the evidence that oxygen radicals are important *in vivo* iii) what needs to be done to establish a role for oxygen radicals and lipid peroxidation in human disease.

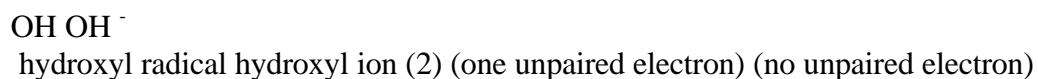
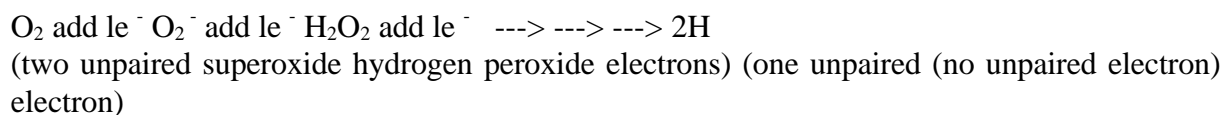
What are the oxygen radicals and how are they produced?

Electrons within atoms and molecules occupy regions of space known as "orbitals". Each orbital can hold a maximum of two electrons. A single electron alone in an orbital is said to be "unpaired" and a radical is defined as any species that contains one or more unpaired electrons. Such a definition embraces the atom of hydrogen (one unpaired electron) and the ions of such transition metals as iron, copper and manganese (cf. Holmberg, this volume).

The diatomic oxygen molecule, O<sub>2</sub>, has two unpaired electrons and thus qualifies as a radical. Most of the oxygen taken up by human cells is reduced to water by the action of the cytochrome oxidase complex in mitochondria. This requires the addition of four electrons to each oxygen molecule,



For chemical reasons (reviewed in ref. 21 and 28), O<sub>2</sub> likes to receive its electrons one at a time, producing a series of partially reduced intermediates

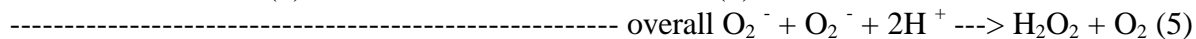
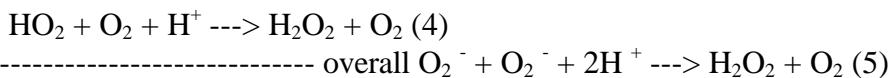
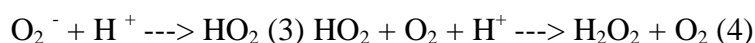


||||| add  $e^-$   $H^+$  | add  $H^+$   $H_2O$   $H_2O$

Cytochrome oxidase keeps the partially reduced intermediates on the pathway to water tightly bound to its active site (21); they do not escape into free solution.

### Superoxide

Superoxide ion is the one-electron reduction product of oxygen. Dissolved in organic solvents, it is an extremely reactive species, e.g. it can displace chlorine from such unreactive chlorinated hydrocarbons as carbon tetrachloride ( $CCl_4$ ) (40). In aqueous solution  $O_2^-$  is poorly reactive, acting as a reducing agent (e.g. it will reduce cytochrome c or nitro-blue tetrazolium) and slowly undergoing the dismutation reaction, in which one molecule of superoxide reduces another one to form hydrogen peroxide ( $H_2O_2$ ). The dismutation reaction occurs in stages;  $O_2^-$  must first combine with a proton to yield the hydroperoxyl radical,  $HO_2$ ,



At physiological pH the low concentration of  $H^+$  ions slows the rate of dismutation.

Despite the low reactivity of  $O_2^-$  in aqueous solution, systems producing it do a great deal of damage in vitro (e.g. they fragment DNA and polysaccharides, kill bacteria and animal cells in culture) and in vivo (e.g. when  $O_2^-$  generating systems are injected into the footpads of rats inflammation is produced, their instillation into the lungs of rats and rabbits produces oedema and cell death, and infusion of them into vascular beds produces endothelial cell damage and extensive leakage from the blood vessels) (21,26,28). Depending on the circumstances, damage caused by  $O_2^-$  generating systems might be attributed to

- (i)  $O_2^-$  itself, e.g. exposure of tissue fluids to  $O_2^-$  causes formation of a factor chemotactic for neutrophils that brings more of them into the area and hence can potentiate inflammation;
- (ii)  $HO_2$  radical, which is more reactive than  $O_2^-$  (6). Formation of  $HO_2$  is favoured at pH values lower than "physiological", but the phagocytic vacuole operates at an acid pH and the pericellular pH of macrophages has been reported to be 6 or less (15);
- (iii)  $H_2O_2$  (see below) (iv) hydroxyl radical (see below) (v) singlet oxygen. Singlet  $O_2$  is an especially reactive form of oxygen capable of rapidly oxidising many molecules, including membrane lipids. Its formation in  $O_2^-$  generating systems has often been proposed but clear-cut evidence for a damaging role of singlet  $O_2$  in such systems has not been obtained. One of the problems is that the "scavengers" of singlet  $O_2$  frequently used react with other radical species as well (for reviews see ref. 26 and 28).

### What is the evidence that $O_2^-$ is formed in vivo in human cells?

Any electron transport chain operating in the presence of  $O_2$  "leaks" some of the electrons, passing them directly onto  $O_2$ . Since  $O_2$  prefers to take electrons one at a time,  $O_2^-$  is produced. Such  $O_2^-$  production can be demonstrated in vitro using mitochondria and microsomes from a range of animal tissues. The rate at which  $O_2^-$  is produced rises as the concentration of  $O_2$  in the system is raised (e.g. see ref. 20). A number of compounds slowly become oxidised on exposure to  $O_2$  and  $O_2^-$  is generated; these include adrenalin, tetrahydrofolate, reduced FMN and oxyhaemoglobin (21,24).

Since human cells contain mitochondria, endoplasmic reticulum, oxidisable compounds and oxygen, it is likely that  $O_2^-$  is formed within them in vivo. Backing up this evidence, for those

who do not like extrapolating from in vitro experiments, is the fact that human cells contain high levels of superoxide dismutase (SOD) activity (45). This enzyme, for which  $O_2^-$  is the specific substrate (35), is known to be a very important anti-oxidant in bacteria and small mammals (26) and its presence in human cells is good evidence that  $O_2^-$  is formed in vivo. During the maturation of erythrocytes most enzymes are lost, but SOD remains. It is not a great stretch of the imagination to associate this with the ability of oxyhaemoglobin to release  $O_2^-$  radical and methaemoglobin.

Another source of  $O_2^-$  in vivo is the respiratory burst of phagocytic cells such as neutrophils, monocytes, eosinophils and macrophages (3, 16, 25). The amount of  $O_2^-$  produced might sometimes be controlled by the  $O_2$  tension of body fluids (14). Host defence against invading bacteria is dependent on the circulating neutrophils, which respond to contact with particles they recognise as foreign by producing a "burst" of  $O_2^-$  radical. The particle is engulfed (the piece of membrane surrounding it being the segment that produces  $O_2^-$  on contact; cf. Segal, this volume), and other vesicles then fuse with the phagocytic vesicle. This exposes the engulfed particle to other anti-bacterial mechanisms, including cationic proteins, lysosomal enzymes and myeloperoxidase (3, 16, 25).

Which of these processes is the most important in bacterial killing? Human and other animal neutrophils can kill some strains of bacteria under anaerobic conditions, when  $O_2^-$  cannot form. Obviously, the other mechanisms are important here. Many other bacterial strains are not killed in the absence of  $O_2$ , however, even though engulfment and vesicle fusion proceed normally. In chronic granulomatous disease (CGD), an inborn error of metabolism, the respiratory burst does not occur but other aspects of phagocytic action proceed normally. CGD was first described in humans because it is accompanied by severe and recurrent infections affecting lymph nodes, skin, lungs and liver (43). The symptoms of CGD provide direct evidence for the production of  $O_2^-$  by human phagocytic cells in vivo and for its role in bacterial killing.

It follows therefore that if neutrophils become activated in the wrong place, or to excessive extents (as in the autoimmune diseases, 25) then the oxygen radicals they release could do a lot of damage. It must be remembered, however, that phagocytic cells also produce hydrolytic enzymes (elastase, neutral proteases etc.), chemotactic factors, prostaglandins, leukotrienes and other chemicals, so that damage by activated phagocytes could be due to any one of these factors or to any combination of them. It cannot be attributed a priori to oxygen radicals.

### Hydrogen Peroxide

$O_2^-$  generating systems produce  $H_2O_2$  by the dismutation reaction (eqn. 5) and a number of oxidase enzymes produce  $H_2O_2$  directly, examples being glycollate oxidase and amino acid oxidases. SOD enzymes remove  $O_2^-$  by greatly accelerating the dismutation reaction, so if we accept that  $O_2^-$  is formed in vivo in humans then we must accept that  $H_2O_2$  vapour is present in expired human breath (48), a likely source being  $H_2O_2$  released from alveolar macrophages (3, 25) although a contribution from peroxide-producing oral bacteria (10) cannot be ruled out.

That  $H_2O_2$  is formed in vivo in humans is further supported by the presence of enzymes specific for its removal, such as catalase and glutathione peroxidase. The latter enzyme requires selenium for its activity (13; cf. Diplock, this volume).  $H_2O_2$  is probably more damaging than is  $O_2^-$  in in vitro experiments in aqueous solution, but many cells seem to tolerate its presence and bacteria often produce  $H_2O_2$  (e.g. ref. 10). On the other hand, the toxicity of  $O_2^-$  generating systems to several animal cells in culture has been attributed to

formation of  $\text{H}_2\text{O}_2$  (e.g. ref. 44). Why this should be so is discussed in the next section.

### **Hydroxyl radical**

Hydroxyl radical is produced when water is exposed to high-energy ionising radiation and hence its properties have been well documented by radiation chemists (6, 49). Unlike the hydroxyl ion, the hydroxyl radical is fearsomely reactive, combining with most molecules found *in vivo* at near diffusion-controlled rates. Hence any OH produced *in vivo* will react at or close to its site of formation. The extent of the damage done would therefore depend on what the site of formation was (e.g. production of OH close to DNA could lead to strand breakage whereas production close to an enzyme molecule already present in excess in the cell, such as lactate dehydrogenase, might have no biological consequences).

Hydroxyl radical is produced whenever  $\text{H}_2\text{O}_2$  comes into contact with copper (I) ions ( $\text{Cu}^+$ ) or iron (II) ions ( $\text{Fe}^{2+}$ ). Dr. Gutteridge has reviewed in this volume the substantial evidence that metal complexes capable of causing hydroxyl radical formation are present *in vivo* in human cells (also see ref. 28). Particularly important *in vivo* are complexes of iron salts with phosphate esters such as ATP and GTP (17, 19) or with DNA (18). Organisms take great care to ensure that as much iron or copper as possible is bound to transport proteins or functional proteins such as transferrin, caeruloplasmin or haemoglobin. Metals bound to these proteins are inactive or only weakly active in catalysing OH production (28, 50).

Since both  $\text{H}_2\text{O}_2$  and metal complexes are present *in vivo* in humans, it is logical to assume that OH radicals can form. Direct evidence for this is difficult to obtain. Many methods exist for demonstrating the existence of OH *in vitro* (see ref. 24 and 28 for reviews) but *in vivo* any OH formed is likely to react so close to its site of formation that the use of these methods is impractical, although some new techniques (such as the ability of OH to convert dimethylsulphoxide into methane (36) or its ability to hydroxylate aromatic rings in characteristic ways (37) show promise for *in vivo* use. One can also attempt to infer the formation of OH radical *in vivo* by observing the damage done (as in rheumatoid arthritis, see below). *In vitro*, phagocytic cells have been shown to produce OH radical (11-13) and the killing of bacteria can sometimes be prevented by reagents that react with this species (3,16, 25).

It was mentioned in the previous section that the killing of animal cells in culture by  $\text{O}_2^-$  generating systems can sometimes be attributed to  $\text{H}_2\text{O}_2$ . It could, of course, be achieved by  $\text{H}_2\text{O}_2$  itself; some enzymes are known to be inactivated by  $\text{H}_2\text{O}_2$  although the best examples come from plant rather than animal systems (11). There is another possibility, however,  $\text{H}_2\text{O}_2$  generated externally crosses cell membranes easily and could penetrate inside the cell and cause OH to be formed. Externally added scavengers of OH would not prevent this since they could not reach the correct place. By contrast,  $\text{O}_2^-$  crosses cell membranes only slowly (42) unless there is a specific channel for it (the only known example of this being the erythrocyte membrane, which has an "anion channel" through which  $\text{O}_2^-$  can move (3). Hydroxyl radical will never cross a membrane: it will react with whatever membrane component it meets first.

### **What is lipid peroxidation and is it of medical importance?**

Lipid peroxidation has been broadly defined by A. L. Tappel in the USA as "oxidative deterioration of polyunsaturated fatty acids", i.e. fatty acids that contain more than two carbon-carbon double bonds. Oxygen-dependent deterioration, leading to rancidity, has been long recognised as a problem in the storage of fats and oils and is even more relevant today with the popularity of "polyunsaturated" food products. Some of the best studies on peroxidation chemistry have been carried out by food chemists.

Initiation of peroxidation in a membrane or polyunsaturated fatty acid is due to the attack of any species that can "pull off" a hydrogen atom from one of the -CH<sub>2</sub>- groups in the carbon chain. Hydroxyl radical and possibly HO<sub>2</sub> can do this, but H<sub>2</sub>O<sub>2</sub> and O<sub>2</sub><sup>-</sup> cannot.

Hence O<sub>2</sub><sup>-</sup> does not initiate lipid peroxidation. Since a hydrogen atom has only one electron, removing it leaves behind an unpaired electron on the carbon. The resulting carbon radical -CH<sup>•</sup>-, undergoes molecular rearrangement to form a conjugated diene, which then combines rapidly with O<sub>2</sub> to give a:

O<sub>2</sub> | peroxy radical, -CH<sup>•</sup>-. Peroxy radicals are capable of abstracting a hydrogen atom from other fatty acids and so setting off a chain reaction that can continue until the membrane fatty acids are completely oxidised to hydroperoxides (eqn. 6);

O<sub>2</sub> | -CH<sup>•</sup>- + -CH<sub>2</sub>- ---> peroxy adjacent fatty acid radical carbon chain;

O<sub>2</sub>H | -CH<sup>•</sup>- + -CH<sup>•</sup>- (6) carbon radical, lipid forms another hydroperoxide peroxy radical;

Lipid hydroperoxides are stable under physiological conditions until they come into contact with transition metals such as iron or copper salts. Cu<sup>2+</sup>, Fe<sup>2+</sup> or Fe<sup>3+</sup> salts as well as haem and haem proteins (e.g. cytochromes, haemoglobin) can interact with lipid peroxides. These metals or their complexes cause lipid hydroperoxides to decompose in very complicated ways, producing radicals that can continue the chain reaction of lipid peroxidation (as in eqn. 6), as well as cytotoxic aldehydes and hydrocarbon gases. Most attention is paid in the literature to malonaldehyde, but this is a very minor endproduct of lipid peroxidation (for reviews see ref. 4, 26, 32).

### **Does lipid peroxidation occur normally in vivo in humans?**

This question is surprisingly difficult to answer: little evidence for lipid peroxides or their decomposition products can be found in healthy human tissues (28). Expired human breath contains gaseous hydrocarbons that might have originated from decomposition of lipid hydroperoxides, but they might also have been produced by bacteria in the gut or even on the skin. Animal cell membranes contain tocopherol (vitamin E), which is a powerful inhibitor of lipid peroxidation, and proteins such as caeruloplasmin and glutathione peroxidase probably help to protect against this process in vivo (27).

Diseased tissues, or tissues isolated after exposure of animals to such toxins as ethanol, phenylhydrazine and paraquat often show evidence of increased peroxidation. Simple in vitro experiments demonstrate quite clearly that dead or damaged tissues peroxidise more rapidly than living ones, presumably because of membrane disruption by enzymes released from lysosomes, release of metal ions from their storage sites and failure of antioxidant mechanisms. Thus evidence that a toxin increases lipid peroxidation in vivo does not prove the sequence of events:

toxin ---> lipid peroxidation ---> damage (7)



but is equally explained by the sequence

toxin ---> cell damage or death ---> lipid peroxidation (8)

Of course, toxins released by dead or dying cells undergoing peroxidation might cause further damage to healthy cells, although there is little evidence for this *in vivo*. Among the many claims I have seen in the literature for lipid peroxidation as an agent of the damage induced by a toxin, I have seen clear evidence for sequence 7 only in the case of the hepatotoxic effects of carbon tetrachloride (32). Sequence 8 is a much better explanation of the *in vivo* effects on membrane lipids of, for example, paraquat.

An often quoted illustration of the importance of lipid peroxidation *in vivo* is the accumulation of "age pigment" in various human tissues. Chemical analysis of age pigment shows convincingly that it is an endproduct of oxidative damage to lipids (41). However, the lipids in question seem to be taken into lysosomes before they are degraded; they are not "normal cell lipids". The exposure of lipids to hydrolytic enzymes and metal ions within lysosomes no doubt facilitates their peroxidation, and so more peroxidised material accumulates within cells as lysosomes get older and have engulfed more lipid material.

### **The TBA test**

The TBA (thiobarbituric acid) test is one of the most widely used (and abused!) tests for measuring lipid peroxidation. The simplicity of performing the test (the material under study is merely heated with acid and TBA and the formation of a pink colour measured at 523 nm) conceals its essential complexity.

Consider a typical experiment. A lipid system, perhaps with added metal ions, chelating agents or other reagents, is incubated in the presence of air. Then TBA plus acid are added and the mixture heated at 100 degrees Celsius. The air, metals and other reagents are still present, so as much or even more oxidative damage to the lipid can be done during the TBA test itself as happened during the initial incubation.

The pink colour is due to the formation of an adduct between TBA and malonaldehyde (MDA) under acidic conditions. Indeed, the TBA assay is often calibrated with MDA and the results of peroxidation assays are often expressed as "amounts of MDA formed". Some papers in the literature give the mistaken impression that TBA reacts only with free MDA and so measures the production, but it was shown as long ago at 1958 in studies with peroxidising fish oil that 98 % of the MDA that reacts in the TBA test was not present in the original sample assayed but forms from lipid peroxides that decomposed during the acid-heating stage of the TBA assay. More recent studies confirm this and show that the apparent "TBA reactivity" of say, serum, varies with the exact concentration of acid, type of acid and period of heating used in the TBA assay (23). The amount of MDA formed during the initial incubation of the system as opposed to during the assay depends on such factors as the iron salt concentration (4, 23, 32). An apparent "inhibitor" of lipid peroxidation as detected by the TBA test might actually inhibit the peroxidation process, but could equally well interfere with decomposition of the peroxides during the acid-heating stage of the assay. Similarly, absolute values for the "TBA reactivity" of body fluids or tissue extracts are meaningless, although changes in these values may be significant provided that the same assay is employed in the same way each time.

Of course, many scientists are aware of these problems with the TBA assay and there are ways around them (2, 41), including the use of other assay systems in conjunction with the TBA test (4, 27). I have included these cautions to encourage a more critical attitude to some of the

published literature.

### **Oxygen Radicals and Disease**

Free radicals have been suggested to be involved in the pathology of a number of diseases. In several cases the evidence consists only of observations of increased lipid peroxidation in diseased tissues, which is ambiguous (see above). I have chosen to look in detail at two cases where the evidence at first sight is more convincing, cancer and inflammatory joint disease.

#### **Cancer**

Any substance that reacts with DNA is potentially carcinogenic. Exposure of DNA to  $O_2^-$  generating systems causes extensive strand breakage and degradation of deoxyribose (9, 39), an effect shown in vitro to be due to formation of OH. Both bacteria and animal cells in culture suffer DNA damage on exposure to  $O_2^-$  generating systems, which can be shown to be mutagenic (46, 47). It is therefore tempting to attribute the increased risk of development of cancer in chronically inflamed tissues to generation of oxygen radicals by phagocytic cells, although there is no direct evidence for this.

Great excitement was generated by reports that cancer cells in culture and from some transplantable tumours in animals are deficient in SOD activity, especially in their mitochondria (for a review see ref. 34). The relevance of these studies to human cancer is not at all clear, however, since human tumours biopsied during surgery show no defects in any SOD activity (31, 45).

#### **Rheumatoid arthritis**

I have already speculated on the role of oxygen radicals in the autoimmune diseases. Rheumatoid arthritis has some of the features of an autoimmune disease but its exact cause is unknown. The synovial fluid of the inflamed joint swarms with neutrophils. Since the fluid contains increased concentrations of products that activated neutrophils release (including lactoferrin, 5) and end-products of arachidonic acid metabolism), then at least some of these neutrophils must be activated and thus producing superoxide, and hence  $H_2O_2$  in vivo. Human synovial fluid is poor in SOD, catalase and glutathione peroxidase activities (8) but does contain iron complexes capable of catalyzing a reaction between  $O_2^-$  and  $H_2O_2$  to form OH (38). There is as yet no direct proof that OH is formed in vivo, but evidence consistent with its formation includes the observation that the hyaluronic acid in synovial fluid is degraded in rheumatoid joints, and the type of degradation observed can be reproduced by exposing pure hyaluronic acid in vitro to OH radical (22). TBA-reactive material is also present in serum and synovial fluid of rheumatoid patients. There are significant correlations (38) between the content of TBA-reactive material in synovial fluid, its content of catalytic iron complexes and both clinical ("knee score") and laboratory ("white cell count" and "fluid content of C-reactive protein") assessments of disease activity.

Thus there is certainly evidence for oxygen radicals being produced in the rheumatoid joint and having some deleterious effects. The question to be answered is how important are oxygen radicals in relation to other agents of damage. The pathology of rheumatoid arthritis is very complex and the number of potentially damaging agents, including hydrolytic enzymes, prostaglandins and leukotrienes, is enormous (29). Some scientists have tried to assess the importance of oxygen radicals by examining the effects of injecting SOD directly into inflamed joints (33; see Marklund, this volume), whereas our group, reasoning that iron complexes are

required for  $O_2^-$  dependent formation of highly reactive OH radical, is examining the effect of iron-chelating drugs that can prevent OH formation (such as desferrioxamine, 12) on animal models of acute and chronic inflammation (7).

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# Pioneers in Ozone Therapy

From: The Use of Ozone in Medicine  
Second Revised Edition  
First English Edition  
S. Rilling/R. Viebahn

## **Christian Friedrich Schonbein**

Born on 18th October 1799 in Metzingen, Swabia (near Stuttgart); died on 29th August 1868 in Baden-Baden. 1840 is given as the year in which ozone was discovered. Schonbein was a contemporary of famous scientists such as Volta, Jenner, Dalton, Cuvier, Humboldt, Ampere, Berzelius, Fraunhofer, Ohm, Faraday, Wohler, and Liebig, to name but a few.

Apart from his discovery of guncotton, which was just as important as ozone, Schonbein was the author of 343 scientific publications in 837 editions. During his studies at the University of Erlangen, he was a co-student with the famous chemist, Baron Justus von Liebig. He also enjoyed a long personal contact with the philosopher Friedrich von Schelling who, with his post-Kantian philosophy concerning the "nature of the elements", exerted a great influence on him. Schonbein taught at a private school in Epsom, England, and attended lectures held by the famous French physicist Gay-Lussac. At the age of 29 (in 1828) he received a call to the University of Basle in Switzerland, where he was appointed professor of physics and chemistry in 1835.

In a letter dated 20th May 1866 to his friend Liebig, he himself describes the circumstances of his discovery:

"I am of the opinion that, for the history of science, those who discover facts of even minor significance should always communicate to colleagues the manner by which they have come across them. This matter is, regrettably, often neglected, for which reason even important discoveries appear to have been made by hazard - which they certainly never were and, indeed, never will be, as they must always be preceded by an idea, even if the initial impulse leading up to it frequently consists of a phenomenon observed by chance. For my part, I have observed this in myself in a small way: the perception of the 'electric' smell of electrolytically produced oxygen was simply a chance phenomenon - however, everything emerging from this observation cannot be attributed any longer to pure hazard."

In 1832, Schonbein published the famous little book on this 'remarkable substance' entitled "The Production of Ozone by Chemical Means" (Erzeugung des Ozons auf chemischem Wege).

Initially, he still believed that ozone was a component of nitrogen. Liebig, who wished for a comprehensive essay on ozone by Schonbein in his journal ("Liebig's Annalen"), proposed using in place of the word 'ozone', the less exceptionable term 'ozonized oxygen'. Almost the entire part of his later work was devoted to oxygen, the "hero of chemistry".

Buttersack, a known German writer, once defined ozone as "a set of oxygen atoms in transit within a system (or organism)".

In 1857, with the "superior induction tube" developed by Werner von Siemens (the engineer and inventor), the first technical ozone unit was constructed.

## **Erwin Payr**

Born on 17th February 1871 in Innsbruck (Austria); died on 5th April 1946. At the age of 28, in 1899, he received his lectureship (habilitation) at the University of Graz in Carinthia: in 1907 he was regular professor at Greifswald University (in present-day Eastern Germany), in 1910 at Königsberg (East Prussia), and in 1911 at Leipzig (Saxony).

His major fields were surgery of the joints, thyroid operations, brain surgery and the suture of blood vessels: this changed in 1932, however, when he himself became a patient and experienced ozone treatment on his own body through his dentist, E.A. Fisch.

In an autobiographical description, Payr has left us a few statements which were important for the scientific situation of his times; they are still valid today.

"When using references, I have always insisted on absolute honesty: it is not correct to put foreign feathers in one's cap";

"Unexpected difficulties have always brought out my best efforts and performances";

As regards his literary productions (medical writings):

"One can make life easier or more difficult respectively if one does not go through the relevant references carefully in the original instead of the review, which is often inadequate; this avoids superimposing one's own trains of thought unjustly or carelessly on those of others already expressed previously."

"Perception and error are paths which run very close to each other."

Mental work is a private sanctuary, and one must not allow it to be disturbed or desecrated."

### **E.A. Fisch (1899-1966)**

As a dental physician and surgeon, Fisch has recorded his large range of experience with ozone in a number of publications in Italian, French and German: finally, in the 1950's he prepared a comprehensive doctoral thesis on this subject.

Actual ozone therapy found its origins in the dental practice of E.A. Fisch, as this is where Payr was able to make his acquaintance with the method as a patient in the chair.

The patent for the apparatus bearing the name CYTOZON, now used in modern ozone generators for dental medicine, was also applied for by E.A. Fisch as the first piece of laboratory equipment.

### **Joachim Hansler**

Was born in Hirschberg, Upper Silesia (now Jelenia Góra in West Poland), on 17th December 1908 and studied physics, mathematics and chemistry, first of all at Breslau (Wrocław, now Poland), and then at Berlin. These three related fields formed, in combination, the fundamental background for his interdisciplinary research and construction.

Born on the same day as the chemist and glass manufacturer Friedrich Otto Schott, who invented the world-famous Jena glass, and on the same day as the unique musical phenomenon Beethoven, he created the prerequisites for the technical application of medical ozone. Although Joachim Hansler died on 11th November 1981, his name will be remembered as long as medical ozone therapy is used.

Without his pioneering work, the problem of accurate medical ozone application would probably have remained unsolved up to the present time.

### **Hans Wolff**

Was born on 4th April 1924 in Stentsch (now Szczaniec) near the West Prussian border (now Poland). Like many others of his generation, his life was marked by the war and subsequent events. After hostilities and life as a prisoner of war with the Americans, he completed his

medical studies at the Goethe University in Frankfurt am Main (FRG) and spent his years of internship at the same city, before receiving his licence to practice there on 15th May 1953, where he then started up his own practice as general practitioner, which he continued until his untimely death of 22nd July 1980. Not only an impassioned physician, he also inspired enthusiasm in those about him, and his dynamic manner also affected his patients. The words of a colleague in his obituary thus become understandable when he writes: Hans Wolff's entire medical activity and research was a life dedicated to ozone. He also wrote this under the impression obtained from Wolff's book "Medical Ozone" ("Das Medizinische Ozon"). A virtuoso in rhetoric and gesture, the innumerable participants in his courses and training sessions will never forget him. His never-ceasing interest was devoted to planning a world-wide spreading of ozone application in medicine. It was on this basis that the Statutes of the Medical Society of Ozone Therapy were founded in 1972. Hans Wolff gave the signals for this idea.



# **What you need to know about ozone/oxygen therapy.**

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1987

from: Medical Society for Ozone Therapy

## **What is ozone?**

Ozone is an oxygen compound which also occurs in nature. In fact, it is known to almost everyone on account of its unpleasant odor which is often produced after a heavy thunderstorm, in mountains, by the seaside, or when artificial (ultraviolet) sunlight is applied. Approximately 30 kilometers above the earth's surface, a layer of ozone is present, called the ozonosphere: it ensures that the damaging parts of the sun's high-energy UV radiation are filtered out before they reach us. It was this part of the atmosphere which made life on our planet possible at all!

However, ozone has also come to our attention as a component of smog where it is produced as a result of the interaction between industrial waste gases (nitrogen and sulphur compounds) and oxygen in the air under the sun's influence: it can be used to measure the extent of pollution present in the environment. Apart from its name, this has absolutely nothing in common with medical ozone.

## **How and where is ozone generally used?**

Most of the properties of ozone are shown in table 1, and these are applied throughout the world for the treatment (dressing) of drinking water and the regeneration of waste water - such as in Moscow (with the largest installation in the world), Singapore, Brussels/Belgium, Essen/Germany, Florence/Italy and Marseille/France. In Southern Germany, an installation of this type supplies more than two and a half million persons in the Stuttgart area with the very best drinking water from Lake Constance (Bodensee) - pretreated with ozone!

## **Why is ozone in medicine, what disease are treated with it and how is it applied?**

In addition to the properties described, the following are particularly important when ozone is used medically:

its bactericidal effect - it destroys bacteria  
its fungicidal effect - it acts against all fungus infections (on the skin and mucous membranes)  
its virucidal effect - viruses become ineffective against ozone protected cells.

In addition to this, ozone possesses a number of other properties in the biological system, whose effect may be described as that of improving the circulation. This means that ozone has a positive influence on the oxygen supply and oxygen-processing facilities in the tissue. As a result, the medical application of ozone can be for the following diseases:

Infected wounds, decubitus ulcers (bedsores in chronically ill patients), badly healing wounds

('open leg') and similar complaints, in addition to fungal infections (nowadays widespread). It is also effective in the case of diseases caused by bacteria and viruses, such as for example herpes simplex (a highly infectious outbreak of small blisters on the skin) and herpes zoster (shingles, inflammation and blisters surrounding the abdomen), as well as jaundice (yellow fever) in all its different form.

Another application of medical ozone which is extremely important also belongs to this category, i.e. that in circulatory disturbances ('senile' gangrene, open black rot, smoker's leg, leg sores, etc.), but naturally also for circulatory disturbances in conjunction with arteriosclerosis and diabetes!

Medical ozone is a mixture of (at maximum) 5 parts pure ozone gas and 95 part oxygen (for external application only!) and a mixture consisting of only 0.05 parts ozone (and therefore 99.95 parts oxygen) when applied as an agent for improving circulation and accelerating healing tendencies.

### **The applications of medical ozone**

1. Intraarterial application ((of the ozone/oxygen mixture): This is principally used in arterial circulatory disturbances.
2. Intestinal insufflation: This application has proved itself to be invaluable in mucous colitis (a fungal infection in the intestine) and fistulae (abnormal openings): this technique was already applied by the Austrian physician Payr in 1935 and the French therapist Aubourg in 1936. It had been discovered already at that time that the ozone content of the blood is increased after rectal ozone/oxygen gas application!
3. Intramuscular application: This method is prominent in the treatment of inflammatory infections and allergic diseases.
4. Major and minor autohemotherapy: Based on the studies and methods of Wehrli, one of the most famous modern therapists, H. Wolff, devoted his attention to these two technical applications from 1968 until his untimely death in 1980: he continuously demonstrated their efficacy in arthritis, hepatitis, allergies and herpes infections with a weakened reticuloendothelial system (RES).
5. Ozonized water: Is used in the field on dental medicine, e.g. for disinfection during surgery.
6. Intraarticular injection: in other words, injections into diseased joints, this is a method reserved for practical application in surgery and into diseased joints, this is a method reserved for practical orthopedics, e.g. in rheumatic complaints.
7. External application: Is indicated in cases of fungal infections, ulcus cruris (leg ulcers) and infected or badly healing wounds: the ozone/oxygen gas mixture is applied over the skin inside an ozone resistant plastic hood.

### **The Present-day uses of ozone in Medicine (alphabetical order)**

Abscess, Acne, AIDS, Allergies(hypersensitivity), Anal fissure, Antiviral effect, Cerebral sclerosis, Circulatory disturbances arterial, Cirrhosis of the liver, Climacterium (menopause), Constipation, Cystitis, Decubitus, (Bedsore) Dermatology, Dermatology/Allergology, Dermatology/Proctology, Fistulae, Fungus-caused diseases, Furunculosis, Gangrene, Gastroenterology, Gerontology, Hepatitis, Herpes, Hypercholinesteremia, Mucous colitis, Neurology, Odontology (dental medicine), Oncology (tumours), Oncological additive (special additional cancer treatment), Orthopaedics, Osteomyelitis (inflammation of the bone marrow), Parkinson's disease, Polyarthritis, Proctology gynecology, Radiology, Raynaud's disease (attacks of Scars (after radiation) vascular cramp), Spondylitis (inflammation of Stomatitis

(inflammation of the the vertebrae) mouth cavity), Sudeck's disease (vegetative Surgery distrophy in all joints), Surgery/Dermatology, Thrombophlebitis (inflammation of the veins), Ulcus cruris (open leg sores), Urology, Vascular surgery, Wound healing disturbances.

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**Table 1 - The properties of ozone according to Rilling/Viebahn**

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- Oxygen saturation
  - Disinfection (bacteria and germs)
  - Inactivation of viruses
  - Fungicide
  - Reduction of fetor (wound odor)
  - Reduction of taste
  - Elimination of fecal bacteria (Biochemical oxygen demand/Chemical oxygen demand reduction)
  - Elimination of sulphur
  - Oxidation and flocculation of Mn and Fe
  - Oxidation of cyanide and phenol
  - Elimination of detergents
-

This is a very detailed description of vitamin C and free radical interaction. It is interesting to note that  $\text{H}_2\text{O}_2$  can act as a reductant and supply 2 high energy electrons, as ascorbate can, under the right conditions. This makes for some interesting ramifications. Under the right redox potential,  $\text{O}_2$  could recycle dehydroascorbate back to ascorbate.

Unfortunately, the references were lost from the original source during downloading. We have not attempted to correct the problem due to possible errors that could be made.

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## A UNIQUE FUNCTION FOR ASCORBATE

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### ABSTRACT

Vitamin C is a reducing substance, an electron donor. When vitamin C donates its two high-energy electrons to scavenge free radicals, much of the resulting dehydroascorbate is rereduced to vitamin C and therefore used repeatedly. Conventional wisdom is correct in that only small amounts of vitamin C are necessary for this function because of its repeated use. The point missed is that the limiting part in nonenzymatic free radical scavenging is the rate at which extra high-energy electrons are provided through NADH to rereduce the vitamin C and other free radical scavengers. When ill, free radicals are formed at a rate faster than the high-energy electrons are made available. Doses of vitamin C as large as 1 to 10 grams per 24 hours do only limited good. However, when ascorbate is used in massive amounts, such as 30 to 200+ grams per 24 hours, these amounts directly provide the electrons necessary to quench the free radicals of almost any inflammation. Additionally, in high concentrations ascorbate reduces NAD(P)H and therefore can provide the high-energy electrons necessary to reduce the molecular oxygen used in the respiratory burst of phagocytes. In these functions, the ascorbate part is mostly wasted but the necessary high-energy electrons are provided in large amounts.

### DEFINITION AND QUALIFICATION

In this paper, the words, vitamin C, will refer to the substance  $\text{C}_6\text{H}_8\text{O}_6$  used in tiny doses as a vitamin and an electron carrier. The word, ascorbate, will mean the same substance but when used in massive amounts for its high-energy electrons themselves.

This paper is not meant to be an exhaustive review of the subjects of oxidation-reduction reactions, free radical scavenging, electron- transport-chains, or oxidative phosphorylation, etc. Readers are referred to excellent texts on these subjects ( , , , ).

Many of the biochemical processes are deliberately simplified. Some intermediate steps are omitted. Certain generalizations are made so that the importance of a very simple but

overlooked idea can be described in terms a non-biochemist can understand. The overlooked idea is that massive doses of ascorbate can actually be the source of high-energy electrons used in the process of free radical scavenging and not just an electron carrier used repeatedly in an electron- transport-chain resulting in free radical scavenging.

## INTRODUCTION

Clinically, a few physicians have found massive doses of ascorbate to be effective in the treatment of a wide variety of diseases. It was apparent to those using ascorbate in these doses that there is some physiologic or pharmacologic action much different from what might be expected of a mere vitamin.

Nevertheless, most physicians remained critical of these treatments and remained convinced that the usefulness of ascorbate is only as vitamin C. Many had recognized that one vitamin C function is as a free radical scavenger. In this function, vitamin C donates high- energy electrons to neutralize free radicals and in the process becomes DHA (dehydroascorbate). DHA is either further metabolized, releasing more electrons, or is rereduced back to vitamin C to be used over and over again. This regeneration and repeated use of the vitamin has led to the thought that it does not take much to do its functions. Other nonenzymatic free radical scavengers such as glutathione and vitamin E function in a similar manner. The purpose of taking the nutrients making up the free radical scavengers is ordinarily to replace the small percentage inadvertently lost.

Much of the original work with large amounts of ascorbate was done by Klenner ( , , ) who found that most viral diseases could be cured by intravenous sodium ascorbate in amounts up to 200 grams per 24 hours. Irwin Stone ( , , ) pointed out the potential of ascorbate in the treatment of many diseases, the inability of humans to synthesize ascorbate, and the resultant condition hypoascorbemia. Linus Pauling ( , , ) reviewed the literature on vitamin C, particularly its usefulness in the prevention and treatment of the common cold and the flu. Ewan Cameron in association with Pauling ( , , ) described the usefulness of ascorbate in the treatment of cancer.

In 1970 I noted an increasing bowel tolerance to oral ascorbic acid with illness. In 1984 I wrote, ( ) "Based on my experience with over 11,000 patients during the past 14 years, it has been my consistent observation that the amount of ascorbic acid dissolved in water which a patient, tolerant to ascorbic acid, can ingest orally without producing diarrhea, increases considerably somewhat proportionately with the "toxicity" of his illness. A person who can tolerate orally 10 to 15 grams of ascorbic acid per 24 hours when well, might be able to tolerate 30 to 60 grams per 24 hours if he has a mild cold, 100 grams with a severe cold, 150 grams with influenza, and 200 grams per 24 hours with mononucleosis or viral pneumonia. The clinical symptoms of these diseases and other conditions previously described, are markedly ameliorated only as bowel tolerance dose levels (the amount that almost, but not quite, causes diarrhea) are approached ( , , , , )."

This amelioration of symptoms at a high dosage threshold combined with the knowledge that ascorbate functions as a reducing substance suggested that the beneficial effect was achieved only when the redox couple, ascorbate/dehydroascorbate, became reducing in the tissues affected by the disease. It is a characteristic of oxidation- reduction reactions that their redox potential is determined by the logarithm of the concentrations of the substances and certain constants. The logarithmic effect would explain the threshold; the redox potential would suddenly become reducing in the diseased tissues only when a large amount of ascorbate was forced into those tissues sufficient to neutralize most of the oxidized materials in those tissues (

).

### **FREE RADICAL SCAVENGING**

Radicals are molecules that have lost an electron. When a radical escapes its normal location, it becomes a free radical. These free radicals are very reactive and will seize electrons from adjacent molecules. Inflammations whether due to infectious diseases, autoimmune diseases, allergies, trauma, surgery, burns, or toxins involve free radicals. Cells injured by free radicals will spill free radicals onto adjacent cells injuring those cells and generating more free radicals, etc. The body must confine these free radical cascades with free radical scavengers.

Some free radicals spontaneously decay and others are destroyed by enzymatic free radical scavengers such as superoxide dismutase and catalase that act on free radicals in such a way that they neutralize themselves without the addition of extra electrons.

The remainder must be destroyed by the high-energy electrons carried by the nonenzymatic free radical scavengers. Free radicals that escape all the above mechanisms cause symptoms and damage.

It is helpful to remember through all the following descriptions that technically it is the high-energy electron that is neutralizing the free radical, not the free radical scavenger. The free radical scavenger carries the high-energy electron that does the neutralizing.

### **HIGH-ENERGY ELECTRONS THE LIMITING FACTOR**

The energy of the electrons which neutralize free radicals comes ultimately, like all energy used by living things on Earth, from the Sun. Plants store this energy by photosynthesis in carbohydrates, fats, and proteins which are then eaten by animals. As animals metabolize these substances, this energy is passed from one molecule to another in the form of high-energy electrons which often, but not always, are in association with hydrogens. Together with a high-energy electron, one such hydrogen can be called a hydride anion.

As glucose is metabolized,  $\text{NAD}^+$  (nicotinamide adenine dinucleotide) is reduced to  $\text{NADH}$  (the bolded H is to emphasize the included high-energy electron). The high-energy electron in the hydride anion (H) is added to the  $\text{NAD}^+$ .

The most critical but generally unrecognized fact here is that  $\text{NAD}^+$  can be reduced to  $\text{NADH}$  only at a limited rate by the addition of the hydride anion with its high-energy electron derived from the metabolism of carbohydrates, fats, or proteins. Therefore, this  $\text{NADH}$  is not without cost. Moreover, the energy it carries must be shared among several other critical functions. Most must be used in the process of oxidative phosphorylation to make ATP (adenosine triphosphate) which is used as a source of energy by the various tissues of the body. When phagocytes engulf pathogens into its vacuoles,  $\text{NADPH}$  (nicotinamide dinucleotide diphosphate, reduced form) provides the high-energy electrons the phagocytes need to make the oxidizing substances (radicals) with which they kill various pathogens. The process of making the necessary oxidizing substances is called the respiratory burst. Paradoxically, the first oxidizing substance, superoxide, ( $\text{O}_2^-$ ), in the respiratory burst is made by the reduction of molecular oxygen ( $\text{O}_2$ ) by  $\text{NADPH}$ .  $\text{NADP}^+$  is rereduced back to  $\text{NADPH}$  in the hexosemonophosphate shunt. Glucose is metabolized for the source of the high-energy electron. This process is also rate-limited and the glucose comes from the metabolism of carbohydrates, fats, and proteins. Therefore,  $\text{NADH}$  and  $\text{NADPH}$  have a common source of

energy and can be made available only at some limited rate.

Remaining NAD(P)H can be used by the body in regenerating free radical scavengers so that the body may protect itself from free radicals. As NAD(P)H is used in these various processes, it gives up the hydride anion with its extra high-energy electron and becomes NAD(P)<sup>+</sup> again. When the limited rate of availability of these hydride anions is exceeded by the formation of free radicals, then symptoms and damage caused by the free radicals occur.

### **RESPIRATORY BURST LIMITED BY ACCUMULATION OF FREE RADICALS**

As these high-energy electrons are used up within the phagocytes, the phagocytes are unable to produce more oxidizing substances within their vacuoles to kill pathogens. Some of the previously made oxidizing substances leak from within the vacuoles into the cytoplasm thereby becoming free radicals. With the exhaustion of the high-energy electrons, the nonenzymatic free radical scavengers cannot be rereduced. The free radicals damage the phagocytes and interfere with phagocytosis. The phagocytes bog down in their own oxidizing substances.

### **REDUCED GLUTATHIONE**

To understand the unusual function of massive doses of ascorbate, let us follow the most important pathway whereby the extra electrons are passed off to the free radicals thereby neutralizing them. Follow the high-energy electron in the hydride anion through all this process. Certain nutrients that could be limiting factors in all this will be mentioned along the way.

NAD(P)H reduces oxidized flavin adenine dinucleotide (FAD<sup>+</sup>), to reduced flavin adenine dinucleotide (FADH<sub>2</sub>), and becomes NAD(P)<sup>+</sup> again. FADH<sub>2</sub> reduces oxidized glutathione (GSSG) to reduced glutathione (GSH). (Part of NAD(P)H is from vitamin B3, and part of FADH<sub>2</sub> is from vitamin B2).

The high-energy electrons of reduced glutathione (GSH) can directly reduce some free radicals. But also, some reduces dehydroascorbate back to ascorbate. In the process the GSH is oxidized back to GSSG. Two hydride anions are added to the dehydroascorbate reducing it back to vitamin C. (The enzyme glutathione peroxidase and its coenzyme selenium catalyze these reactions).

Ascorbate (C<sub>6</sub>H<sub>8</sub>O<sub>6</sub> or C<sub>6</sub>H<sub>6</sub>O<sub>6</sub>H<sub>2</sub>, the bolded and separated H<sub>2</sub> is to emphasize the hydrogens containing the high-energy electrons) differs from dehydroascorbate (C<sub>6</sub>H<sub>6</sub>O<sub>6</sub>) in that it has two extra hydrogen atoms with two high-energy electrons in its molecular structure which it can donate to reduce free radicals.

The high-energy electrons of ascorbate, C<sub>6</sub>H<sub>6</sub>O<sub>6</sub>H<sub>2</sub>, can directly quench free radicals. But some may reduce to cophenyl quinone (an oxidized form of vitamin E) back to α-tocopherol (vitamin E). Some high-energy electrons are passed to the α-tocopherol and then quench free radicals.

The point I want to emphasize is that these free radical scavengers cycle from the reduced form carrying the hydride anion with the high-energy electron back to the oxidized form lacking the hydride anion. Although there is a little loss, most of the free radical scavengers are rereduced and used over and over again. This repeated use with only a little loss is why it ordinarily takes a small amount of these substances to do their electron carrying function to the maximum allowed by the availability of the hydride anion.

The limiting factor in all this, in a well nourished person, is this rate-limited availability of the hydride anion with its high-energy electron. The body can make NAD(P)H available for this purpose only at a limited rate. When the need to scavenge free radicals exceeds this rate, then

symptoms, damage, and ageing occur. Adding more vitamins and other nutrients, even the ones noted as being free radical scavengers, notably vitamin C, vitamin E, vitamin A (especially  $\beta$ -carotene), cysteine, selenium, etc. do not, under ordinary circumstances, add much to all this. All these free radical scavengers are cycled several times an hour when a person is sick. The NAD(P)H keeps rereducing these free radical scavengers so they are used repeatedly. Taking of the usual amounts of nutrient free radical scavengers only assures that there are no critical deficiencies that would limit this free radical scavenging electron-transfer chain described above. Still there is a normal limit to the free radical scavenging ability of this system.(),(),().

### **ASCORBATE TO THE RESCUE**

. . .except. . .ascorbate,  $C_6H_6O_6H_2$ , used as the source of electrons, not just as the electron carrier, can change all this. The  $C_6H_6O_6H_2$  used in massive doses substitutes for the limited availability of the NAD(P)H. The  $C_6H_6O_6$  part of the  $C_6H_6O_6H_2$  used this way is thrown away; the  $C_6H_6O_6H_2$  is only used for the electrons it carries. Amounts of 30 to 200+ grams of  $C_6H_6O_6H_2$  provide ample high-energy electrons to directly scavenge the large amounts of free radicals generated in disease processes and provide enough high-energy electrons to rereduce  $NAD(P)^+$ ,  $FAD^+$ , GSSG, to copheryl quinone, etc. back to their reduced forms.

Lewin () pointed out that although the  $C_6H_6O_6H_2 / C_6H_6O_6$  redox couple is usually reduced by GSH at the concentrations in which these substances are ordinarily present, when  $C_6H_6O_6H_2$  is present in large concentrations, it will reduce GSSG to GSH. The usual direction of the redox reaction is reversed and the  $C_6H_6O_6H_2$  supplies the high- energy electrons reducing the GSSG. If there was some substance that was cheaper, better tolerated by the body, and had fewer uisance problems associated with its administration than sodium ascorbate,  $NaC_6H_6O_6H$ , intravenously and intramuscularly, or ascorbic acid,  $C_6H_6O_6H_2$ , orally, I would use it. So far,  $C_6H_6O_6H_2$  and  $NaC_6H_6O_6H$  are the premier sources of high-energy electrons and therefore the premier free radical scavengers.The dehydroascorbate,  $C_6H_6O_6$ , part of the ascorbate,  $C_6H_6O_6H_2$ , used this way is excreted rapidly in the urine or metabolized further by the body. Although the complete pathway has not been described and involves some uncertainty, it is known that certain breakdown products of dehydroascorbate supply even more high-energy electrons.

Bearing in mind that it is the high-energy electron that is doing the free radical scavenging, one can see that animals which can synthesize ascorbate within themselves have a higher amount of the electron carrier available and will not ever suffer from scurvy. However, the high-energy electrons ultimately come from the same sources as in humans. Ascorbate producing animals still must make the ascorbate and the high-energy electrons available by various metabolic steps using glucose. This process is rate- limited. Comparing the ability of a human to make  $C_6H_6O_6H_2$  to a dog is like comparing a human's ability to fly in a Concorde with a humming bird. The human can make enormous amounts of  $C_6H_6O_6H_2$  in his chemical plants. Humans just have to learn to use it properly. The usefulness of ascorbate in treating diseases involving free radicals bears no relationship to how much vitamin C animals make or consume unless one is satisfied with achieving only the level of health of that animal. We are using a natural substance in an unnatural way to achieve these effects. It is the high-energy electrons, not the ascorbate, that is most important here.

The mechanism I am describing is a pharmacologic effect of the high- energy electrons carried by the  $C_6H_6O_6H_2$  that transcends the normal ability of any species of animal to ameliorate or



conquer diseases involving free radicals. Any disease process that involves free radicals can be ameliorated by the high-energy electrons carried by ascorbate when used properly in massive doses.

It is true that there are certain logistic problems involved in delivering the massive doses of  $C_6H_6O_6H_2$  containing the enormous numbers of electrons sufficient to quench the excessive free radicals of certain severely toxic diseases but it is surprising what massive doses of ascorbate will accomplish.

### **RAPID UTILIZATION OF THE HIGH-ENERGY ELECTRONS**

Calculations of the total amount of ascorbate in a healthy person (pool size) with an intake of about 100 milligrams of vitamin C per day is roughly 2-3 grams and the turnover half time is about 20 days (). When a person who when well can ingest only 15 grams of ascorbic acid per 24 hours before it causes diarrhea, can take over 200 grams in 24 hours when ill with mononucleosis, one obtains a suggestion of the numbers of extra electrons involved. If 185 grams (200 minus 15) extra is used, whatever the amount of high-energy electrons carried in that divided by the amount in 3 grams means that if ascorbate was the only carrier of electrons (which it is not), that 3 grams of ascorbate would be rereduced about every 23 minutes. There are so many facts such as the amount of high-energy electrons carried by the other free radical scavengers that this number is almost valueless. Still, it makes one think in terms of minutes to a few hours for the rereduction of all the free radical scavengers of the body when one is seriously ill. This emphasizes the futility of using vitamin free radical scavengers in the doses described in the RDA () to provide the necessary high-energy electrons.

### **A SIMPLE ANALOGY**

Suppose you had a house out in the country that had a water well about 300 yards away. Between the house and the well are two high fences. Your house catches on fire and your neighbors come running with their buckets. One group sets up a bucket brigade between the well and the first fence and pours the water through a hole in the fence into the buckets of the second bucket brigade. The second bucket brigade runs to the second fence to pour the water through a hole in the second fence into the buckets of the third bucket brigade who throw the water on the fire.

Unfortunately, the fire goes out of control and it is not possible to pump the water out of the well at a rate fast enough to put out the fire. The arrival of more neighbors does no good because there are already enough for the three bucket brigades. A couple of neighbors run from their homes with their buckets full of water but that does not help very much.

Then the fire engine roars up and puts out the fire with hoses that draw water from the fire engine. The firefighters do not rely on the water from the well. We have to stretch the analogy here a little but imagine microscopic buckets with C painted on their sides carrying the water out of the fire hose. The little buckets are wasted. Their only function is to carry the water.

### **CONCLUSION**

Free radical scavenging is a very dynamic process. The nutritional free radical scavengers in the diet, including vitamin C, are not for the purpose of providing the large number of high-energy electrons necessary to meet the rate with which free radicals are made. The purpose of dietary

free radical scavengers is to replace those scavengers incidentally lost. The process of reducing a free radical does not destroy a free radical scavenger if it is rereduced before being further broken down. The free radical scavengers are intermediaries. It is up to other metabolic processes to provide the high-energy electrons with which the free radical scavengers reduce free radicals.

The rate at which free radicals are formed becomes excessive and causes symptoms when it exceeds the rate of reduction of those free radicals. Part of the reduction is spontaneous and part is enzymatic. The remainder must be reduced by the high-energy electrons carried by the nonenzymatic free radical scavengers.

Ascorbate in massive doses can perform an unusual function. When doses of 30 to 200+ grams per 24 hours are used, the high-energy electrons carried in on the administered ascorbate adds significantly and decisively to the actual electrons doing the reducing. The ascorbate is not used as the vitamin C where it is rereduced by NAD(P)H and used repeatedly; it is used for the high-energy electrons it carries.

In high concentrations ascorbate reduces NAD(P)H and provides the high-energy electrons necessary to reduce molecular oxygen used in the respiratory burst of phagocytes. In these functions, the ascorbate part is mostly wasted but the necessary high-energy electrons are provided in large amounts.

The opportunity to reduce the human suffering from the free radicals of infectious diseases, autoimmune diseases, allergies, trauma, burns, surgery, toxins, and to a degree ageing, etc., which could be neutralized by high-energy electrons carried by high doses of  $C_6H_6O_6H_2$  is immense.

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# GENERATION OF H<sub>2</sub>O<sub>2</sub> IN BIOMEMBRANES

T. Ramasarma

Biochemica et Biophysica Acta, 694 (1982) 69-93

From pages 70-71

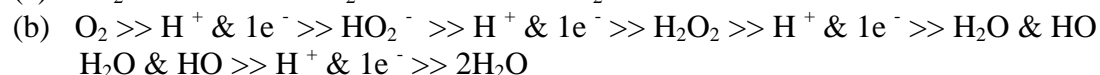
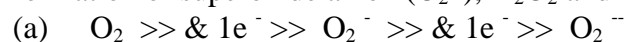
## I. Introduction

Knowledge of the generation of H<sub>2</sub>O<sub>2</sub> in cellular oxidations has existed for many years. It has been assumed that H<sub>2</sub>O<sub>2</sub> is toxic to cells and the presence of catalase is indicative of a detoxication mechanism. Other radicals of oxygen were recently recognized to be more potent destructive agents of biological material than H<sub>2</sub>O<sub>2</sub>. Also catalase and other peroxidases utilize H<sub>2</sub>O<sub>2</sub> in some cellular oxidation processes leading to several important metabolites. Thus, the generation of H<sub>2</sub>O<sub>2</sub> in cellular processes seems to be purposeful and H<sub>2</sub>O<sub>2</sub> can not be dismissed as a mere undesirable byproduct. Biological formation of H<sub>2</sub>O<sub>2</sub> is not limited to the previously known flavoproteins and some copper enzymes, but other redox systems, particularly heme and non-heme iron proteins, are now found to undergo auto-oxidation yielding H<sub>2</sub>O<sub>2</sub>. The capacity for generation of H<sub>2</sub>O<sub>2</sub> is now found to be widespread in a variety of organisms and in the organelles of the cells. The reduction of oxygen to H<sub>2</sub>O by mitochondrial cytochrome oxidase being the predominant oxygen-utilizing reaction had overshadowed the importance of the quantitatively minor pathways.

Under aerobic conditions generation of H<sub>2</sub>O<sub>2</sub> by a variety of biomembranes has now been found to be a physiological event interlinked with phenomena such as phagocytosis, transport processes and thermogenesis in some as yet unidentified way. The underlying mechanisms of these processes seem to involve generation and utilization of H<sub>2</sub>O<sub>2</sub> in mitochondria, microsomes, peroxisomes or plasma membranes. This review gives an account of the potential of the biomembranes to generate H<sub>2</sub>O<sub>2</sub> and its implication in the cellular processes.

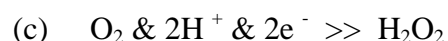
### I A. Steps in the reduction of oxygen

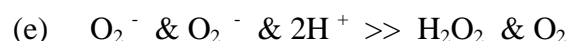
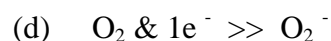
Molecular oxygen has two unpaired electrons each of which goes into separate antibonding pi-orbitals with parallel spins giving the molecule the stability and paramagnetic property in the ground state. The reductions of O<sub>2</sub> by addition of one, two and four electrons lead to formation of superoxide anion (O<sub>2</sub><sup>-</sup>), H<sub>2</sub>O<sub>2</sub> and H<sub>2</sub>O, respectively.



Only two electrons can be accommodated by each oxygen atom. The antibonding orbital of molecular oxygen receives the added electrons and each addition weakens and increases the length of the O to O bond, from 1.274 angstrom in O<sub>2</sub> to 1.480 angstrom in H<sub>2</sub>O<sub>2</sub>, leading to rupture [1].

The two electron reduction of oxygen directly to H<sub>2</sub>O<sub>2</sub> is restricted by symmetry considerations [2] that can be overcome by binding of O<sub>2</sub> to the electron donor and consequent perturbation of the molecular orbitals.





The flavoprotein oxidases appear to follow this type of direct two electron reduction process (reaction c) with no intermediate step [3]. Other  $H_2O_2$  generating systems seem to use one electron reductions forming superoxide anions ( $O_2^-$ ) (reaction d)[4] two of which then dismutate yielding a molecule each of  $H_2O_2$  and  $O_2$  either spontaneously or catalyzed by the enzyme superoxide dismutase (reaction e)[5]. The flavoprotein dehydrogenases and possibly the theiron protein generating  $H_2O_2$  seem to adopt this mechanism and are mostly membrane-localized. It is now found that superoxide formation is a property shared by large number of redox components. In view of the ubiquitous nature of superoxide dismutase and easy nonenzymatic dismutation of superoxide, generation of  $H_2O_2$  accompanying oxidation of these redox components with molecular oxygen becomes equally widespread.

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# The Wizard of Ozone

*Is this Philadelphia businessman peddling Quackery? Or is the profit-driven American Medical Establishment ignoring Jim Caplan's Miracle Treatment?*

by Brenda Fullick

"I knew my foot would have to be amputated, but I didn't think it would be this soon," says Adaria Young, 31, of Philadelphia. She has been a diabetic since she was 4. Because diabetes reduces the feeling of pain, Young didn't realize she had been walking around for several days with a thumbtack stuck in her right foot. The foot became infected, the infection spread to her bone, and her foot was amputated in September.

"At first it was frustrating, but it was something I have to live with," Young says. "I have a 6-year old, and I knew I had to be strong for him."

So far, her left foot seems to be OK. "I have to be really careful," she says. "I have to keep something on my feet at all times, and when I take a shower I have to check between my toes (for infection or drainage). So far, I've been really lucky."

According to the Centers for Disease Control in Atlanta, Young is among an estimated 13 million Americans with diabetes, though only half of all diabetics have been diagnosed. Diabetic circulatory disorders like Young's contributed to more than 162,000 deaths in 1990, making it the seventh-leading cause of death that year, according to CDC records.

In 1994, the National Institutes of Health (NIH) earmarked \$301.3 million for diabetes research. It is among this country's most broadly studied diseases, with 17 different institutes at NIH funding research on everything from blood-sugar levels to peripheral-nerve destruction. Despite all the researchers have learned, American doctors still are poorly equipped to handle diabetic gangrene and infections that lead to amputations.

Meanwhile, for decades, doctors in Germany have been healing diabetic wounds with ozone, a very strong form of oxygen applied directly to the wound. But the German technique is not available in the United States, partly because bringing it to market could cost tens of millions of dollars--or more--and no company could recoup that kind of an investment with a simple, unpatentable chemical.

"It feels like somebody's stabbing you with a knife," says Dorothy Simmons Hardy of Philadelphia. "It's constant, sharp, achy pain. It never lets up. The pain is real severe, and it's real constant."

Simmons Hardy is one of about 72,000 people in the United States who suffer from sickle cell anemia. When the oxygen level in her blood drops too low, her blood cannot flow normally. The pain usually hits her legs, but sometimes she has arm and stomach pain. Frequent hospital stays make it hard for her to hold a job. She almost died twice during pregnancy because of sickle-cell complications, including a blood clot on the lung.

NIH spends about \$70 million a year to study sickle cell anemia. Statistically, relatively few people suffer from this disease, compared to other ailments. But American scientists say a disproportionate amount of energy is focused on sickle cell because they consider it a great medical challenge: In 1954, Linus Pauling won a Nobel prize for identifying sickle cell anemia as a genetic defect, making it the first genetic defect found in humans.

For years, NIH has funded research into lowering the percentage of sickle hemoglobin in the

blood. Drugs such as hydroxyurea and butyrate are being tested at Children's Hospital in Philadelphia and throughout the country. But now those drugs are on the back burner, and the hottest sickle-cell research is in gene therapy, the idea that technology could permanently alter people's cell structures to cure diseases. Dr. Junius Adams, a health-scientist administrator at NIH in Bethesda, MD., says gene therapy is "really the only thing we've got going that has potential to cure sickle-cell disease."

Some scientists predict gene therapy could become reality within five years; others say it's closer to 40 years, maybe more. Meanwhile, Philadelphia businessman and ozone proponent Jim Caplan has convinced doctors in Cuba to treat sickle cell anemia with ozone, much as the Germans are treating diabetics.

At the moment, the best American doctors can do is put their sickle-cell patients on antibiotics to stave off infections while the blood circulation is limited, and give them painkillers to help them ride out the painful crises. But Cuban doctors have documented that in their research, the use of ozone cut the length and the severity of painful episodes in half. So far NIH grant reviewers have opted not to put research money toward this treatment.

As his immune system has steadily fallen apart, one Philadelphia man says he has lost 40 pounds in four months from AIDS diarrhea, what doctors call "AIDS wasting."

"It's a severe problem," says this resident of Betak, a Philadelphia nursing home for AIDS patients. The man, who asked not to be named, is resigned to his unrelenting diarrhea. "It doesn't really ever go away. They try to control it with medicines. It works a little, but it's an ongoing thing...It has a tendency to drain you, make you very tired."

At the end of 1993, there were 54,000 AIDS patients across the United States who had AIDS wasting. NIH has set aside \$1.3 billion for AIDS research in 1995. At least \$4.6 million a year is reserved specifically to study AIDS wasting, which hit 14 percent of Philadelphia AIDS patients in the last year.

Some vaccines are being tested on AIDS patients in the United States, but most of the NIH-funded research focuses on the basic science of how HIV works, what causes the virus and how it spreads.

Meanwhile, a San Francisco researcher conducted a study in which four out of five AIDS-wasting patients found relief with ozone therapy. A virologist in New York found that ozone was able to attack HIV-infected cells in the laboratory, but healthy cells were not affected. Neither of them has been able to get NIH funding to continue their ozone research.

### **Too little research, too little profit**

What if scientists came up with a stunning medical breakthrough that might be able to help doctors treat a variety of diseases, but nobody had the chance to get rich from it?

Thought Young, Simmons Hardy and the AIDS patient all suffer from different maladies, there are American researchers who say there is reason to believe that each of them could be helped with the same incredibly cheap, incredibly simple drug: enriched oxygen, a.k.a. ozone.

Ozone is used to treat patients in other countries, but not in the States. Here, in the country with the highest medical standards in the world, it has hardly been tested. The same costly, lengthy, bureaucratic approval process that protects Americans from potentially hazardous drugs also is keeping Americans from lifesaving therapies.

This is a story about a potential cure that on one has been able to research thoroughly in the United States, in part because trying to sell ozone would be like trying to sell air--there wouldn't be enough private profit in it.

This is a story about the American medical establishment considering itself more scientific and ethical than the medical systems of other countries--and, as a result, looking skeptically at what doctors in the rest of the world are doing.

Finally, this is a story about an idealistic man who wanted to do good in the world by introducing German successes to the American medical establishment. He found that it isn't so easy.

Some say the American medical system is working as it should--that if ozone turns out to be a legitimate therapy, someday it will get its due. Others say ozone research is held back because it's an unconventional approach competing with more conventional experimental treatments, in a system that bases its agendas on long years of preliminary laboratory testing. Because there has been little American research to determine whether Germany's medical results are valid, there's no jumping-off point for the theory in the United States.

"It was a fresh idea," Rosemount resident Jim Caplan says. "I just thought, 'My gosh, you open the window for them and they're going to fly.' They didn't fly."

### **Ozone: Dangerous and wonderful**

Ozone (O<sub>3</sub>) is a form of oxygen (O<sub>2</sub>) produced when an electric spark or ultraviolet light is passed through air or oxygen. When you flip a light switch and see a spark, you've created a small amount of ozone. "Any electrical discharge cross in the air will create a certain amount of ozone," says Bob Steeves, a lawyer and pharmacist at the Food and Drug Administration's Office of Orphan Products Development in Rockville, Md. Ozone easily reverts to regular oxygen again.

Ozone has both very bad and very good properties. It's good in the sky, bad in the lungs.

The ozone layer in the earth's atmosphere protects us from harmful ultraviolet radiation, which causes skin cancer and other problems. That's why environmentalists and public-health organizations are so concerned about automobile exhaust fumes combining with the sun's rays to burn holes in the ozone layer.

Ozone also is a severe lung toxin. People working with it must be careful not to release it into the air they breathe.

"Ozone can do many, many things. It's amazing," says Toshio Asakura, an M.D. and Ph.D. at Children's Hospital in Philadelphia, as well as a professor at the University of Pennsylvania. "Ozone is also a very dangerous chemical."

Ozone "pretty much kills every known microbial thing out there," says Lt. Col. and Dr. Donald Skillman, chief of infectious diseases at Fitzsimons Army Medical Center in Denver. It causes free radicals, chemicals that can kill. It can lead to cancer. "Like anything else, it's toxic in high concentrations."

Ozone is very unstable: The third oxygen atom likes to break off and attach to other things, including bacteria and viruses that do not grow in an oxygen environment. The human immunodeficiency virus (HIV), for example, dies when exposed to air. Ozone is the most powerful oxidant known.

In Japan, ozone has been bubbled into fish tanks with amazing results, Asakura says. He doesn't know how it works, but "the fish grow so big as compared to the sibling fishes. This is a fact."

Germans began using ozone as early as World War 1 for cleaning and disinfecting wounds, but it was difficult to handle because oxygen with just 5 percent ozone would corrode rubber and various metals. The development of modern plastics made it possible for Germans to resume ozone therapy in the 1960s.



Since then, German doctors have been working with ozone to treat a variety of problems. They've had especially good results treating infections and wounds, like diabetic ulcers. Sometimes they draw blood from the patient, bubble ozone into that blood and then re-infuse the oxygen-rich blood into the patient. Sometimes they apply ozone to the skin in a closed container, like a plastic boot. Sometimes they give ozone enemas. In each scenario, oxygen atoms break off from the ozone and bond to oxygen-poor blood or stubborn infections. Ozone kills bacteria and fungi as well as improving circulation, according to German doctors S. Rilling and R. Viebahn, authors of *The Use of Ozone in Medicine*. They write that ozone stimulates the body's ability to carry crucial, life-giving oxygen to the body's tissues. American doctors know that oxygen helps tissues heal, but they're not always sure how to get oxygen to where it's needed. Simply breathing oxygen doesn't seem to do much good. Neither does putting people in pressure chambers with oxygen. "I think in theory, ozone has potential to be helpful in eradicating many types of infections," Skillman says. "It could be used in many different fields."

### **Starting with strawberries**

For one thing, ozone is useful for shipping strawberries. When Jim Caplan was 17 years old, he and his father started installing ozone generators on rail cars carrying strawberries from California and Texas to the East Coast. The ozone, O<sub>3</sub>, would quickly decompose into more stable oxygen molecules, O<sub>2</sub>. The extra oxygen atoms would attach themselves to mold spores and protect the delicate fruit.

As a teenager, Caplan was intrigued by ozone, in the 33 years since, Caplan has spent much of his spare time reading about, thinking about and talking about ozone.

For six years now, Caplan has been pushing and cajoling American doctors and researchers to consider ozone as a treatment for sickle cell disease. His crusade, reminiscent of the parents' chase for an ADL cure in Lorenzo's Oil, hasn't made him a lot of friends in the American medical establishment. "Oh God, not that guy. Ozone Enemas himself," came the response from Adams at NIH.

"Mr. Ozone Enemas" actually is a comfortable businessman, husband and father to four children living in a white house in the suburbs. He has a bachelor's degree in economics from Penn State. As a National Science Foundation fellow, he studied at the London School of Economics and Yale.

Even as a child growing up in suburban Philadelphia, Jim Caplan was something of an independent spirit who like intellectual challenges.

"Growing up as an only child, you learn to fight your own battles," he says. Without brothers or sisters, "there's no one to confer with."

He liked playing sports. He read a lot. When he was about 12, he read a Clarence Darrow biography and decided to become an attorney. That thought was short-lived.

"I didn't like the idea that you could end up defending an argument you didn't believe in," he says. "I didn't want to be a lawyer after that."

"I wanted to understand everything about people," he says. "I was interested in the labor movement. I was interested in how people lived, how you had poor people and rich people, and what made the system what it was."

So Caplan studies economics to become a businessman, and he continued thinking about ozone. Then while he was living in Tegernsee, Germany, from 19696 to 1972, Caplan found himself at a Waldfest drinking beer with Dr. Josef Issels, a German cancer specialist who tried to bring about remissions in terminal patients. Issels told Caplan of his efforts to build up the

immune system and reduce the spread of cancer with ozone.

Meanwhile, Caplan read about the work of Dr. Ottokar Freiherr von Rokitansky, chief surgeon at a Vienna hospital. Rokitansky reportedly used ozone to decrease the number of gangrene-related amputations by 40 percent. In 1983, Caplan met Rokitansky at an ozone conference in Washington, D.C., where the researcher was reporting on his work with ozone to treat circulatory problems.

In 1987, Caplan became CEO of his father's Philadelphia business, Capp, Inc. The business primarily makes temperature controls for melting things like metals, plastics, pharmaceuticals and Hershey's chocolate. Caplan says the work sharpens his determination to find answers to technical problems. "You can't leave a company like DuPont up in the air," he says, "or they won't do business with you anymore."

In 1988, he saw one of his employees, Dorothy Simmons Hardy, trying to recover from a sickle-cell crisis. "At 2 o'clock in the afternoon I would see her with her head on her desk, terribly fatigued," Caplan says.

He wanted to help. He turned to a general medical text, Boyd's Pathology, and looked up sickle cell anemia. The book described red blood cells that lose their shape and elasticity when the blood's oxygen partial-pressure falls below 45 millimeters of mercury.

Oxygen pressure. Caplan remembered the strawberries. He remembered the doctors in Germany. Then he wondered: Why not use German ozone techniques to treat sickle-cell crisis? If Germany can do it, why not the United States?

### **Closed doors at Children's**

"I reviewed the material Mr. Caplan sent me," says Dr. Alan Schechter, a sickle-cell specialist and chief of the Laboratory of Chemical Biology in NIH's National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda. "I was very impressed. The data looked very nice." "He's right," Schechter says. "If you could increase the partial pressure of oxygen, it would probably have a beneficial therapeutic effect (on sickle-cell patients). I think it's an interesting idea."

Schechter suggested that Caplan take his idea to Children's Hospital in Philadelphia, because Asakura is the person in the United States with the technology best able to measure the sickling of cells. Ironically, Caplan says he already tried to interest Children's.

Caplan says he first took the concept to Children's, which receives \$1.5 million a year from NIH as well as large private grants specifically to study sickle cell anemia. It has 22 sickle-cell studies going at the moment.

"I wanted them to join me and do the scientific research (one ozone therapy) in the United States," Caplan says.

Caplan says he left an ozone generator and other equipment at Children's, and that he spoke every week with Asakura for two years. "I think Asakura was very interested in the possibilities here," Caplan says. He says he hosted Asakura, his wife and other Children's staffers in his home to witness German doctors using ozone therapy.

Asakura says he is "very interested" in studying the effects of ozone on sickle cell anemia, and that he remembers the hospital being approached by someone to study ozone. He says he can't remember who it was, but that it definitely wasn't Caplan. "The hospital rejected the company because their interest is not the research, but the name on our hospital," Asakura says. "This hospital decided that it is inappropriate that I conduct the research for the company.

"(Children's) Hospital is very interested in any good research," Asakura says. But Children's doesn't want him to accept research money from a for-profit company because there could be

pressure to come up with certain findings, Asakura says. However, "I may (research ozone) in the future, when I have time and money."

If Asakura can't remember Caplan by name, his supervisor certainly does.

"We just could not be pushed or coerced into an area of research we have no preparation for," says Dr. Kwaku Ohene-Frempong, who heads up Children's Sickle Cell Center.

"Ozone kills bacteria," he says. "It will also supply a lot of oxygen to tissues that need to be repaired." However, he adds, "medicine, or science, doesn't just run in fits and starts. You have to develop some scientific basis for something."

He points to acupuncture, the ancient Chinese therapy that ever-so- slowly is gaining credibility in the United States. It takes time for the momentum and scientific paperwork to build up, Frempong says. "If I propose an ozone study to my institutional review board, they will think I'm crazy."

### **Cutting the pain in half**

After months of trying to interest American doctors, Caplan attended a 1989 ozone conference in New York. A delegation of Cuban scientists was reporting on their use of ozone to treat retinitis pigmentosa, a progressive retina disease that leads to blindness. Caplan mentioned sickle cell to them.

Cuban doctors Sylvia Menendez, Manuel Gomez, and E. Espinosa were intrigued. Perhaps they could use a therapy they already were using safely, but for a new purpose. Statistically, sickle cell anemia strikes about 1 percent of all blacks--which is a significant number of people in a country that is more than half black. Caplan sent Gomez his notes.

At the National Center for Scientific Research and the Institute of Hematology and Immunology, both in Havana, the Cuban doctors started their research with animals to prove the ozone-enema treatment wasn't toxic. By May 1990, they already had conducted clinical trials with more than 100 sickle-cell patients.

The complex system of capillaries in the colon was able to pick up the oxygen and help the sickled blood cells flow more smoothly. The doctors reported that ozone helped patients resolve their sickle-cell crises in half the time, and that patients treated with ozone suffered fewer recurrences in the six months afterward. (Their findings are published in the January 1995 issue of the Townsend Letter for Doctors, which calls itself "an informal letter magazine for doctors communicating with doctors.") By November 1990, the Cuban Minister of Health approved ozone as a treatment for sickle cell anemia.

As Caplan figures it, the Cuban doctors who conducted the sickle-cell research are "wonderful, caring human beings" who work 12 hours a day, six days a week. "They seem to be extremely dedicated to patient care."

American doctors also want to improve patients' lives, but it's harder for them, Caplan says. American doctors have to fight for their positions at hospitals, they have to plan their studies around grant money available if they work at research institutions, and they have to watch every step for fear of a lawsuit.

Cuban doctors "don't go through what our doctors go through," Caplan says. "They can really practice medicine."

Caplan presented a paper on Cuba's ozone successes at the 18th annual meeting of the National Association for Sickle Cell disease, held in May 1993 at Children's Hospital in Philadelphia. More than 100 care-givers were present, but not one doctor showed interest.

Several medical experts told the Welcomat they dismiss evidence from Cuba because they see it as a troubled Third World country without so much as a free press.

### **A tortoise among hares**

It isn't easy to get the American medical establishment to pay attention to the work of doctors in other countries.

When American researchers hear of foreign data, "they tend to say 'Who are these people? Are they running a monkey-gland clinic?'" says Art Caplan, director of the Center for Bioethics at Penn.

"The fact that (a therapy) is used in Europe doesn't really imply that it really is valuable," says Schechter at NIH.

Realistically, the research findings might be less accurate outside the U.S. because, in most countries, researchers are allowed to try experimental treatments on people without double-blind studies. In a double-blind study, neither the patient nor doctor knows who's getting the drug and who's getting a placebo. Theoretically, patients could improve from a treatment simply because they expect to.

Other countries also are more willing to allow human experimentation without preliminary tests in test tubes and on animals, American researchers say. Plus, researchers in other countries don't face the same significant studies to demonstrate a treatment is effective.

When American pharmaceutical companies have an idea, they often start their research in Europe. By going overseas, drug companies can evaluate a drug faster and put it on the market there long before it hits the States, if it ever does.

"Their (European) procedures are much easier, so it takes less time," says Mark Grayson, a spokesperson for the Pharmaceutical Research and Manufacturers of America. "The drug agencies aren't quite as intrusive, and they move much quicker than our FDA."

Schechter and other researchers are quick to point out that Americans don't want a drug that could be harmful to, say, one patient in 50.

It seems odd to talk about researching a toxic cure. But German doctors seem to be able to use ozone without killing people, points out Art Caplan. To study the effects ozone on people, American researchers first would have to prove that it can be delivered without hurting people--which would be redundant when it's already being used safely in Europe, Art Caplan says.

Unfortunately, Americans "don't have a way for systematically incorporating safety finding" from other countries, he says.

Perhaps worse yet, ozone's reputation in the U.S. suffers from people outside the medical profession who make claims before they have the scientific data. Certain people have offered ozone to desperate AIDS patients as a cure-all without the research to back their promises, Poiesz says. "If a concept gets associated with that, sometimes it's hard to break out of that cache of illegitimacy."

Many American researchers, people who like to know the microscopic scientific steps within the overall process, are befuddled by ozone. It isn't completely understood.

"If you look at the studies that are done by the Cubans, it looks like they have major effects...on their patients," says Frans Kuypers, a Ph.D. research scientist who has studied ozone at the Sickle Cell Center at Children's Hospital in Oakland, Calif. But "none of those (Cuban) studies clearly defines why it is effective."

### **Test anxiety**

The people who think ozone has potential therapeutic benefits are among the first to say ozone should be scrutinized with big, scientific American tests. They just want those tests to be done.

Because so many people have promoted the use of ozone, "it deserves some legitimate study to say does this stuff have a potential or not, just to put it to rest," says Dr. Bernard Poiesz, a virologist who has studied the effect of ozone on the HIV virus at the State University of New York at Syracuse. "There's a lot of clinicians that are using it for all kinds of things."

Here in the United States, Dr. Michael Carpendale of San Francisco has been studying the potential uses of ozone for 15 years. He says all of his research has confirmed what German doctors have been saying about ozone's benefits.

Carpendale studied five AIDS patients who had suffered from AIDS diarrhea for an average of 38 weeks. He found that four of the five patients improved after ozone-enema treatments. The results were published in 1993 in the *Journal of Clinical Gastroenterology*.

"Although it was only five patients, it was very meticulously studied, very rigid," Carpendale says. "We thought once we published that, that it would be easy to get funding for a proper study with 50 patients or 60 patients."

A large study would be relatively expensive--\$500,000 or so--because repeated lab tests would have to be done to track the treatment's progress, Carpendale says. But "ozone isn't expensive in itself. It's just the price of oxygen, and that's very cheap."

Carpendale got some Veteran's Administration research money 10 years ago, and later he got some private funding that he stretched over two years, but he hasn't been able to catch the eye of NIH review committees. As he sees it, that's because ozone has no credibility in the "official party line" of conventional American medicine.

"It's very hard to take that," Carpendale says. "The thing is, I wouldn't mind if there were one good scientific study done...to say 'Look, it doesn't work.'"

Double-blind "is certainly the right way to go," Carpendale says. "But to put something down which they haven't done any tests on..."

"AIDS diarrhea is such a bad disease to have. To die of it is really very hard. But you really need to ask someone who's more dispassionate than I am."

### **At State University of New York, Poiesz has been frustrated, too.**

In his study, he found that ozone could be used for "almost seemingly complete destruction" of HIV without affecting blood protein. It's too early to jump to conclusions, he says, but the HIV-infected cells were more vulnerable to ozone than healthy cells. This raises the possibility that AIDS patients could be treated with ozone.

His study also showed that a system to sterilize human plasma with ozone could be safe for handlers, he says. He thinks that theoretically, ozone could protect medical staff and patients from HIV and other viruses that have not yet been identified. The results were published in 1991 in *Blood*, the leading medical journal on blood and blood diseases.

Poiesz collaborated with Medizone, a New York company that hopes to get approval to use ozone to decontaminate blood products as well as treat viral diseases, including hepatitis B, herpes and HIV. Medizone International has worked with the Italian Scientific Society for Ozone Oxygen Therapy (ISSOT) on clinical trials at the University of Naples. If the process is approved, Medizone has patent rights to the process in the United States, Canada, Japan, Hong Kong and other countries.

Poiesz is interested in doing more ozone studies, but his research hospital can't afford it. Medizone president Joe Latino has tried to find additional funding, but he hasn't gotten very far. NIH generally funds just 15 percent of research proposals, and this idea wasn't among them.

"The government deemed it not worthy of funding," Poiesz says. He says there was a bias

among certain project reviewers that ozone wouldn't be very useful. "They just didn't think it had a priority."

"What I really think we know about (ozone) is somewhere between nothing and not much." Penn's Art Caplan says. "What bothers me is that people aren't trying to push hard to get it tested" in the U.S.

### **A matter of money**

American scientists spend many years studying individual steps in the basic science long before actual human beings are introduced to the equation. Then the clinical trials go on for years. Schechter has spent the last 10 years at NIH studying three drugs to try to increase fetal hemoglobin in the blood of sickle-cell patients. "It's very slow going," he says. "We probably will not know the answers for three or four years."

"Historically, maybe on in 100 people who advocate an offbeat approach to medicine will turn out to have something important," Schechter says. Unfortunately, nobody knows which Wonka bar has the golden ticket.

"I can tell you that there are 25 or 50 other types of compounds that people are advocating for sickle-cell therapy," he says, adding that of 20 to 30 sickle-cell proposals in the '70s, "virtually none" are considered viable today.

At least half a dozen companies have potential sickle-cell drugs in the pipeline right now, he says. "They're having the same type of frustration. What Mr. Caplan is experiencing with ozone is not unique.?"

### **Realistically, researchers say, choices must be made.**

"There are always many more important questions that can't get answered for lack of funds," says Dr. David Asch, a senior fellow at the Leonard Davis Institute of Health Economics, University of Pennsylvania. Getting federal research money is a matter of convincing people that an idea has merit, he says. "You can't test everything. I don't know if sucking on truck tires will cure cancer, but my guess is it won't."

Scientists know that oxygen can make sickled cells normal again, but ozone studies would have to progress from test-tube studies to animal studies and then to human studies, says Frempong at Children's Hospital. "You can't jump over all those steps and just say, 'I'm going to test this on humans.' You can't just have a hunch and test it."

All this research takes money, and most of the money for research in this country comes from private industry. The pharmaceutical industry spends more than \$13 billion a year on research--far more than the \$700 million NIH allocates for studies, Grayson says.

Some of the proposals never pan out. On average, pharmaceutical companies spend \$359 million per drug to get FDA approval, Grayson says. As a result, drug companies spend their research dollar "where they feel they've got a real breakthrough. You don't set up to do something somebody else is already doing."

Financially, it doesn't make sense for drug companies to pump research money into ozone because drug companies are for-profit businesses. Ozone is a naturally occurring compound that can't be patented.

The FDA realized that these financial realities and its strict regulations limit research into potentially useful drugs. So the agency set up an orphan drug designation to encourage research on disease that affect 200,000 or fewer people in the United States.

The orphan drug program provides \$9 million in grants each year, tax credits on research done, and a seven-year exclusive license if the process is approved by the FDA for that particular

disease.

Jim Caplan has orphan-drug designation for ozone to treat sickle-cell anemia. If the process is approved, he would own the patent on the delivery process in sickle-cell cases for seven years. He says he hasn't even applied for orphan-drug research funding yet because he doesn't have the American scientists to conduct ozone research on sickle cell anemia.

### **An outsider looking in**

Jim Caplan says he's frustrated. He doesn't feel he's being taken seriously because he doesn't have "the right pedigree," a medical degree.

People from outside the medical world can be seen as the equivalent of snake-oil peddlers with "the latest bottle of feel-good stuff," Art Caplan says.

But it's also hard for people within the system, Schechter points out.

As Poiesz puts it, a businessman suggesting a medical idea is like a doctor trying to get a bill through Congress. He says he's not surprised Caplan, an outsider to the medical establishment, has met with such resistance.

"Oftentimes, they get pretty chilly receptions," Art Caplan agrees.

"Always there are people who like to make money," says Asakura at Children's Hospital. He says he would not be willing to join forces with a business that would sell ozone generators. "For pure science I am interested."

"I wonder if they ever asked people like Frempong and Asakura how much Children's Hospital makes on sickle cell anemia," Jim Caplan says.

He says that if he were interested in profits, he wouldn't have devoted about 15 percent of his business week for years on end to an idea that might never see the light of day. "I've gone all over the world and pursued this thing," he says. "My whole motivation was to establish this mode of thinking and treatment. There are many other areas where I can make a profit."

### **Improving lives**

If a large, wealthy pharmaceutical company were steering ozone through the testing process, perhaps it would have a better shot. But the fact remains that pharmaceuticals would have no reason to take on a product as simple as ozone. As soon as the seven-year protection period ends, says Whitmore at the FDA, "29 companies are pumping it out in New Jersey."

### **Jim Caplan doesn't care.**

"So you've got competition," he says. "So you make a better product." The real issue, he says, is the number of people whose lives might be improved with this cheap and simple process that needs to be tested.

"I grew up playing an awful lot of athletics. I like to win. If I think I'm right, I will persevere." Jim Caplan says. He's trying to get as many people on his team as he can. "There are people out there who will fight to fight. You just have to find them."

Even if he gets a seven-year ozone delivery patent for sickle-cell treatment, Jim Caplan believes he could not make nearly as much money from ozone therapy as the American health system could save if it were approved.

Take the use of ozone to prevent diabetic amputations, for instance. He clicks some conservative numbers into his adding machine: "If you had 50,000 amputations a year and you reduced it by 35 percent, that would be...let's say the operation is \$15,000, conservatively, with a stay in the hospital, and the rehabilitation afterwards is another \$15,000..."

Let's see...17,500 people at \$30,000 a head...

"That would be a savings of \$525 million in this society."

That's every single year. And that's beyond the humanitarian side of things.

In May 1990, Jim Caplan saw a young Cuban woman lying on a treatment bench. "I came into the ward, and she was actually being treated for the ulcers on her leg," he says. With repeated ozone treatments, he says her sores were going away.

"I was introduced as the man from the United States who introduced the ozone/oxygen treatment to Cuba," Jim Caplan says. "The gal's eyes lit up...(Through an interpreter) she said, 'You know, all my life I've had these ulcers on my legs. I've never been able to wear a dress.'

"She hugged me, and tears came to her eyes, and tears came to my eyes," Jim Caplan says. "It was an extremely moving experience. It just makes you want to fight it through."

Source: Welcomat Newspaper. (The Philadelphia Weekly: News, Arts & Opinion) Volume XXIV, No. 26, January 11, 1995.



# **Canadian Medical Research Mystery DOD Positive Ozone / HIV Results Ignored**

by Ed McCabe,  
Investigative Reporter, and author of the bestseller  
"Oxygen Therapies"  
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The story of a mystery within the modern Canadian Medical Establishment. A proven safe and effective treatment for alleviating AIDS symptoms is being hidden from view.

Summary: Various Canadian government and military and commercial representatives got together in 1989-1990 to allegedly test the safety and effectiveness of "ozone therapy" in the treatment of AIDS. Two small pilot studies were undertaken. This resulted in the 1991 Publication: The use of ozone-treated blood in the therapy of HIV infection and immune disease - a small pilot study (phase 1 was 10 patients, phase 2 was 14 patients) of medical ozone's safety and efficacy. "AIDS" 5:981-984. G. Garber, D Cameron, N Hawley-Foss, D Greenway and M. Shannon(1). The methods used were antiquated, and the device quality control was non-existent by any objective standard, and the actual published conclusions were exactly opposite to the conclusions written up by one of the chief investigators.

This is a study the rare detractors of medical ozone like to quote, to falsely try and promote a viewpoint that it doesn't work. I say falsely, because we know for a fact that such detractors parade the false published version of this study out instantly, while hundreds of positive medical ozone references held in their possession remain strangely ignored. Hundreds of references were sent to one of them, the U.S. FDA, and they have admitted having them - in writing, yet they never mention them.

Modern Medical Ozone therapy consists of taking three combined very active atoms of pure oxygen (ozone) and surrounding all the anaerobic (can't live in oxygen) primitive cell bacteria, viruses, fungi and parasites with it. This active form of pure oxygen makes it impossible for the quickly oxidized microbes to live, and ozone is also harmless to normal healthy human cells when used correctly. All the secondary infections, and possibly even the prime infection either go away, or enter a level of remission concurrent with the procedures and methods applied, including the pre-treatment health of the patient. When applied properly, meaning using correct procedures, delivery methods, concentrations, volumes, and durations, ozone is extremely safe and effective, according to published animal and human studies over the past one hundred years (2,3,4).

In an early (early for North American research), Canadian establishment attempt to see if there is any validity to the overwhelmingly positive reports on medical ozone coming out of Europe, and, to see if it was safe, an outdated and poorly executed ozone protocol was used in a "small pilot" study by researchers inexperienced in the use of ozone therapies. Outdated because the method chosen was deemed painful and ineffective in 1938(5), and inexperienced, because they

had never used ozone before.

Modern medical ozone application has a few significant procedures that classically trained scientists outside the field know nothing about, since the many ozone therapy procedures are not taught in North American and Canadian medical schools. These investigators incorrectly chose the delivery method of minor autohemotherapy as their starting point. This was a backwards decision when we consider that ozone has been in use by thousands of European physicians for over 50 years, and far better methods are currently in use worldwide. The minor autohemotherapy method (min AH) they chose involved withdrawing a small amount of blood, mixing ozone into it - to kill the viruses, and then re-injecting the dead viruses - this is the immunization theory. Minor autohemotherapy is a poor cousin to major autohemotherapy, which is itself now giving ground to even more successful modern delivery methods.

The most modern of the successful ozone therapies skip this unneeded dead virus inoculation step, and directly flood the blood, lymph, and cells with virus destroying pure medical ozone gas. This is done in a variety of ways, IV, dialysis type recirculatory systems, ear, vaginal, penile, and rectal insufflation, sauna bags and devices, breathing ozonated air, and drinking ozonated water. Our bodies soak it right up harmlessly because we evolved in an oxygen environment. Starting in the late 1800's up to the present, hundreds of thousands, perhaps millions use some of these methods daily.

The small pilot trial we are discussing was sponsored by the Ottawa General Hospital Infectious Disease Division, the Canadian Department of Health and Welfare, the Canadian Federal Center For AIDS, the Canadian Department Of National Defence, and The Mueller Medical Company of Canada, now Vas-O-Gen. My analysis: If you compare the protocols used in this study with the known to be more effective modern ozone methods, and then also compare the internal letters of the investigators reporting their documented findings against the final published version of the study, it immediately becomes apparent that the published study was, if not fraudulent, then close to it. How can I make such an accusation? Let's look closely at the facts.

Of prime importance is the fact that the very design of the study was so out of touch with current known worldwide private ozone medical practices that it should never be labeled "ozone therapy." It is a travesty to call it anything other than a poor distant cousin to modern ozone therapy.

However, on the plus side, one fact stands out on the very first page (981) of this study published in "Aids."1 The authors plainly state: "Preliminary work has suggested that ozone does inactivate HIV in vitro." Then they also state that they proved ozone does indeed kill HIV-1. They withdrew 10cc's of blood, and interfaced 3 mcg/ml<sup>3</sup> of ozone with it, and the ozone destroyed all the HIV-1 viruses, and didn't hurt the blood. "The resulting inoculation presents a killed virus antigen preparation." These statements alone prove ozone deserves further study!

Let's examine the materials and methods used. Here's a comparison of the outdated protocols employed in the study and modern medical ozone delivery methods:

1990 antiquated (MinAH) Standard private medical Canadian study ozone protocol

- Treat outside body. - Inject directly into the vein, or constant recirculation. - Withdraw 10cc's of blood. - Inject/recirculate up to 500ccs, or whole blood supply. -Treat with 3 mcg/ml<sup>3</sup>  
-Minimum of 27 to 42 mcg/ml<sup>3</sup> concentration. concentration. - Ozone was heated. - Ozone never heated. Heat destroys ozone. - Injected into huge gluteus - Always infused into maximus

muscle. veins/arteries. - Injected only three times - Best applied once or twice per week. per day.

Also ignored results. The published document ignored the results of Phase 1A wherein 3 of the few patients who had any immune system left - each with CD4 T-cells above 200 - had their counts go from 220-230 up to 500. The patients gained weight, and reported feeling great. Instead, the published document stated: "no difference was seen between placebo and ozone treated patients." Reason: I learned from a personal interview with the ozone generator manufacturer's technician that in Phase 1B, the second half of the study, either the ozone generator mysteriously "broke," or someone deliberately sabotaged it, because The ozone generator was producing very little or no ozone! and when the Meuller medical technician dutifully reported this to the investigators, he and this fact were ignored, and the study was written up without reflecting the facts!

Incorrect dosage schedules and volumes. Phase 1A and Phase 1B treated only 10cc's of patient blood on only three times a week treatment days.

Wrong procedure. This is fine to make an inoculation, but inoculations only work on people whose immune system are fully functional, certainly innoculations are not applicable to a study of AIDS patients and their compromised immune systems with only 50 to 500 T cell count ranges.

Ozone is used to sterilize municipal drinking water all over the world. How are you going to clean up the microbe infested waters that the human patients are made up of, by putting only 10cc's (less than a teaspoon) of barely touched with ozone blood into a muscle - and only three times a week?

Compare this choice of minor autohemotherapy (MinAH), with its only thrice weekly injections against the obvious objective of getting rid of this disease by cleaning all the viruses, bacteria, funguses, and parasites out of the 100 POUNDS+- of water that the human body consists of. The injected small amount of oxygen/ozone is used up when the oxygen tries to oxidize the existing and incoming pollution and microbes. The total cleansing objective is challenged daily by the added burden of leaving 2 1/3rd days of normal daily living between treatments. This skipping treatment days allows the environmental and dietary toxic intake load to continually tend to undo this miniscule attempt at the cleaning process. There is no way you could ever hope to "keep up" with this method by cleaning faster than the body absorbs new toxic burdens, especially under the stress of a disease like AIDS and its constant bacterial and viral replications! 10cc's of minor autohemotherapy is to be considered only a drop in the pond of the diseased body waters.

Incorrect concentrations. The tiny 10cc's of withdrawn patient blood was treated with an equally tiny 3 microgram per cubic millimeter by weight, ozone concentration (assuming a functioning ozone generator). Private clinics using ozone know that a minimum of 27 to 42 mcg/ml<sup>3</sup> concentration is necessary for maximum viral kill with a minimum of hemolysis (Standard acceptable levels of normal cell damage). This study used only a drop in the pond of acceptable concentrations.

Wrong delivery method. The tiny amount of blood with the (possibly intermittent or non-existent) tiny concentration of ozone was introduced into the body by injecting it into a large muscle. No-one who really knows how to use ozone has employed this method since 1938, when Dr. Paul Aubourg used it in his study in two Paris hospitals. He proved that although other methods of the application of ozone, like rectal insufflation, gave excellent effectiveness, the intramuscular injection method was "painful and ineffective." (5)

The actual data does not match the published conclusions. Even more suspect than the above

errors is a detailed comparison between the actual investigators' internal inter-office correspondence, and the final published document. Let's look at excerpts from a letter by Captain Michael Shannon, now Commodore Shannon of the Canadian Department of National Defence (the Canadian military forces) written to Dr. D.W. Boucher on January 24, 1990.

Note: A copy of the letter to Dr. Boucher and the accompanying data was stamped CONFIDENTIAL and handed / leaked to me at a health show in a plain brown envelope by an interested party who said, "You don't know where you got this." The party was outraged at the following duplicity, but too self-protective to directly challenge "the system." Actually, there was no need of all the cloak and dagger stuff, because a copy of the exact same letter - not marked confidential - had previously been published by Barry Bruder in his work "Ozone Therapeutics, A Current Compendium" in August of 1993.

M.E. Shannon CD,MA,MSC,MD one of the principal investigators wrote the following in his final report and recommendations to the superior official representing the government funding, Dr. D.W. Boucher, of the Bureau of Biologics, Health Protection Branch, Health and Welfare, Tunney's Pasture, Ottawa, Canada, on January 24th, 1990:

"Ozone Therapy In AIDS/Project #231 Summary of Findings."

Dr. Shannon:

This trial yielded... "encouraging results"

"There has been no clinical, biochemical or immunological evidence of adverse/toxicological effects."

"An improved sense of well being characterized the clinical responses of all patients..."

"...several patients reported a return of appetite and concomitant weight gain."

"4 patients suffering from arthralgic pain reported a significant amelioration of symptoms."

3 out of 4 "reporting complete relief of what was well documented to have been a chronic condition."

"The lack of bruising at the site of injection was somewhat surprising."

"Three patients showed a significant positive response..." in their CD4 measures.

"There were no detrimental effects on absolute CD4 counts for any of the patients."

"One patient showed a 52% reduction in the initial P24 antigen levels with a corresponding increase in absolute CD4 count."

The earlier Sept to October 1989 series of investigations by Dr. M.O. Shaughnessy at the Virology Division of the Bureau of Laboratories and Research Services "clearly support the contention that the technology has potent virucidal (virus inactivating) effects." "It would appear that this form of therapy constitutes a potent means of inactivating HIV-1 in contaminated blood supplies, and may also provide a means for patient specific "autovaccination" in selected cases." ("Selected cases" meaning those with enough of an immune system left so that an inoculation will make the immune system respond.)

"These results are considered well beyond the error limits for the particular assays, and indicative of potential therapeutic benefits which should be further investigated."

"As reported in earlier correspondence, (1988/89 Ottawa General/NDMC) several cases of long standing sciatica and one case of severe facial pain secondary to an invasive naso-pharyngeal carcinoma responded dramatically to this form of therapy."

"As the understanding of ozone biochemistry increases and potential toxicological concerns dissipate, analgesic applications of this therapy should be pursued."

"Since a subgroup responded, consideration should be given to the need for extended follow-up, and administration of a "booster cycle" to commence as soon as possible."

DR. SHANNON'S RECOMMENDATIONS AFTER COMPILING THE TRIAL DATA

"The results of this Phase I clinical trial are sufficiently encouraging that the research team at the Ottawa General Hospital would like to pursue an extension to the subject trial as outlined..."

"The potential benefits of this inexpensive, safe, and possibly efficacious treatment for the rapidly growing HIV-1 pandemic warrants further attention. Your assistance in this regard is respectfully solicited."

### **THE ACTUAL WRITTEN AND PUBLISHED PAPER**

Remember, these two following statements are being quoted and passed around by government agencies as "proof" that ozone "doesn't work."

1. "In summary, these small pilot studies have shown that the Meuller Ozon-O-Med ozone therapy protocol appeared to have no detectable beneficial effect."(?,!)(Emphasis mine.)

2. "Our work does not, therefore, support the continued use of this technique in patients with HIV associated immune disease."(?,!)(Emphasis mine.)

Even with all the problems this study had, they never said "ozone doesn't work," only that the delivery method didn't work! So, if someone or some agency tries to use this study as proof that ozone doesn't work, they are blatantly guilty of deception.

Although 5 investigators were listed as principals on the published paper, exactly who were the actual final paper-writing authors? From Dr. Shannon's communication to The Bureau of Biologics: "Be advised that Dr.'s Garber and Cameron (Ottawa General Hospital) have formally submitted an abstract related to this trial to the International Conference on AIDS presentation this June."

It is also extremely interesting to further note that Dr. Shannon was never given a review copy to sign off on before the paper was published. In other words, although his name appears upon the published version, he was denied any input into the final version of what was said.

What forces would promulgate this obvious perversion of truth? One source I interviewed, an enthusiast for Canadian ozone research, stated that he understood "the word on the street" to be that Dr. Garber was looking forward to proudly announcing the positive results at the upcoming big AIDS conference, but when the second phase didn't produce as good results as the first phase, he became crestfallen and couldn't make the announcement. He turned his back on the project. Of course, the non-existent daily quality checking of the ozone generator was his responsibility. So then he either had to go on record admitting that the trial he was responsible for was flawed, or alternatively, make the claim ozone is worthless. History shows the decision that was made.

There is another aspect that I attribute to no one person, but I believe it must be considered as a possible shadowy, yet powerful, influence. Although it is shocking to any sane person to consider this scenario, we must also ask ourselves ask who would financially loose the most if AIDS and a host of other diseases, like cancer, etc., were to actually be improved, cured, or at least treated back to a level of remission? Hint. You wouldn't need huge AIDS specialized government oversight agencies, and their supervisors, huge sums of private or federal research funds, billions of dollars in drug sales yearly, or healthcare workers, or hospitals, or grassroots AIDS groups, and their directors, and their funding. That is, of course, unless all these people and institutions were willing to clean up their lives, stop "going along", and be directed into POSITIVE life affirming employment and enterprises.

Was this influence at work when Dr. Shannon was seeking labs to possibly continue the research, yet was told "All the labs are booked up for years on other work."(8) Who would have enough money to tie up all the labs and lock ozone out?

Why wouldn't Captain, now Commodore, Shannon come forward and publicly withdraw his support of the study? Who can blame him, we all know what happens to military "whistleblowers." Even though he hasn't spoken out, he remains absolutely pro ozone to this day.(8)

Why would the investigators, and all the connected agencies, ignore, and continue today to ignore, the notification of the broken machine? Perhaps to have spent or taken the money to do such an expensive study, and being known as a "respected department," or "respected investigator" with a reputation to protect, and above all a need to continue the funding, maybe it is just too hard to admit your people, or you, personally, didn't do an expensive study correctly by completing such a basic daily task as quality checking the ozone producing machine. Let us hope that more nefarious forces were not in play.

And finally, Why would the published data suddenly and mysteriously change its obviously positive data into a negative published summation?

Unfortunately, the stench from this rotting carcass now infests my country as well. The U.S. FDA uses this same study as a reference, and seriously oversteps the truth and their boundaries to make the unjustified, and way too broad pronouncement that, based upon this Canadian report, "Ozone therapy does not enhance parameters of immune activation nor does it diminish measurable p24 antigen in HIV-infected individuals." From an actual FDA letter to one of our elected U.S. representatives, Congressman Sherwood Boehlert. Remember, the false published paper clearly never says that ozone doesn't work, but that only the particular delivery system of minor autohemotherapy, as used, incorrectly, and with its broken generator, doesn't work. Quell suprise!

I agree wholeheartedly that the protocols, as used here, are terribly ineffectual when compared to normal medical ozone therapies as practiced daily worldwide by thousands. Especially if you try it with a faulty generator. Even with this handicap, the plain facts remain that the investigators used a comparatively ineffectual ozone delivery method, an antiquated protocol, and a possibly broken generator, to create only a killed virus antigen preparation, and then injected too little of this mixture in the wrong place. Even these inadequate methods yielded such surprisingly positive results (when given time to do their work in a few of the patients whose immune systems were still functioning) that these amazing results had to be hidden from the public.

So, in summary, a protocol that any serious practitioner would laugh at was used, their conclusions were based upon false data - if the machine was broken, and their fraudulent conclusions were written in total disregard for human suffering, not caring how far back ozone research would be set, or how many lives were at stake.

The tragedy of allowing such abberant summations to be published, and to allow such pronouncements to be made based upon the mysterious summations, is that this errant information is repeated by supposedly impartial agency officials to our elected representatives and to news reporters, while these very agencies ignore the thousands of studies that show ozone does work(3,4.) This downright intellectual dishonesty is used to politically justify barring further real research into ozone in North America that would immediately prove we have something ready right now to eliminate suffering and save lives. We know this is true, because ozone has been in use for 100 years by thousands of physicians. (2,3,4,5,6,7)

The miscarriage of justice and perversion of facts here is so overwhelmingly evident that I don't know what more to say, but I will say this: Exactly what factors came into play in the minds of the authors, the "reputable scientists" that we have trustingly given the care of ourselves and our loved ones to, when they obfuscated the truth needed by the sick and dying,

so as to further delay the introduction of ozone medical therapies in the U.S. and Canada? Why would any sane person deny a very badly needed therapy to the sufferers of disease? May God have mercy on their Souls, for they know not what they do when men trade their honor for convenience. Where are the positive thinking Canadians attempting to go from here? Quoting Commodore Shannon:(8)

"Allister Clayton, the Director of the Federal Center for AIDS went to bat for our funding." "The book is not closed on the efficacy of ozone therapy for the treatment of AIDS." "We need more funding." "There is a role for ozone in medicine."

In March/April of 1995 Medizone International from New York will be announcing the results (which logically would be successful) of their preliminary 300 patient HIV/Hepatitis ozone trials going on in Italy under the auspices of several universities and The Italian Medical Ozone Society.

In March/April 1995, Cornell University is expected to announce the results of their ongoing ozone blood safety and sterilization trials.

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1. The Use of Ozone-Treated Blood in the Therapy of HIV Infection and Immune Disease: A Pilot Study of Safety and Efficacy. AIDS 1991, 5:981-984
2. Safety - January 1980, The German Medical Society for Ozone Therapy commissioned Marie Theresa Jacobs and Prof. Dr. Dr. Hergetbegan from the University Kilnikum Giessen and the Institute for Medical Statistics and Documentation of Giessen University to begin an inquiry entitled "Adverse Effects and Typical Complications In Ozone Therapy." 2,815 questionnaires were sent out to all western German ozone therapists known by the Medical Society for Ozone Therapy (AGO, Arztliche Gesellschaft fur Ozontherapie). 884 went to physicians and 1931 to therapists. They collected 1,044 replies, or 37% of the total. The replies that were returned stated 384,775 patients were treated with ozone with a minimum of 5,579,238 applications and the side effect rate observed was only .000005 per application! The report also stated "The majority of adverse effects were caused by ignorance about ozone therapy (operator error)." The University of Innsbruck's Forensic Institute published Dr. Zacob's dissertation quoting this in The Empirical Medical Acts of Germany.
3. "Ozone Vs. AIDS, The history and suppression of ozone therapy in the United States as of May 1994" Energy Publications 305/759-8710 (Referencing 120+ ozone medical references).
4. Get a computer with a modem, and get on the Internet, and write an "email" message to list@oxytherapy.com On the first line of the message, put the word "Subscribe" if you wish to be on the computer mailing list ozone discussion group. Worldwide Web users web to: <http://www.oxytherapy.com> Or call 305/759-8710 to order the proof.
5. "Medical Ozone: Production, Dosage, and Methods of Clinical Application". Parisian Medical Bulletin - Bul Med Paris 52 or 42:745-749,
6. 1885 Florida Medical Association published "Ozone" by Charles J. Kenworthy, M. D., M.R.S.V. from Jacksonville Florida. Dr. Kenworthy was bubbling ozone through blood to sterilize it. This proves that ozone was in regular medical usage in the U.S. before 1885, and therefore predates the 1906 Pure Food and Drug Act.
7. 1993 Sept 2, World premier of Canadian 1/2 hour video "Ozone and The Politics of Medicine" by Geoff Rogers and Riener Diedrau at the International Ozone Association meeting, San Francisco California. Dr. Horst Kief from Germany states there are over 8,000

- doctors using ozone in Germany and Austria alone today.
8. Cmdr. Shannon personal interview with Ed McCabe 12/19/94.



# H<sub>2</sub>O<sub>2</sub> has a role in cellular regulation

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Unfortunately the figures mentioned in this paper could not be reproduced.

## **Abstract:**

H<sub>2</sub>O<sub>2</sub>, in addition to producing highly reactive molecules through hydroxyl radicals or peroxidase action, can exert a number of direct effects on cells, organelles and enzymes. The stimulations include glucose transport, glucose incorporation into glycogen, HMP shunt pathway, lipid synthesis, release of calcium from mitochondria and of arachidonate from phospholipids, poly ADP ribosylation, and insulin receptor tyrosine kinase and pyruvate dehydrogenase activities. The inactivations include glycolysis, lipolysis, reacylation of lysophospholipids, ATP synthesis, superoxide dismutase and protein kinase C. Damages to DNA and proteoglycan and general cytotoxicity possibly through oxygen radicals were also observed. A whole new range of effects will be opened by the finding that H<sub>2</sub>O<sub>2</sub> can act as a signal transducer in oxidative stress by oxidizing a dithiol protein to disulphide form which then activates transcription of the stress inducible genes. Many of these direct effects seem to be obtained by dithiol-disulphide modification of proteins and their active sites, as part of adaptive responses in oxidative stress.

Molecular oxygen, also termed dioxygen, has two unpaired electrons. These go into separate antibonding n-orbitals which parallel spins. The stability and paramagnetic property of oxygen are due to this. The reductions of O<sub>2</sub> to superoxide, hydrogen peroxide and water are made possible by adding one, two and four electrons to the anti-bonding orbitals of dioxygen (1). These reactions are shown in Fig. 1 along with two dismutation reactions for superoxide and hydrogen peroxide.

The formation of H<sub>2</sub>O<sub>2</sub> in cellular oxidation is known to occur by direct 2-electron reduction by flavoprotein oxidases (2), or by 1-electron reduction to superoxide anions, two of which dismutate yielding a molecule each of H<sub>2</sub>O<sub>2</sub> and O<sub>2</sub> by the enzyme superoxide dismutase (3). By its facility for electron exchange H<sub>2</sub>O<sub>2</sub> can act both as an oxidant and a reductant typically found in catalase reaction itself. In presence of Fe<sup>2+</sup> and other metal ions, H<sub>2</sub>O<sub>2</sub> can also generate hydroxyl radicals which are known to cause molecular damage. H<sub>2</sub>O<sub>2</sub> is toxic to cells and is indeed responsible for killing internalized bacteria in phagocytosis (4). This led to the misconception that H<sub>2</sub>O<sub>2</sub> is undesirable by-product of oxidase reactions that the aerobic cells tackle by providing themselves with high concentrations of degrading enzymes such as catalase and glutathione peroxidase, which ensure adequate protection. Peroxidases are of ubiquitous occurrence and utilize H<sub>2</sub>O<sub>2</sub> to oxidize a wide range of compounds to yield important metabolites. Therefore generation of H<sub>2</sub>O<sub>2</sub> in cellular processes seems to be purposeful, and has been found to be widespread in occurrence in aerobic cells and cellular organelles (5,6). But reduction of oxygen to H<sub>2</sub>O<sub>2</sub> by cytochrome oxidase, the major O<sub>2</sub> user, had over-shadowed the importance of the qualitatively minor pathways.

Generation of H<sub>2</sub>O<sub>2</sub> appears to be a natural process in aerobic cells as part of the of the

reactions of a number of oxidases and dehydrogenases, essential in cellular activities. Only the endomembranes, plasma membranes (7,8) and microsomes (9), have the special property of dormant NAD(P)H oxidation that can lead to very high rates of H<sub>2</sub>O<sub>2</sub> generation in presence of decavanadate (10) or in phagocytosis (11). Under normal conditions the rates are small and account for H<sub>2</sub>O<sub>2</sub> no more than 2% of total O<sub>2</sub> consumed. Thus, in the presence of excess catalase and glutathione peroxidase in cells, the limited H<sub>2</sub>O<sub>2</sub> has little chance of exhibiting its purported toxicity.

With respect to mitochondria the accumulated information indicates the presence of H<sub>2</sub>O<sub>2</sub> generator distinct from the respiratory chain (12). The parallel utilization of substrates has provided a false facade of sharing dehydrogenases. The two activities, substrate- dependent dye reduction and H<sub>2</sub>O<sub>2</sub> generation, respond differently. Only the H<sub>2</sub>O<sub>2</sub> generation is inhibited by phenolates (12), increased in cold exposure (13) and noradrenaline treatment (14) and decreased in heat exposure (15,16). This regulated activity therefore must have a meaningful physiological role.

A specific need for H<sub>2</sub>O<sub>2</sub> in killing the phagocytosed bacteria is established. While lysosomes undertake the task of dissolving out the components of the injected particles, the killing of pathogenic bacteria requires a H<sub>2</sub>O<sub>2</sub> dependent reaction, yet to be defined. This process utilizes the latent capacity of NAD(P)H oxidation of the plasma membrane unmasked by a serum component picked up during opsonization and requires the phagosome structure (17). The explanation for these peculiar features is not available (18).

Intrinsic high rates of H<sub>2</sub>O<sub>2</sub> generation, an apparent metabolic necessity, seems to be a characteristic of protozoa. Parasitism in the case of trypanosoma and plasmodium may indeed be characterized by the removal by the host cell of such metabolically generated H<sub>2</sub>O<sub>2</sub>, otherwise self-destructive in view of the absence of H<sub>2</sub>O<sub>2</sub> detoxifying systems in these protozoa. This is exemplified by the decreased survival of these disease-causing parasites in the host cells with defective H<sub>2</sub>O<sub>2</sub> scavenging mechanism or on treatments that lead to increased H<sub>2</sub>O<sub>2</sub> generation (19).

Since seventies it is increasingly realized that H<sub>2</sub>O<sub>2</sub> is not a mere wasteful by-product but fulfills functional, metabolic needs. Inter- relationship of hormone H<sub>2</sub>O<sub>2</sub> dithiol proteins-metabolic control is suggested in the case of insulin-mimicking action of H<sub>2</sub>O<sub>2</sub> (20). The hormonal response of NADH dehydrogenase of plasma membrane (21) that is known to generate H<sub>2</sub>O<sub>2</sub> (22) is documented. An ubiquitous, regulated phenomenon must have a role in cellular activities. The small rates, in fact, are best designed for that purpose in view of its toxicity and high reactivity. A number of direct effects of H<sub>2</sub>O<sub>2</sub> on metabolism and enzyme activities are described (Table 1) and this review projects the importance of H<sub>2</sub>O<sub>2</sub> in this regard.

### **Carbohydrate Metabolism**

As early as 1958 Warburg and coworkers (23) and Holzer and Frank (24) recognized that the presence of H<sub>2</sub>O<sub>2</sub> depressed glycolytic flux. This direct effect on tumour cells, confirmed by others (25,26), can be partially reversed by addition of endogenous NAD (24,25). Interestingly this effect was traced to decrease in activity specifically of glyceraldehyde-3-phosphate dehydrogenase (GAPD) raising the possibility of an oxidative inactivation by H<sub>2</sub>O<sub>2</sub> of this known sulphhydryl enzyme (27,28).

In a comprehensive study with P388D1 cells, Hyslop et al. (29) showed that a large, rapid inhibition of GAPD was obtained with IC<sub>50</sub> of 100 μM concentration of H<sub>2</sub>O<sub>2</sub>. Purified rabbit muscle enzyme was inhibited completely at this concentration. Similar inhibition on exposure of

cells or tissue to  $H_2O_2$  of this enzyme was reported for human lung carcinomal cells (30) which can be partially reversed by DTT, and for rat heart which cannot be reversed by DTT (31). In these studies on treatment with  $H_2O_2$ , Hyslop (29) and Radda (32) and coworkers found that only GAPD showed rapid decreases (Fig.2) but some glycolytic enzymes, among the following tested, remained unaffected: hexokinase, phosphoglucose isomerase, phosphofructokinase, aldolase, triose-P-isomerase, kinases of pyruvate and phosphoglycerate, enolase and dehydrogenases of G-6-P and lactate. As expected the fructose 1, 6-diphosphate and aldolase-products (triose phosphates) accumulated in cells under conditions of inhibition of GAPD by  $H_2O_2$ . Some indication of decrease in hexose monophosphates as well as glucose-1, 6-diphosphate was obtained with P388D1 cells which appears to be more due to lack of ATP than by modifications of the enzymes involved.

$H_2O_2$  was shown to stimulate transport of glucose (33) and glucose C-1 oxidation (34) as well as glucose incorporation into glycogen (35) in rat adipocytes, and insulin-responsive tissue. These effects follow the known stimulation of HMP shunt activity in such as tissue by oxidants and  $H_2O_2$  (36,37).

In P388D1 cells treated with  $H_2O_2$ , the net glucose uptake decreased, coinciding with decrease in lactate production, but not the glucose transporter rate (29). It appears that G-6-P-dehydrogenase was not the target of action of increased overall activity of HMP shunt and the step affected is yet to be identified.

In intact spinach chloroplasts,  $H_2O_2$  treatment caused drastic inhibition of  $CO_2$  fixation that can be reversed by catalase or DTT (38). This resulted in increase of incorporation of  $^{14}CO_2$  in hexose and heptulose biphosphates and pentose phosphates, and decrease in hexose monophosphates and ribulose 1,5-biphosphate. Since oxidative pentose phosphate cycle and G-6-P-dehydrogenase are known to be inactivated by dithiols (39), the  $H_2O_2$  activation is conjectured to be a reversal of this effect by 'oxidation of light-generated SH- groups'.

### **Lipid Metabolism**

$H_2O_2$  was found to inhibit lipolysis stimulated by theophylline (40) or isoproterenol (41). Some of these compounds used are prone to oxidation by  $H_2O_2$  and thus in principle the effect of  $H_2O_2$  may simply be to destroy the stimulator. Using ritodrine (100 nM), a B- adrenergic agonist resistant to oxidative destruction, and glucagon (1nM), Little and deHaen (42) were able to show that stimulated lipolysis in epididymal fat cells was indeed inhibited by  $H_2O_2$  similar to insulin.

On  $H_2O_2$  treatment stimulation of [ $^{14}C$ ]glucose incorporation into lipids, particularly glyceride-fatty acids, had been reported similar to insulin response (43,44). Accompanying this effect the active form of pyruvate dehydrogenase showed rapid increase, without changing the total amount of the enzyme protein (44). This stimulation, like with insulin, was found to occur in the absence of glucose in the medium and therefore is independent of increased glucose due to its enhanced transport (33), also known to stimulate the active form of enzyme (45). The response of pyruvate dehydrogenase increase was obtained as early as 5 min after treatment of adipocytes with  $H_2O_2$  (0.31 mM) and was maximal at 15 min followed by decrease consequent to degradation of  $H_2O_2$  (Fig. 2). These and other experiments led May and deHaen (20,44) to propose that  $H_2O_2$  plays a second messenger role. In further experiments deHaen and coworkers (46) found that in cells treated with 100 nM of phenyl (isopropyl) adenosine, a potent inhibitor of lipolysis, and exposed to insulin in the presence of medium glucose, glycerol production and cyclic AMP concentrations were unaffected, whereas free fatty acid release was inhibited coinciding with increase in  $H_2O_2$  production. Therefore they considered that

"H<sub>2</sub>O<sub>2</sub> production is a metabolic consequence of insulin action distal to the receptor and is correlated with the fall of free fatty acids."

Irreversible brain injury during ischemia is thought to be due to released unsaturated fatty acids through their peroxidation products. The fatty acid hydroperoxides (LOOH) were found to inhibit reacylation of phospholipid in neural membranes (47), an essential step in repair of damaged membranes.

H<sub>2</sub>O<sub>2</sub> treatment of alveolar macrophages inhibited 5-lipoxygenase and stimulated release of arachidonic acid and synthesis of thromboxane A<sub>2</sub> (48). Conditions that promote lipid peroxidation, however, stimulated lipoxygenase activity (49).

In the case of soybean lipoxygenase, H<sub>2</sub>O<sub>2</sub> behaves as a potent activator (5).

### **ATP and NAD Metabolism**

One of the striking effects of H<sub>2</sub>O<sub>2</sub> treatment of cells is the rapid depression of intracellular ATP (51,52) and NAD<sup>+</sup> (refs 53,54) concentrations. In P388 d1 cells, the t<sub>1/2</sub> for decrease of levels of ATP and NAD<sup>+</sup> were found to be about 15 and 4 min, respectively, on treatment with 50 μM concentrations of H<sub>2</sub>O<sub>2</sub>. Calculations of data on ADP phosphorylation in these experiments revealed that both glycolytic and mitochondrial contributions were inhibited and results in loss of pool of ATP and eventual cellular death. The decline in ADP phosphorylation appears to be related more to inactivation of the ATPase-synthase rather than to the decline in the rate of electron transport according to Hyslop et al. (29).

Both NAD<sup>+</sup> and NADH concentration decline in H<sub>2</sub>O<sub>2</sub> treated cells. This appears to be due to the use in ADP ribosylating nuclear proteins during this stress (55) on activation of the nuclear enzyme, poly (ADP ribose) polymerase, also known to occur (53,54).

### **Protein Phosphorylation**

Another relationship exists between H<sub>2</sub>O<sub>2</sub> and insulin through the mechanism of protein phosphorylation. Insulin receptor is a self phosphorylating insulin-sensitive protein kinase. This protein phosphorylation was found to be dramatically potentiated by H<sub>2</sub>O<sub>2</sub> in intact Fao cells (56), and was inhibited by antagonists such as phorbol ester and cyclic AMP. Such effects were also obtained with vanadate (26) which was found in our laboratory to generate H<sub>2</sub>O<sub>2</sub> on oxidation of NADH by plasma membranes (8). Thus, the effects with reduced naphthoquinones (57) and vanadate (58) on stimulation of protein tyrosine phosphorylation in plasma membrane appear to depend on generation of H<sub>2</sub>O<sub>2</sub>. Further studies by Heffetz et al. (59) indicated that H<sub>2</sub>O<sub>2</sub> (3mM) and vanadate (0.1 mM) in combination far exceeded insulin in stimulating phosphorylation of four proteins in Fao cells and part of this effect was obtained by marked inhibition of protein-tyrosine phosphate hydrolysis.

Purified protein kinase C was found to be inactivated by H<sub>2</sub>O<sub>2</sub> and the susceptibility increased in the presence of calcium ions and phorbol ester (6). This phenomenon seems to be complex because mild oxidation showed a small increase but further oxidation damaged both regulatory and catalytic domains. Also, the membrane-bound enzyme, which increased on activation of x-adrenergic receptor by adrenergic agonists (61) and also by decavanadate (62), was more susceptible to inactivation by H<sub>2</sub>O<sub>2</sub> produced in situ as a result of such treatment (14,63). Intracellular free calcium (64) itself registered fast rise on H<sub>2</sub>O<sub>2</sub> treatment and also in synaptosomes on addition of menadione bisulphite which released endogenous H<sub>2</sub>O<sub>2</sub>. Thus, all the effects of H<sub>2</sub>O<sub>2</sub> seem to favour inactivation of protein kinase C to keep the dependent signal transduction inoperative.

### **Damage to Biopolymers and Cytotoxicity**

Damage to DNA on  $H_2O_2$  treatment of cells had been noted in several systems (51-53,66). This effect may occur through calcium, as indicated by its prevention by its intracellular chelator, Quin 2 (ref. 67).

Hyaluronic acid in proteoglycan aggregates was found to be fragmented on  $H_2O_2$  treatment of neonatal human articular-cartilage. This effect was apparently obtained through hydroxyl radicals and also involved cleavage of link protein to remove a trideca-peptide as well as modification of His (16) and Ala and Asn (21) to Asp (68).

Inactivation of superoxide dismutase of the Cu-Zn and Fe-types, but not Mn-type, occurred on treatment with  $H_2O_2$  (69,70) and in the case of the bovine liver enzyme release of copper was responsible for this.

The above effects contribute to the cytotoxicity of  $H_2O_2$ . The reactive oxygen radicals generated from  $H_2O_2$  in presence of iron or trace metal ions are likely to cause strand breaks in DNA (71) or leaky membranes (72) or cytoskeletal plasma membrane perturbations (73).  $H_2O_2$  insult to mammalian (74) and bacteria (75) cells leading to killing include a variety of processes such as DNA strand breaks, poly ADP ribosylation, protein modifications, membrane perturbations and energy transducing systems. Cell survival seems to depend on its ability to restore the cellular reductive process and thiol status (76).

### **Thiol-disulphide Status of Proteins**

Glutathione redox cycle was affected in presence of  $H_2O_2$  and intracellular thiols were oxidized (29,77,78). The effects of such oxidations of proteins sulphhydryls will be seen in their respective activities and in metabolism involving them. This was established in cases of GAPD and pyruvate dehydrogenase described above. It is apparent that  $H_2O_2$  in small quantities generated in cells can exert powerful regulatory actions by modifying enzymes capable of redox changes of thioldisulphide type. Ziegler (79) presented a case for such regulation of enzyme activity. The enzymes thus affected are: phosphorylase a, fructose bisphosphatase, G-6-Pase, G-6-P dehydrogenase, acetyl CoA hydrolase, and pyruvate dehydrogenase are increased, while glycogen synthetase, phosphofructokinase, hexokinase, phosphoenol-pyruvate carboxykinase, GAPD, HMGC<sub>o</sub>A reductase, N-acetyl tranferase, protein kinase, guanylate cyclase and mevalonate kinase are decreased.

The cellular response to oxidative stress in the first place is adaptive and is likely to use redox reaction for counteracting the stress. An excellent example of this is provided by the studies of Ames and coworkers (80) on direct activation by oxidation of a protein responsible for transcription of oxidative stress-inducible genes. They found that the gene product of oxy R, a 34 kDa protein oxy R, which binds with promoter region of the oxy R, was oxidized rapidly and reversibly to disulphide form when the bacterial cells were exposed to  $H_2O_2$  and was then able to activate transcription for at least 9 proteins, including catalase. The purified oxy R, protein was found to bind to DNA in both reduced-inactive form and oxidized- active form, albeit differently as characterized by the foot- printing. While both oxidized and reduced forms of the protein oxy R repress own expression in vitro, only the oxidized form was capable of stimulating expression of katG gene in a concentration dependent fashion that was sensitive to DTT. It may be expected that other such proteins will be discovered where oxygen species are involved in metabolic regulation.

Long exposures and high concentrations of  $H_2O_2$  do destroy the biological structures and lead to irreversible damage. It appears that such lethal actions are initiated by oxygen radical species. This happens only in certain conditions such as phagocytosis. Under normal

physiological conditions, H<sub>2</sub>O<sub>2</sub> is generated in small quantities and is rapidly used or degraded. It is now clear that this regulated generation of H<sub>2</sub>O<sub>2</sub> is not only used as a substrate for peroxidases, where present, but also for protein-thiol oxidation. The use of H<sub>2</sub>O<sub>2</sub> for this additional role in cellular regulation has only revealed a vignette of its vast potential in modification of proteins and their activities. H<sub>2</sub>O<sub>2</sub> can perform a role similar to protein phosphorylations in cellular regulations.

### Acknowledgment

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### Figure 1.

Reduction of oxygen [The reductions of dioxygen by 1.2 and 4 electrons to superoxide, hydrogen peroxide and water, respectively are shown. It may be noted the O-O distance progressively increases on reduction. The two dismutations of superoxide and hydrogen peroxide by enzymes are indicated. The formation of radical species of hydroxyl and lipid hydroperoxide are also shown]

### Figure 2.

The changes in activities of glyceraldehyde-3-phosphate dehydrogenase and pyruvate dehydrogenase on incubation with H<sub>2</sub>O<sub>2</sub> [The data are adapted from Hyslop et al. (2) for P388 D1 cells, Chatham et al. (32) for heart tissue and May and deHaen (44) for adipocytes]

### Table 1. Metabolic effects of H<sub>2</sub>O<sub>2</sub> treatment

(Some of the effects described in the text for direct effects of H<sub>2</sub>O<sub>2</sub> treatment of tissues/cells/enzyme systems are summarized. The time periods and mode of treatment are different in each case.

Tissue/cells H<sub>2</sub>O<sub>2</sub> Test System % Control Ref. conc. No. mM

Adipocytes, rat 0.20 [U-14C]Glucose --> 170 44 TG-fatty acids 0.31 Pyruvate dehydrogenase 185 44 0.06 Lipolysis, glycerol Decreased 42 release (B-adrenergic stimulated)  
P3888 D1, cells 0.10 Net glucose uptake 40 29 0.10 Glucose-->lactate 50 29 0.10 HMP shunt pathway 510 29 0.10 Glyceraldehyde-3-P 50 29 dehydrogenase  
Carcinoma cells 1.0 Glyceraldehyde-3-P Decreased 30 dehydrogenase (ROOH)  
Glyceraldehyde-3-P Decreased 31 dehydrogenase  
Heart, rat 0.15 Glyceraldehyde-3-P 25 32  
Fao cells 3.0 Insulin-receptor Potentiated 56 tyrosine phosphorylation 3.0 Protein-tyrosine-P-50 59 phosphatase  
Protein kinase 5.0 Ca-dependent protein 20 60 C phosphorylation  
ADP-ribose -- Poly ADP ribosylation Increased 54 polymerase of proteins  
Pseudomonas 0.42 Dismutation of 50 60 superoxide superoxide dismutase  
Chloroplasts, 0.6 CO<sub>2</sub> fixation 10 38 spinach into sugar phosphates  
Soybean 0.5 5-Lipoxygenase Increased 50  
Synaptosomes, 0.025 Reacylation of 50 47 rat brain  
E. coli 0.06 Transcription of Increased 80 oxy R gene controlled oxidative stress inducible genes

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May 24th 1990

# Artificial Ionization of the Air

by Roger Wiesenbach

(also mentioned: air purification, filters, ozone, disinfection)

First of all, a properly designed ionizer subjects your body to nothing \*unnatural\*, only the kind of air you'd find in a pine forest.

Second, I have nothing to sell you, nothing to gain but maybe your thanks if you have benefited from this information.

Third, there is not too much of certainty that can be said about the effects of ionization; some studies seem to have shown significant effects, but few scientists have followed up on it nor has there been much publicity. It seems that there are some aspects that have shown real value and merit serious study, and can be analysed at little expense with existing technology.

The 'claimed' effects of negative ionization (of oxygen molecules, mainly):

- improved exchange of O<sub>2</sub> and CO<sub>2</sub> in the lungs (important if lungs function poorly),
- better metabolism, each negative ion said to permit the passage of ~75 neutral O<sub>2</sub> molecules into a cell, (animals died after some days in atmosphere without neg. ions),
- improved 'beating' of cilia in the respiratory system to expel particles,
- neutralisation of harmful free-radicals in the blood stream
- destruction or precipitation of bacteria, pollen and certain germs,
- certain maladies & symptoms are provoked or aggravated by positive ionization, reduced by negative ionization, such as asthma, cardio, arterio, hepa, rhuma, cancer, stress, digestion, better healing of scars, less pain (by production of cortisol), reduced recovery time after anaesthesia, reduced stress by regulation of serotonin (without the side-effects of anxiolytics/benzodiazepines),

An ionizer is typically a ventilator with filters on the air intake and little needles charged to about 4000 volts on the output end. In France the price for a modest but acceptable model from Philips is about \$175. More on the technical aspect follows later. The value of breathing the air from an ionizer depends very much on the individual and the milieu. Note that some people benefit very much from Prozac (which works on the serotonin) while others in a seemingly identical condition feel nothing. If you live in a pine forest, an ionizer would be of little value (unless you want to 'supercharge' on negative ions for some kind of therapy).

Some people are very aware of the presence of ionization, others not, and the sensation can change with the weather and personal mood. You might try turning the ion generator on/off while keeping the fan going to see if you can detect the difference, whether the air seems 'fresher'.

Even if ionization had no physiological value, there is still the advanced filtering unit and the precipitating effect of ionization which greatly reduce the air pollution. With an active charcoal filter, household smells are also removed.

The 'healthy' air has at least several hundred negative ions per cubic centimeter. It is still considered healthy if there is slightly higher percentage of positive ions. Conditions which reduce the negative ions or increase the positive ions include:

- too many people in a confined and unventilated room,
- pollution: smoking, car fumes, fog,
- electric appliances: TV screens, copiers, motors,
- hot & dry winds: Santa Ana, Chinook, Foehn, Sharav, etc.,
- the onset of storms, relieved when the rain comes,
- synthetic interior fabrics.

The interior of an automobile is a particularly critical milieu, considering that people sit for a long time in a confined space, the container is a metallic cage, and one person has to keep in a good state of alertness.

Ionization is easily confounded with ozone, oxygen & hydrogen peroxide treatment, especially since they may present the same condition to the target organ. Ionization improves the exchange of carbon dioxide and oxygen, so it means more oxidation of the hemoglobin. More can be said on this in a later article.

### **Technical discussion:**

A good ionizer contains (typically) a three-stage filter. The first, a washable large-mesh, catches the dust & lint and other large particles before they can clog the non-renewable following stages. The second may be an electrostatic filter of many fine threads, which should among other things catch many varieties of germs. The third is an active-charcoal filter to absorb gases.

The electrostatic filter becomes quite dark in a few months, and normally you must exchange the assembly at a cost of about \$15. I got some bulk material instead as replacement. A mask as used in surgery might be put in front of this filter to extend its life. Some one of you might have suggestions for a good, low-priced filter material.

I first became fascinated with ionization in my activities as physicist, work that often results in large sparks. I noticed how the air very quickly took on a fresh sensation, odors disappeared. I finally did an experiment, bringing out a wire from the very high voltage circuit of a TV receiver (up to 20,000 volts -- don't try this without great caution!!), attaching needles to the end of the wire. From the points came nice little corona discharges. Placing a cigarette in the vicinity, the fumes swirled into the electric field and then deposited on the surrounding metal cage. Adding a fan caused the air of the room to become quite fresh.

On further study, though, I began to worry that this might be producing free radicals of large carcinogenic molecules, so I settled on a store-bought ionizer of lower voltage and needles with points designed to give just enough voltage gradient to spray out negative ions of light molecules like oxygen. This did not have such a strong effect but was more reassuring.

A powerful ionizer (or ozone generator) still interests me for disinfecting purposes. Put your bedding, shoes, whatever in a zip-up bag and make a closed-circuit circulation of ions or ozone. Sick rooms & toilets could be closed off for regular treatment. A very useful device would be a low-priced ionometer to measure the amount and size of the various kinds of ions and particles in the air, both to gauge the 'healthiness' of the air and then the effectiveness of an ionizer.

Medical scientists are beginning to worry about 'pm10' particulates, those below 10 microns (10 millionth of a meter) which pass through the body's filter system. Ionization might assure that they are at least partly neutralized or precipitated.

Somebody's going to make big money from \*membrane\* technology, filters that let through only the smaller molecules. One use is desalination, passing H<sub>2</sub>O while blocking salt. Another

use is in hospital bedding, letting the mattress & pillow covers breathe air and humidity while blocking viruses, etc.

Another money-maker will be instruments to measure various substances in the blood stream, including oxygenation and medication, as well as the nutritive value of vegetables & fruit. These are topics on which I am gathering info.

A compendium of information about ionization is found in a book by Dr. Herve Robert: "Ionisation, Sante, Vitalite", in French, 1989. He might be considered 'marginal', but the preface is by a leading French professor/clinician who decries the lack of interest by the medical establishment in this subject.

The book cites studies by, eg. NASA on capsule climatization, Dutch re. the attentiveness of children in school, the French transport institute on driver fatigue, Swiss on sick-leave and food industry hygiene, Finns on hospital infections, others on the growth of plants, French on aging,

Otherwise, I have noted that Matsushita (Panasonic, etc.) has embarked on trials in Osaka and Mexico City on large-scale pollution reduction by electronic means.

Perhaps someone among you would like to research what is available in the English language? There is much more that can be said on these topics, but I will wait for some feedback from your part to provide inspiration to gather and collate more from this end.

# Hyperbaric oxygen therapy

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## Abstract

Hyperbaric oxygen (HBO) therapy involves intermittent inhalation of pure oxygen under a pressure greater than one atmosphere. During the 1960s, HBO was proposed as a treatment for cancer, heart attack, senility, and other conditions, but research studies did not obtain reproducible results. The skepticism engendered among medical personnel by these failures extended to HBO's use for treating clinical conditions that it had been shown to help. A review of these conditions is provided. HBO acts both mechanically, due to its pressure component, and physiologically, due to its oxygen component. HBO therapy has been effective in treating decompression sickness (the illness resulting from too-rapid changes in pressure by divers or aviators), and air embolism (introduction of air into the circulatory system, often unintentionally by medical personnel) by mechanically reducing the size of gas bubbles, and increasing oxygen levels in the blood. Oxygen is essential for proper function of certain cells of the immune system and, in certain injuries, such as burns and crush injuries, HBO treatment can increase the supply of oxygen to tissues otherwise deprived of it. Complications of HBO treatment include trauma to or rupture of cavities, neurotoxicity resulting from exposure to 100 percent oxygen for long periods, and other sequelae. HBO therapy is indicated for decompression sickness, air embolism, carbon monoxide poisoning, acute traumatic ischemia (crush injuries that deprive tissues of oxygen), and bacterial invasion of a necrotic wound (in which tissue has died). HBO may also stimulate regrowth of blood vessels in damaged tissue adjacent to areas treated by radiation therapy and may promote bone formation in cases of osteomyelitis (bone infection) that have not responded to other treatments. This therapy also shows promise for treating a variety of 'problem wounds', but randomized, prospective studies are lacking. Overall, HBO therapy is safe and effective for certain conditions, and well-formulated clinical trials could help extend its use to others. (Consumer Summary produced by Reliance Medical Information, Inc.)

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## HYPERBARIC OXYGEN THERAPY

Hyperbaric oxygen therapy involves intermittent inhalation of 100% oxygen under a pressure greater than 1 atm. Despite over a century of use in medical settings, hyperbaric oxygen remains a controversial therapy. The last 20 years have seen a clarification of the mechanism of action of hyperbaric therapy and a greater understanding of its potential benefit. However, despite the substantial evidence that hyperbaric oxygen may have a therapeutic effect in certain carefully defined disease states, many practitioners remain unaware of these findings or are concerned about using hyperbaric therapy because of the controversy it has engendered. This review examines the indications currently considered appropriate for hyperbaric oxygen and

briefly evaluates animal and clinical data substantiating these indications. Areas in which the mechanism of action of hyperbaric oxygen is still not well understood, as well as possible new areas of applications, are discussed. HYPERBARIC oxygen (HBO) therapy involves intermittent inhalation of 100% oxygen under a pressure greater than 1 atm. [1] Both therapeutic and toxic effects result from two features of treatment: mechanical effects of increased pressure and physiologic effects of hyperoxia. Hyperbaric oxygen therapy has long been accepted as a primary treatment for decompression sickness [2]; however, other proposed indications have been controversial. During the 1960s there was widespread enthusiasm for hyperbaric treatment of myocardial infarction, stroke, senility, and cancer. Enthusiasm waned after results of clinical trials (and direct experience) showed little benefit for these diseases. The overzealous claims about the effectiveness of HBO therapy have left a legacy of skepticism among physicians. [3] However, animal studies, clinical trials, and greater clinical experience over the last two decades have produced a set of indications for which HBO therapy appears beneficial. These clinical conditions are substantially different from those in the 1960s. However, there has been no recent interdisciplinary review of HBO therapy delineating these current indications, despite their broad applications. Thus, while substantial evidence supports use of HBO therapy in certain carefully de fined settings, many patients who might benefit go untreated because of their physician's unfamiliarity with recent research and overall uncertainty about the legitimacy of HBO as therapy. We discuss the mechanism of action of HBO therapy and the commonly accepted clinical indications (Table 1) as delineated by the Undersea and Hyperbaric Medical Society, [1] the professional association of physicians administering HBO therapy, and we briefly review the data supporting current indications.

## **MECHANISMS OF ACTION**

**Pressure** In disease such as air embolism and decompression sickness, the therapeutic effect of HBO therapy is achieved through the mechanical reduction in bubble size brought on by an increase in ambient pressure. A 5 atm a bubble is reduced to 20% of its original volume and 60% of its original diameter. Increasing pressure in HBO therapy is often expressed in multiples of atmospheric pressure absolute (ATA); 1 ATA equals 1 kg/c[m.sup.2] or 735.5 mm Hg. Most HBO treatments are performed at 2 to 3 ATA. In air embolism and decompression sickness, where pressure is crucial to therapeutic effect, treatments frequently start at 6 ATA. This additional pressure, when associated with inspiration of high levels of oxygen, substantially increases the level of oxygen dissolved into blood plasma. This state of serum hyperoxia is the second beneficial effect of hyperbaric oxygen therapy. Hyperoxia: Life Without Blood

At sea level in room air, hemoglobin is approximately 97% saturated with oxygen (19.5 vol% oxygen, of which approximately 5.8 vol% is extracted by tissue). The amount of oxygen dissolved into plasma is 0.32 vol%. An increase in P[O.sub.2] has a negligible impact on total hemoglobin oxygen content; however, it does result in an increase in the amount of oxygen dissolve directly into plasma. With 100% inspired oxygen the amount of plasma oxygen increases to 2.09 vol%. At 3 ATA plasma contains 6.8 vol% oxygen, a level equivalent to the average tissue requirements for oxygen. Thus, HBO treatment could and has sustained life without hemoglobin. [4] The immune system, wound healing, and vascular tone are all affected by oxygen supply. Oxygen alone has little direct antimicrobial effect, even for most anaerobes [5]; it is, however, a crucial factor in immune function. Neutrophils require molecular oxygen as a substrate for microbial killing. The oxidative burst seen in neutrophils after phagocytosis of bacteria involves a 10-to 15-fold increase in oxygen consumption. [6] Here oxygen serves as

a substrate in the formation of free radicals, which directly or indirectly initiate phagocytic killing. [7] This endogenous antimicrobial system virtually ceases functioning under conditions of hypoxia. A tissue [PO.sub.2] of at least 30 mm Hg of oxygen is considered necessary for normal oxidative function to occur. [8] Oxygen partial pressures below this are often seen in damaged and infected tissues. Increasing the oxygen level in this tissue can allow restoration of white blood cell function and return of adequate antimicrobial action. [9] The cardiovascular effects of hyperbaric oxygen include a generalized vasoconstriction and a small reduction in cardiac output. [10] This ultimately may decrease the overall blood supply to a region, but the increase in serum oxygen content results in an overall gain in delivered oxygen. In conditions such as burns, cerebral edema, and crush injuries, this vasoconstriction may be beneficial, reducing edema and tissue swelling while maintaining tissue oxygenation. [11]

## **COMPLICATIONS**

Usual complications of HBO therapy are listed in Table 2. They are a result of either barometric pressure changes or oxygen toxicity. The most common complications involve cavity trauma due to change in pressure. [12] Any air-filled cavity that cannot equilibrate with ambient pressure, such as the middle ear when the eustachian tube is blocked, is subject to deformity and barotrauma during pressure changes in HBO therapy. Pneumothorax is a rare complication of HBO treatment, usually occurring only in patients with severe lung disease. Air embolism, presumably resulting from a small tear in the pulmonary vasculature, is another rare complication. [13] One hundred percent oxygen under high pressure is neurotoxic and can lower the seizure threshold and affect central nervous system control of respiration. However, neurotoxicity is rare with the low-pressure, short-duration treatments used clinically in HBO therapy. In one series the incidence was reported as 1.3 seizures per 10 000 treatments. [14] Pulmonary oxygen toxic reactions can occur with 100% inspired oxygen at less than 1 ATA with prolonged exposure. Almost all patients will show pulmonary toxicity after 6 continuous hours of inspired oxygen at 2 ATA. [15] No clinical HBO protocol requires this length of continuous exposure to 100% oxygen. However, HBO treatments may contribute to the pulmonary oxygen toxicity seen in critically ill patients who receive high concentrations of inspired oxygen between hyperbaric treatments. Although a concern in premature newborns, retrolental fibroplasia has not been noted in infants, children, or adults undergoing HBO therapy. [16] Development of cataracts has been reported in patients receiving more than 150 HBO treatments. [17]

## **HBO ADMINISTRATION**

Hyperbaric oxygen can be administered in either a multiplace or a monoplace chamber. Multiplace Chamber Multiplace chambers are large tanks accommodating 2 to 14 people (Fig 1). They are usually built to achieve pressures up to 6 atm and have a chamber lock-entry system that allows personnel to pass through without altering the pressure of the inner chamber. Patients can be directly cared for by medical staff within the chamber. The chamber is filled with compressed air; patients breathe 100% oxygen through a face mask, head hood, or endotracheal tube. Although fire hazards restrict the use of certain electronic equipment, some monitors and ventilators with solid-state circuitry can be used within the chamber, allowing intensive care of critically ill patients. [18] The multiplace chamber's ability to maintain pressures of 6 atm or more, makes it the chamber of choice for decompression sickness and air embolism. Monoplace Chamber Monoplace chambers (Fig 2) are far less costly than their larger counterparts and have allowed hospitals to institute HBO programs without prohibitive

capital outlays. Most chambers are sized to allow a single patient to lie supine under a transparent acrylic dome or viewing port. The internal environment of a monoplace chamber is maintained at 100% oxygen; thus, the patient does not wear a mask. This high concentration of oxygen precludes the use of any electronic equipment in the chamber. However, specially adapted ventilators and monitoring systems do allow treatment of critically ill patients.

## **CLINICAL INDICATIONS**

**Acute Conditions Decompression Sickness:** Although occasionally seen in aviators, decompression sickness is generally a disease of divers. During a dive, the diver is exposed to pressures greater than 1 atm, and tissue uptake of nitrogen increases according to the principles of Henry's law. With ascent, a pressure gradient develops, and nitrogen leaves the tissue, dissolving into the blood and passing to the lungs, where it is exhaled. With rapid ascent a steep pressure gradient develops and intravascular nitrogen gas bubbles form. [19] These can be detected in asymptomatic divers. [20] With greater pressure gradients, the nitrogen bubbles become large enough and prevalent enough to mechanically deform tissue and obstruct blood vessels. The gas-fluid interface also interacts with blood cells, platelets, and proteins, causing disruption of the intravascular coagulation system. [21] Decompression sickness results. Divers can experience decompression sickness as pain only, usually as a "deep and dull ache" in the extremities. More serious cases can present as paraplegia or cardiovascular collapse due to embolization of bubbles into the cardiac or central nervous system. Hyperbaric oxygen therapy mechanically decreases the size of the bubbles, oxygenates ischemic tissue, and reduces the nitrogen gradient. Any patient with decompression sickness should be transferred immediately to the nearest HBO facility with the capacity to decompress to 3 to 6 ATA, as this has been shown in numerous series to be the most reliable and effective treatment. [22,23] The Duke University Divers Alert Network maintains a 24-hour emergency consultation telephone number, (919) 684-8111, and can identify the closest available HBO facility.

**Air Embolism.** Air embolism can be a complication of uncontrolled ascent in diving but more frequently is seen medically in iatrogenic misadventures. Bubbles can embolize to the cerebral or cardiac circulation, producing either severe neurologic symptoms or sudden death. Hyperbaric oxygen therapy has been part of successful treatment of air embolism due to cardiovascular procedures, [24,25] lung biopsies, [26] hemodialysis, [27] and central line placement. [28] Presumably, HBO therapy decreases the volume of the embolism and oxygenates local tissues. Treatment involves immediate descent to 6 ATA for 15 to 30 minutes on air, followed by decompression to 2.8 ATA, where the patient receives prolonged oxygen treatment.

**Carbon Monoxide Poisoning.** Carbon monoxide poisoning accounts for half of all fatal poisonings in the United States. Multiple series have shown that patients with carbon monoxide poisoning improve markedly following treatment with HBO. [29-31] However, both the mechanism of carbon monoxide toxicity and the therapeutic effect of HBO are poorly understood. Carbon monoxide toxicity was long thought to be due to anoxia alone; [32] however, there is evidence that the pathophysiologic effects occur with carbon monoxide binding to the cytochrome-oxidase system, causing anoxia at the mitochondrial level. [33] In either case, HBO therapy is the most rapid way of displacing carbon monoxide bound to hemoglobin and cytochromes. The serum half-life of carboxyhemoglobin is decreased from 5 hours 20 minutes with room air to 80 minutes with 100% oxygen and 23 minutes with 100% oxygen at 3 ATA. [34] In treating patients with carbon monoxide poisoning, it is important to remember that serum carboxyhemoglobin levels do not reflect tissue levels of carboxyhemoglobin and, therefore, may not correlate with the degree of toxicity. Accompanying signs and symptoms



are as important to guiding therapy as the serum carboxyhemoglobin level. [35] Although HBO therapy remains the preferred treatment for significant exposure (Table 3), only a few controlled human studies with inconclusive results have compared HBO with 100% oxygen at 1 atm. [36,37] Clostridial Myonecrosis. Clostridial myonecrosis occurs when a hypoxic environment within a necrotic wound allows clostridial spores to convert to vegetative organisms. These organisms produce exotoxins that destroy red blood cells, cause tissue necrosis, and abolish local host defenses. The most important exotoxin is alpha toxin. A tissue [PO.sub.2] of 250 mm Hg inhibits the production of alpha toxin by Clostridium. [38] Hyperbaric oxygen is commonly used as an adjunct therapy in clostridial infections. In vivo studies have demonstrated decreased mortality rates and diminished tissue loss in infected mice. [39,40] In a study by DeMello et al, [41] using a dog model of clinical Clostridium infection, 100% of infected control dogs and dogs randomized to either HBO therapy or surgery died. Fifty percent of the dogs that received antibiotics survived, 70% of the dogs that received antibiotics and underwent surgery survived, and 95% of the dogs that received antibiotics and HBO therapy and underwent surgery survived. Multiple series have evaluated the effect of HBO therapy on clostridial infections in humans. [42,43] Surgeons experienced with its use emphasize that early HBO treatment reduces systemic toxic reactions so that patients in shock seem more stable and better able to tolerate surgery, and there is clearer demarcation of viable and nonviable tissue. There have, however, been no randomized, controlled studies. Hyperbaric oxygen therapy has been recommended for treatment of necrotizing fasciitis, since anaerobic bacteria play a role in the disease. [44,45] The diversity of clinical states in retrospective studies and the paucity of experimental data make it difficult to demonstrate the effect of HBO therapy on nonclostridial soft-tissue infection. Although necrotizing fasciitis is an accepted indication for HBO, the benefit HBO therapy may provide is still poorly understood, and surgery remains the cornerstone of therapy. [46]

### **Acute Traumatic Ischemia.**

Acute crush injury to an extremity may cause severe edema and ischemia in tissue and capillary beds not relieved by restoration of arterial perfusion. Hyperbaric oxygen therapy may aid salvage during the acute stages of revascularization by reducing edema via vasoconstriction and increasing oxygen delivery via plasma flow. [47] Investigators have used HBO therapy successfully as an adjunct to surgery in crush injuries. [48,49] Additional evidence has demonstrated that HBO therapy may also serve as an adjunct therapy in the compartment syndrome. [50]

### **CHRONIC CONDITIONS**

**Irradiated Tissue.** Radiation therapy, in addition to its therapeutic effects, can damage normal adjacent tissue. The initial pathologic process is a progressive obliterative endarteritis, resulting in areas of tissue hypoxia and eventual cell death. [51] Large areas of hypocellular, hypovascular, and hypoxic tissue are created that are devoid of functioning fibroblasts and osteoblasts. [52] Hyperbaric oxygen therapy appears to assist in salvaging such tissue by stimulating angiogenesis in marginally viable tissue. [53] Marx and Johnson [54] emphasize that, in reconstructive surgery involving recently irradiated tissue, presurgical HBO treatment can help promote a well-vascularized wound bed that will enhance reconstruction and graft take. Using a specific HBO protocol of presurgical and postsurgical treatments, they demonstrated a satisfactory surgical outcome in 92% of their patients and a complication rate of 9%. In osteoradionecrosis, tissue destruction progresses to breakdown of overlying tissues

and symptomatic destruction of bone. Prior to the introduction of HBO therapy, only 5% to 30% of patients who developed osteoradionecrosis could expect remission with conservative therapy. [55] In a protocol developed by Marx, [56] a series of 58 patients received an initial series of HBO treatments, followed by debridement and further HBO treatment, as dictated by their clinical course. All 58 patients studied had resolution of symptoms of osteoradionecrosis, with good results on long-term follow up. These impressive results have been corroborated by others. [57,58] Successful results have also been demonstrated for radiation-induced cystitis [59] and other radiation-damaged soft tissue. [60] Hyperbaric oxygen therapy is beneficial for patients at risk for the development of osteoradionecrosis, such as irradiated patients requiring tooth extraction. In a randomized trial comparing HBO and penicillin therapy in 74 previously irradiated patients, 30% of the patients who received penicillin developed osteoradionecrosis, while 5.4% of the patients who received HBO developed osteoradionecrosis. [61] Similar results have been reported elsewhere. [62] Refractory Osteomyelitis. Hyperbaric oxygen is currently being used as an adjunctive therapy with debridement and antibiotics in osteomyelitis that has remained refractory to standard therapy. Animal studies have demonstrated that HBO therapy used in experimental models of osteomyelitis has increased osseous repair [63] and promoted callus formation, [64] possibly by promoting osteoclast activity. [65] Human studies involve series of patients in whom standard treatment regimens have failed. Multiple clinical series demonstrate substantial success with HBO therapy in these patients. [66-68] However, to date there have been no randomized trials. Problem Wounds. The rationale for HBO therapy in problem wounds is to intermittently increase the tissue oxygen tension to optimize fibroblast proliferation [69] and white blood cell killing capacity [70] during periods of hyperoxia and to stimulate angiogenesis during periods of relative hypoxia. [71] Series have been published showing improved healing with HBO therapy in problem wounds refractory to standard therapy. [72,73] Patients in whom increased oxygenation of wounds can be demonstrated following HBO therapy are the most likely to benefit. However, unlike osteoradionecrosis, where a well-defined clinical problem has been shown to improve with a carefully designed protocol incorporating HBO therapy, treatment of problem wounds remains an ill-defined field, and HBO data often consist of small series without standardized patient populations or treatment schedules. Hyperbaric oxygen therapy cannot substitute for surgical revascularization in advanced arterial insufficiency and cannot reverse inadequate microvascular circulation. [74] Hyperbaric oxygen therapy may serve as an adjunct in the treatment of certain problem wounds, but it cannot replace meticulous local care based on sound physiologic principles. Special Considerations Certain animal data indicate that HBO therapy may improve the outcome of moderate and severe burns. [75] Few centers use HBO as standard therapy, but recent publications of patient series have demonstrated good response. [76-78] Broad-based justification of the use of HBO in burns, however, will depend on favorable results of randomized clinical trials.

## **SUMMARY**

Hyperbaric oxygen therapy is a safe and effective primary therapy when administered for decompression sickness and air embolism. The role of HBO as an adjunctive therapy in the treatment and prevention of osteoradionecrosis has been impressively documented. Its contribution to the treatment of clostridial myonecrosis has been substantiated by both animal models and clinical experience. The role of HBO therapy in recovery from carbon monoxide poisoning, while probably significant, is poorly understood and awaits clarification of the mechanism of action of both carbon monoxide poisoning and the beneficial effects of oxygen

therapy. Hyperbaric oxygen therapy is clearly of value for carefully defined indications. Successful extension of its use in other situations will be predicated on in vitro and in vivo experimental evidence and appropriate well-controlled clinical trials.

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# **Hyperbaric oxygen: more indications than many doctors realise.**

by Eric P. Kindwall

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## **More indications than many doctors realise**

Many British doctors are ignorant of the indications for hyperbaric oxygen and sceptical of its benefits, according to a recent survey of hyperbaric oxygen facilities. The survey, by the BMA's Board of Science and Education, concluded that given the present level of use then provision was sufficient, although doctors may be underusing the treatment.[1] They need to know for which conditions hyperbaric oxygen works and refer accordingly. The telephone advisory service, run by the Institute of Naval Medicine at Gosport (similar to the National Poisons Unit help line), should be better known. Treatment with hyperbaric oxygen was introduced as an adjunct to cardiovascular surgery before cardiopulmonary bypass techniques and deep hypothermia became available. But when surgery in a hyperbaric chamber was no longer necessary most of the original researchers stopped studying it. Britain helped to pioneer the use of hyperbaric oxygen to treat carbon monoxide poisoning, refractory osteomyelitis,[2] and compromised skin grafts. But with no formal training programmes and little funding, the treatment now attracts little attention in Britain. When administered at pressures greater than one atmosphere, oxygen can assume properties more akin to a drug than a simple support for metabolism. In carbon monoxide poisoning, for example, it stops lipid peroxidation, which spares neuronal cell membranes.[3] It reduces oedema by about 50% in post ischaemic muscle through preserving adenosine triphosphate.[4] In acute burns it reduces fluid requirements by 35% in the first 24 hours, thus reducing oedema.[5-8] It reduces white cell adhesion to capillary walls after ischaemic or traumatic insult, mitigating the no reflow phenomenon.[9] Red cell flexibility is doubled in about 15 treatments.[10] White cell killing of aerobic bacteria and some fungi is greatly enhanced at high oxygen pressures,[11] facilitating control of osteomyelitis[12] and reducing the number of operations and mortality in necrotising fasciitis.[13] Extremely important is its stimulation of new capillary and collagen formation in radiated tissue, normalising tissue oxygen tensions to permit surgery, healing, and even bone grafting.[14 15] Finally, it increases tissue levels of superoxide dismutase, which counters the formation of free radicals after injury, resulting in better tissue survival.[16] This is particularly important in crush injury, replants, and grafts, where free radical formation is responsible for reperfusion injury.[17] Although many doctors believe that good research on hyperbaric oxygen is rare, the converse is true.[18-22] Over 3800 papers have been published on the topic despite the relative scarcity of chambers. The Undersea Medical Society began investigating the claims being made for hyperbaric oxygen treatment in 1977. A committee (which I chaired) considered 64 different allegedly improved by treatment with hyperbaric oxygen. In most of them there was insufficient evidence to warrant its clinical use. In preparing our original report we consulted the largest private insurers in the United States, Blue Cross/Blue Shield, and the Federal Health Care Finances Administration. Since then the report has been continually updated. At present only 12 conditions are approved by the society for reimbursement.[23]

Since 1977 the number of clinical chambers in the United States has grown from 37 to nearly 300. For inclusion on the approved list there had to have been controlled studies or large clinical series indicating not only the efficacy but also the cost effectiveness of treatment with hyperbaric oxygen. In disorders for which prospective controlled trials were impossible or unavailable, evidence adduced for the efficacy of hyperbaric oxygen had to be at least as convincing as that used to support reimbursement of other treatments routinely paid for the insurers. The five major British centres for the most part limit treatment to those disorders on the approved list, despite there being no regulation to that effect. This list can serve only as a guide. Though quite useful in diabetic wounds, hyperbaric oxygen is only part of a programme of total wound care. For some diabetic wounds hyperbaric oxygen is inappropriate if the large vessels distal to the trifurcation at the knee are occluded or severely stenotic. Crush injury and impending compartment syndrome need to be treated immediately if any worthwhile result is to follow. Late referral, which gives time for oedema, reperfusion, and injury; free radical damage; and the no reflow phenomenon to do their work, makes the treatment largely a waster of time and money. For some surgical patients the potential dangers of further trauma to the wound during transportation will militate against the use of hyperbaric oxygen. Experience has shown, however, that patients with severe carbon monoxide poisoning can be transported safely over long distances in a properly equipped ambulance or helicopter. Before transfer a critically ill patient is contemplated it should be ascertained that the receiving chamber facility can deliver the necessary level of intensive care. Whenever the use of hyperbaric oxygen is considered, consultation with the physician in charge of the hyperbaric oxygen facility is mandatory to ensure that referral is appropriate. The timing of hyperbaric oxygen in relation to surgery is also critically important. For example, in necrotising fasciitis, surgery is the accepted primary treatment, with hyperbaric oxygen used as a follow up. With gas gangrene, however, the hyperbaric chamber is used before surgery (other than for fasciotomy). In the treatment of radionecrosis the patient should be treated at least 20 to 30 times in the chamber, to induce the formation of new capillaries, before elective surgery is performed if healing is to be expected.

## NOTES

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# Reactive oxygen species in living systems: source, biochemistry, and role in human disease.

by Barry Halliwell

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## Author's Abstract

Reactive oxygen species are constantly formed in the human body and removed by antioxidant defenses. An antioxidant is a substance that, when present at low concentrations compared to that of an oxidizable substrate, significantly delays or prevents oxidation of that substrate. Antioxidants can act by scavenging biologically important reactive oxygen species ( $O_2$ ,  $H_2O_2$ , OH, HOCl, ferryl, peroxy, and alkoxy), by preventing their formation, or by repairing the damage that they do. One problem with scavenging-type antioxidants is that secondary radicals derived from them can often themselves do biologic damage. These various principles will be illustrated by considering several thiol compounds.

Full Text It is difficult these days to open a medical journal and not find some paper on the role of "reactive oxygen species" or "free radicals" in human disease. These species have been implicated in over 50 diseases[1]. This large number suggests that radicals are not something esoteric, but that they participate as a fundamental component of tissue injury in most, if not all, human diseases. What are "free radicals" and "reactive oxygen species"? Do they cause disease? Are they produced in increased amounts as a result of disease and then contribute to further tissue injury? Are they merely an epiphenomenon of no relevance to clinical medicine? This introductory article attempts to answer such questions.

## WHAT IS A FREE RADICAL?

Electrons in atoms occupy regions of space known as orbitals. Each orbital can hold a maximum of two electrons, spinning in opposite directions. A free radical can be defined as any species capable of independent existence that contains one or more unpaired electrons, an unpaired electron being one that is alone in an orbital. Most biologic molecules are nonradicals, containing only paired electrons. An electron occupying an orbital by itself has two possible directions of spin. Indeed, the technique of measuring electron spin resonance detects radicals by measuring the energy changes that occur as unpaired electrons ~relax' following alignment in response to a magnetic field[2]. Since electrons are more stable when paired together in orbitals, radicals generally are more reactive than nonradicals, although there is a considerable variation in their reactivity. Radicals can react with other molecules in a number of ways[3]. If two radicals meet, they can combine their unpaired electrons (symbolized by \*) and join to form a covalent bond (a shared pair of electrons). The hydrogen atom, with one unpaired electron, is a radical and two atoms of hydrogen easily combine to form the diatomic hydrogen molecule:  $H^* + H^* \rightarrow [H_2]$  (1) Radicals react with nonradicals in several ways. A radical may donate its unpaired electron to a non-radical (a reducing radical) or it might take an electron from another molecule in order to form a pair (an oxidizing radical). A radical may also join onto a nonradical. Whichever of these three types of reaction occurs, the nonradical species becomes a radical. A feature of the reactions of free radicals with nonradicals is that they tend

to proceed as chain reactions, where one radical begets another. For many years, chemists have been interested in free radical reactions. Many plastics, such as polythene, arise by free radical chain polymerization[4]. Combustion is a free radical reaction. The drying and aging of paint also involves free radical reactions. Curators of museums have studied the role of free radical damage in the age-dependent deterioration of paintings and other items[5]. Metabolism of toxins in the human body can produce radicals. For example, carbon tetrachloride (CCl<sub>4</sub>) is metabolized in the endoplasmic reticulum of the liver to produce the damaging trichloromethyl radical, CCl<sub>3</sub> [3].

## HYDROXYL RADICAL

Chemists and biologists have examined in detail the role of free radical reactions in the damage done to living cells by high-energy radiation. When tissues are exposed to, for example, gamma radiation, most of the energy taken up is absorbed by the cell water, largely because there is more water there than any other molecule. The radiation causes one of the oxygen - hydrogen covalent bonds in water to split, leaving a single electron on hydrogen and one on oxygen, thus creating two radicals: [Mathematical Expression Omitted] H<sup>\*</sup> is a hydrogen radical (or hydrogen atom), and \*OH is a hydroxyl radical. The latter is the most reactive radical known to chemistry. It can attack and damage almost every molecule found in living cells at a diffusion-controlled rate, i.e., \*OH reacts as soon as it comes into contact with another molecule in solution. Since it is so reactive, \*OH generated in vivo does not persist for even a microsecond and rapidly combines with molecules in its immediate vicinity. Reactions of \*OH with biologic molecules, most of which are nonradicals, set off chain reactions[1]. Reactions of \*OH include its ability to interact with the purine and pyrimidine bases of DNA, leading to radicals that have a number of possible chemical fates[6]. \*OH can also abstract hydrogen atoms from many biologic molecules, including thiols: R - SH + \*OH

--->] RS<sup>\*</sup> + H<sub>2</sub>O (3) The resulting sulfur radicals (thiyl radicals) have many interesting chemical properties. They can combine with oxygen to generate oxysulfur radicals, such as RSO<sub>2</sub> and RSO<sup>\*</sup>, a number of which damage biologic molecules[7-9]. For example, sulfur-containing radicals derived from the drug penicillamine are able to attack and damage certain proteins[10]. When discussing the use of thiol compounds as free radical scavengers, it is essential to ask what may happen to the resulting sulfur radicals in biologic systems[11]. Perhaps the best-characterized biologic damage caused by \*OH is its ability to stimulate the free radical chain reaction known as lipid peroxidation. This occurs when the \*OH is generated close to membranes and attacks the fatty acid side chains of the membrane phospholipids. It preferentially attacks polyunsaturated fatty acid side chains, such as arachidonic acid. The .OH abstracts an atom of hydrogen from one of the carbon atoms in the side chain and combines with it to form water: CH<sup>-</sup> + \*OH ---> <sup>-</sup>C + H<sub>2</sub>O (4) Reaction (4) removes the \*OH, but leaves behind a carbon-centered radical ( - C - ) in the membrane. Carbon-centered radicals formed from polyunsaturated fatty acid side chains usually undergo molecular rearrangement to give conjugated diene structures, which can have various fates. Thus, if two such radicals collided in the membrane, cross-linking of fatty acid side chains could occur as the two electrons joined to form a covalent bond. Reaction with membrane proteins is also a possibility. However, under physiologic conditions, the most likely fate of carbon-centered radicals is to combine with oxygen, creating yet another radical, the peroxy radical (sometimes abbreviated to the peroxy radical): [Mathematical Expression Omitted] Peroxy radicals are reactive enough to attack adjacent fatty acid side chains, abstracting hydrogen: [Mathematical Expression Omitted] Another carbon-centered radical is generated, and so the chain reaction

[equations (5) and (6)] continues. One  $\cdot\text{OH}$  can result in the conversion of many hundred fatty acid side chains into lipid hydroperoxides. Accumulation of lipid hydroperoxides in a membrane disrupts its function and can cause it to collapse. Lipid hydroperoxides can also decompose to yield a range of highly cytotoxic products, among the most unpleasant of which are aldehydes[12]. A great deal of attention in the literature has been focused on malonaldehyde (malondialdehyde), but this is much less noxious than such products as 4-hydroxynonenal[12,13]. Peroxyl radicals and cytotoxic aldehydes can also cause severe damage to membrane proteins, inactivating receptors and membrane-bound enzymes[14].

## **SOURCES OF OXYGEN RADICALS IN VIVO**

Biochemists (apart from those with a special interest in "background" free radical generation in vivo, due to exposure to ionizing radiation) became interested in radicals only in the 1970s. This interest followed from the discovery in 1968 of superoxide dismutase (SOD), an enzyme specific for a free radical substrate[15]. SOD removes superoxide radical, a species that is formed by adding an extra electron onto the oxygen molecule: [Mathematical Expression Omitted] SOD removes  $\text{O}_2^-$  by catalyzing a dismutation reaction, involving oxidation of the  $\text{O}_2^-$  to oxygen and reduction of another  $\text{O}_2^-$  to hydrogen peroxide: [Mathematical Expression Omitted] In the absence of SOD, reaction (8) occurs nonezymically but at a rate approximately four orders of magnitude less at pH 7.4. The discovery of SOD led to the realization that  $\text{O}_2^-$  is formed in vivo in living organisms, and SOD removes it. Some of the  $\text{O}_2^-$  formed in vivo arises from a chemical accident. For example, when mitochondria are functioning, some of the electrons passing through the respiratory chain leak from the electron carriers and pass directly onto oxygen, reducing it to  $\text{O}_2^-$ [15,16]. Many molecules oxidize on contact with oxygen, e.g., and epinephrine solution left on the bench "goes off" and eventually forms a pink product. The first stage in this oxidation is transfer of an electron from the epinephrine to  $\text{O}_2$ , forming  $\text{O}_2^-$ . Such oxidations undoubtedly proceed in vivo as well[1]. For example, several sugars, including glucose, interact with proteins to produce oxygen radicals. It has been suggested that decades of exposure of body tissues to elevated blood glucose can result in diabetic patients suffering "oxidative stress" that may contribute to the side effects of hyperglycemia[17]. Glycation of proteins involves not only direct reaction with the sugar but also free radical reactions[17]. Thiols can also be oxidized in the presence of oxygen, generating sulfur-containing radicals as well as  $\text{O}_2^-$  and  $\cdot\text{OH}$ . Thiol oxidation is favored by alkaline pH values and by the presence of transition metal ions, especially copper ions[18]. Thus, mixtures of copper ions and thiols can be cytotoxic, as shown for cysteine[19]. Iron ions can also promote free radical generation from thiols under certain circumstances[20]. Attempts to use thiols as anti-oxidants in systems containing iron or copper ions may even result in stimulation of oxidative damage.

**Superoxide and Phagocyte Action** Some of the  $\text{O}_2^-$  production in vivo may be accidental but much is functional. Activated phagocytic cells generate  $\text{O}_2^-$  as shown for monocytes, neutrophils, eosinophils, and macrophages of all types[21]. Radical production is important in allowing phagocytes to kill some of the bacterial strains that they engulf. This can be illustrated by examining patients with chronic granulomatous disease, a series of inborn conditions in which the membrane-bound reduced nicotinamide adenine dinucleotide phosphate (NADPH) oxidase system in phagocytes that makes the  $\text{O}_2^-$  fails to work[21]. Such patients have phagocytes that engulf and process bacteria normally, but several bacterial strains are not killed and are released in viable form when the phagocytes die. Thus, patients suffer severe, persistent, and multiple infections with such organisms as *Staphylococcus aureus*. Another killing

mechanism used by neutrophils (but not by macrophages) is the enzyme myeloperoxidase[22]. It uses  $H_2O_2$  produced by dismutation of  $O_2$  to oxidize chloride ions into hypochlorous acid (HOCl), a powerful anti-bacterial agent:  $H_2O_2 + Cl^- \rightarrow HOCl + OH^-$ . Thiol groups are easily oxidized by HOCl. Hence, low molecular mass thiol compounds such as glutathione (GSH), N-acetylcysteine, and mercaptopropionylglycine are very effective at protecting, for example, proteins against oxidative damage by HOCl[23.24]. Superoxide formed in vivo, whether functionally or accidentally, is disposed of by SOD [equation (8)]. Recent studies using genetic engineering techniques to manipulate SOD levels of organisms, or to delete the genes encoding SOD, provide further evidence of the importance of SOD[25]. It is interesting to note that no complete inborn deficiencies of SOD have been reported in humans, perhaps because they would be lethal mutations.

Reactive Oxygen Species SOD removes  $O_2^-$  by converting it into hydrogen peroxide ( $H_2O_2$ ) and  $O_2$  [equation (8)].  $H_2O_2$  itself can be quite toxic to cells. For example, incubation of cells with  $H_2O_2$  causes deoxyribonucleic acid (DNA) damage, membrane disruption, and release of  $Ca^{2+}$  ions within the cells, leading to activation of  $Ca^{2+}$ -dependent proteases

and nucleases[26]. At least some of this damage may be mediated by a reaction of  $H_2O_2$  with  $O_2$  in the presence of iron or copper ions, to form highly reactive radicals, one of which  $\cdot OH$ . This reaction proceeds in a number of stages, but the overall process is summarized by [Mathematical Expression Omitted] Thus, removal of  $H_2O_2$ , as well as of  $O_2^-$ , is biologically advantageous[27]. SOD therefore works in conjunction with two enzymes, catalase and glutathione peroxidase[27], that remove  $H_2O_2$  in human cells. The study of inborn errors of metabolism suggests that glutathione peroxidase (GSH-Px) is the more important of the two in removing  $H_2O_2$ , probably because it is located in the same subcellular compartments (cytosol and mitochondria) as SOD. GSH-Px has the distinction of being the only human enzyme known requiring the element selenium for its activity; a selenocysteine residue (side chain  $-SeH$  instead of  $-SH$ , as in normal cysteine) is present at its active site. However, it is unlikely that the sole function of selenium in humans is to act as a cofactor for GSH-Px[28]. GSH-Px removes  $[H.sub.2.O.sub.2]$  by using it to oxidize reduced glutathione (GSH) into oxidized glutathione (GSSG):  $2GSH + H_2O_2 \rightarrow GSSG + 2 H_2O$ .  $H_2O_2$  has no

unpaired electrons and does not qualify as a radical. Hence, the term reactive oxygen species has been introduced to describe collectively not only  $O_2^-$  and  $\cdot OH$  (radicals) but also

$H_2O_2$  (nonradical). Hypochlorous acid (HOCl) produced by myeloperoxidase is also a nonradical, having no unpaired electrons.  $H_2O_2$ ,  $\cdot OH$ , and HOCl are sometimes collectively called "oxidants." This is valid description of  $H_2O_2$ ,  $\cdot OH$ , and HOCl, which are oxidizing agents. However,  $O_2$  has both oxidizing and reducing properties. The latter property is used in a popular assay for  $O_2^-$  production by phagocytes:  $cyt\ c\ (Fe^{3+}) + O_2^- \rightarrow O_2 + cyt\ c\ (Fe^{2+})$

## TRANSITIONS METAL IONS AND FREE RADICAL REACTIONS

Many transition metals have variable oxidation numbers, e.g., iron has  $Fe^{2+}$  and  $[Fe^{3+}$  ions and copper has  $Cu^+$  and  $Cu^{2+}$  ions. Changing between oxidation states involves accepting and donating single electrons, e.g., [Mathematical Expression Omitted] Transition metal ions are remarkably good promoters of free radical reactions[29]. Polymer scientists and food chemists have been aware of this for years[4,30], and biochemists are learning it too [1,17-20,26,31-34]. It has already been noted that copper ions promote oxidation of thiols:  $R-SH + Cu^{2+} \rightarrow R-S\cdot + Cu^+ + H^+$  and that  $Fe^{2+}$  ions reduce  $H_2O_2$  to give  $\cdot OH$  [equation (10)].

Transition Metals and Lipid Peroxidation Transition metal ions are involved in lipid

peroxidation in two ways. They can participate in first-chain initiation, which involves attack by any species capable of abstracting a hydrogen atom.  $\cdot\text{OH}$ , which has this property, is produced by the reaction of  $\text{O}_2$  and  $\text{H}_2\text{O}_2$  with iron ion catalysis [equation (10)]. It is also produced by reaction of  $\text{H}_2\text{O}_2$  with copper ions, probably in addition to oxidizing copper(III)-oxygen complexes[26,31]. Several iron ion-oxygen complexes, such as perferryl, ferryl, or  $\text{Fe}^{2+} / \text{Fe}^{3+} / \text{O}_2$  complexes, have also been claimed to initiate peroxidation[32], although their ability to do so is uncertain[33,34]. Transition metal ions also affect lipid peroxidation by decomposing peroxides. Commercial fatty acids are heavily contaminated with peroxides[34]. Cell disruption to isolate membrane fractions increases rates of nonenzymic free radical reactions and activates enzymes (cyclooxygenases and lipoxygenases) that produce peroxides (Figure 1). When transition metal ions are added to lipid systems already containing peroxides, their main action is to decompose these peroxides into peroxy and alkoxy (lipid-O) radicals that in turn abstract hydrogen and perpetuate the chain reaction of lipid peroxidation[34]. This may be represented by the following simplified equations, in which lipid symbolises a carbon-centered radical [Mathematical Expression Omitted]  $\text{lipid O} \cdot + \text{lipid-H} \rightarrow \text{lipid-OH} + \text{lipid} \cdot$ . (18)  $\text{lipid-OO} \cdot + \text{lipid-H} \rightarrow \text{lipid-OOH} + \text{lipid} \cdot$ . (19)  $\text{lipid} \cdot + \text{O}_2 \rightarrow \text{lipid-OO} \cdot$ . (20) Reducing agents, such as ascorbic acid or  $\text{O}^{2-}$ , accelerate these metal ion-dependent peroxidation reactions because  $\text{Cu}^+$  and  $\text{Fe}^{2+}$  ions seem to react with peroxides faster than do  $\text{Cu}^{2+}$  and  $\text{Fe}^{3+}$  respectively. The end products of these complex metal ion-catalyzed breakdowns of lipid hydroperoxides include the cytotoxic aldehydes mentioned previously (malonaldehyde, 4-hydroxynonenal), as well as hydrocarbon gases such as ethane and pentane[1]. Some thiol compounds can also reduce metal ions and accelerate peroxidation of lipids, e.g., cysteine[35]. It has been suggested that some thiol radicals ( $\text{RS} \cdot$ ) initiate peroxidation by abstracting hydrogen atoms from lipids [36]. Different thiols behave differently in peroxidizing lipid systems, presumably depending on their metal ion-reducing ability and the reactivity of their thiol radicals.

## ANTIOXIDANT DEFENSE

Organisms use superoxide dismutases, catalase, and glutathione peroxidase as protection against generation of reactive oxygen species. Organisms also keep as many iron and copper ions as possible safely bound in storage or transport proteins[37-39]. There is three times as much transferrin iron-binding capacity in plasma as iron needing to be transported, so that there are essentially no free iron ions in the plasma[38]. Iron ions bound to transferrin cannot stimulate lipid peroxidation or formation of free  $\cdot\text{OH}$  radicals. The same is true of copper ions bound to the plasma proteins ceruloplasmin or albumin[37-40]. The value of this sequestration is shown by an inspection of the pathology suffered by patients with iron-overload disease, in whom iron ion-citrate chelates circulate in the blood[40]. These patients can suffer liver damage, diabetes, joint inflammation, and hepatoma, among other problems[41]. Metal ion sequestration is an important antioxidant defense. For example, recent papers have referred to ascorbic acid as a major antioxidant in plasma. However, ascorbate can only exert antioxidant properties in the absence of transition metal ions[11].

## Tocopherol

As well as the primary defenses (scavenger enzymes and metal-ion sequestration), secondary defenses are also present. The cell membranes and plasma lipoproteins contain  $\alpha$ -tocopherol, a lipidsoluble molecule that functions as a chain-breaking antioxidant. Attached to the hydrophobic structure of  $\alpha$ -tocopherol is an -OH group whose hydrogen

atom is easily removed. Hence, peroxy and alkoxy radicals generated during lipid peroxidation preferentially combine with the antioxidant, e.g., [Mathematical Expression Omitted] instead of with an adjacent fatty acid side chain. This therefore terminates the chain reaction, whence the term chain-breaking antioxidant. It also converts the [alpha]-tocopherol into a new radical, tocopherol-O., which is poorly reactive and unable to attack adjacent fatty acid side chains, consequently stopping the chain reaction. Evidence exists[43,44] that the tocopherol radical can migrate to the membrane surface and revert to [alpha]-tocopherol by reaction with ascorbic acid (vitamin C). Both vitamin C and [alpha]-tocopherol seem to minimize the consequences of lipid peroxidation in lipoproteins and in membranes, should this process begin. Some thiol compounds, such as GSH, might also be involved in regenerating [alpha]-tocopherol from its radical in vivo[44]. The terms "[alpha]-tocopherol" and "vitamin E" are often used synonymously, which is not strictly correct. Vitamin E is defined nutritionally as a factor needed in the diet of pregnant female rats to prevent resorption of the fetus[45] and compounds other than [alpha]-tocopherol (e.g., [beta-, gamma-, and delta-tocopherols) have some effect in this assay. However, [alpha]-tocopherol is the most effective, and it seems to be the most important lipid-soluble chainbreaking antioxidant in vivo in humans[46]. The content of [alpha]-tocopherol in circulating low-density lipoproteins helps to determine their resistance to lipid peroxidation and thus may affect the development of atherosclerosis, a disease in which lipid peroxidation is involved[47]. Low plasma levels of [alpha]-tocopherol and vitamin C correlate with an increased incidence of myocardial infarction and of some forms of cancer[47].

**Other Antioxidants and Repair Systems** Some other compounds may also function as antioxidants in vivo, such as uric acid, ubiquinol, and bilirubin (reviewed in[11]). Antioxidant defenses are not quite perfect. Cells contain systems that can repair DNA after attack by radicals[48], degrade proteins damaged by radicals[49], and metabolize lipid hydroperoxides[1].

## **WHAT CAN WE EXPECT FROM ANTIOXIDANTS IN THE THERAPY OF HUMAN DISEASE? What Is an Antioxidant?**

"Antioxidant" can be defined in various ways. Often, the term is implicitly restricted to chainbreaking antioxidant inhibitors of lipid peroxidation, such as vitamin E. However, the author prefers a broader definition - an antioxidant is any substance that, when present at low concentrations compared with those of an oxidizable substrate, significantly delays or prevents oxidation of that substrate[1]. The term "oxidizable substrate" includes almost everything found in living cells, including proteins, lipids, carbohydrates, and DNA. Antioxidants act in many different ways (Table I). In proposing antioxidants for use in human disease, it is important to note the following: (a) the precise role played in the disease pathology by reactive oxygen species; and (b) the molecular targets of oxidative damage that need protecting. Thus, oxidative stress can damage a multiplicity of targets in living cells and the initial damage to one target can then affect others[26]. Figure 2 attempts to illustrate some of the complex interacting mechanisms by which excess production of reactive oxygen species can produce cell damage. If, for example, the primary event in damage to DNA, then an inhibitor of lipid peroxidation might offer little or no protection.

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### **Table 1 Questions to Ask When Evaluating the Proposed Role of an "Antioxidant" In Vivo**

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1. What biomolecule is the compound supposed to protect? An inhibitor of lipid peroxidation

is unlikely to be useful if the oxidative damage is mediated by an attack on proteins or DNA.

2. Is the compound present in vivo at or near that biomolecule at sufficient concentration? For example, many compounds have been suggested to act as  $\cdot\text{OH}$  scavengers in vivo. In order to compete with biologic molecules for  $\cdot\text{OH}$ , a scavenger must be present in at least millimolar concentrations in vivo. Most drugs never achieve this sort of concentration.
  3. How does it protect: by scavenging reactive oxygen species, by preventing their formation, or by repairing damage?
  4. For naturally occurring antioxidants, is antioxidant protection the primary biologic role of the molecule or a secondary one? For example, SOD has probably evolved as an antioxidant enzyme. By contrast, transferrin has probably evolved as an iron transport protein, although the binding of iron ions to transferrin prevents them from accelerating radical reactions, giving this protein an important secondary role in extracellular antioxidant defense.
  5. If the antioxidant acts by scavenging a reactive oxygen species, can the antioxidant-derived radicals themselves do biologic damage?
  6. Can the antioxidant cause damage in biologic systems different from those in which it exerts protection?
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### **Free Radicals and Human Disease: Causation or Consequence?**

Does increased formation of free radicals and other reactive oxygen species cause any human disease? Radiation-induced carcinogenesis be initiated by free radical damage[48]. The signs produced by chronic dietary deficiencies of selenium (Keshan disease) or of vitamin E (neurologic disorders seen in patients with inborn errors in the mechanism of intestinal fat absorption) could also be mediated by reactive oxygen species[28,50]. In the premature infant, exposure of the incompletely vascularized retina to elevated concentrations of oxygen can lead to retinopathy of prematurity, which in its most severe forms can result in blindness. Several controlled clinical trials have documented the efficiency of  $[\alpha]$ -tocopherol in minimizing the retinopathy[51], suggesting a role for lipid per-oxidation. For most human diseases, increased formation of reactive oxygen species is secondary to the primary disease process. For example, activated neutrophils produce  $[\text{O}_2^-]$ , and HOCl in order to kill bacteria. If a large number of phagocytes become activated in a localized area, they can produce tissue damage. The synovial fluid in the swollen knee joints of rheumatoid patients swarm with activated neutrophils. There is evidence that reactive oxygen species and other products derived from neutrophils contribute to the joint injury. Whether this is a major or a minor contribution to joint damage remains to be established[52]. In some forms of adult respiratory distress syndrome (ARDS), lung damage seems to be mediated by an influx of neutrophils into the lung, where they become activated to produce prostaglandins, leukotrienes, proteolytic enzymes such as elastase, and reactive oxygen species[53]. Among other effects, reactive oxygen species inactivate proteins (such as  $[\alpha 1]$ -antiproteinase) within the lung that normally inhibit the action of elastase and prevent it from attacking lung elastic fibers. The precise contribution of oxidative damage to lung injury in ARDS is unknown, but deserves investigation in view of the high mortality rate. In both ARDS and in rheumatoid arthritis, increased generation of reactive oxygen species is secondary to the processes that cause neutrophil infiltration, but they then may make an additional detrimental contribution to tissue injury. There are several examples in which injury, by a nonradical mechanism, leads to increased free radical reactions. Mechanical (e.g., crushing) or chemical injury to tissues can



cause cells to rupture and release their contents, including transition metal ions (Figure 1), into the surrounding area. Administration of cytotoxic drugs to patients with acute myeloid leukemia has been shown to create a temporary "iron-overload" state, probably due to extensive drug-induced lysis of the leukemic cells. This increased iron availability could contribute to the side effects of cytotoxic chemotherapy[54]. Perhaps the greatest interest in this area lies in the sequelae of traumatic or ischemic injury to the brain. Some Areas of the human brain are rich in iron. Cerebrospinal fluid has no significant ironbinding capacity, since its content of transferrin is low. It has been proposed[55] that injury to the brain by mechanical means (trauma) or by oxygen deprivation (stroke) can result in release of iron ions into the surrounding area. These ions facilitate further damage to the surrounding areas by accelerating free radical reactions. This proposal has been given some support from animal studies, using antioxidants such as chelating agents that bind iron ions and prevent from catalyzing radical reactions. Promising results have been obtained with amino-steroid-based antioxidants. Thus, one such "lazaroid," U74006F, has been observed to decrease the effects of reperfusion injury upon the brain of cats[56] to decrease post-traumatic spinal cord degeneration in cats[57] and to minimize neurologic damage after head injury in mice[58].

### **Free Radicals in Human Disease: A Triviality?**

Tissue destruction and degeneration can result in increased oxidative damage, by such processes as metal-ion release, phagocyte activation, lipoxygenase activation, and disruption of mitochondrial electron transport chains, so that more electrons "escape" to oxygen to form  $[O_2^-]$  (Figure 1). It follows that almost any disease is likely to be accompanied by increased formation of reactive oxygen species. It is not therefore surprising that the list of diseases in which their formation has been implicated is long and is growing longer[1]. For atherosclerosis[43,59], rheumatoid arthritis[52], some forms of ARDS, reoxygenation injury[60,61], and traumatic or ischemic damage to the central nervous system, there is reasonable evidence to suggest that free radical reactions make a significant detrimental contribution to the pathologic process. As previously stressed[62], it is equally likely that in some (perhaps most) diseases, the increased ROS formation is an epiphenomenon, making no significant contribution to the progression of the disease. Each proposal must be subject to stringent examination, because the likely clinical value of "antioxidant therapy" will depend on how well the exact role of reactive oxygen species is known.

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# Ozone Applications: An In-Depth Discussion

by Brad Hunter

Health Freedom News

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Ozone is a form of oxygen that contains three atoms ( $O_3$ ) compared to the standard two ( $O_2$ ) in an oxygen molecule. Ozone as a gas is blue; both liquid (-111.9C) and solid ozone (-193C) are an opaque blue-black colour. At altitudes from 60-90,000 ft., ozone occurs naturally as a gas in concentrations of 10-20 parts per million (ppm). In these concentrations ozone is a powerful absorber of high frequency light radiation and it stops most of the Sun's ultra-violet rays. At ground level it exists in a greatly diluted state and is always present in minute quantities (.001-.003 ppm) as we breathe it. The human threshold for its unique pungent scent is .001 ppm; below that amount you can't even smell it. It does not become an irritant until levels of .1 ppm are exceeded for an eight hour exposure, and below those levels there have never been any permanent side effects from inhaling it.

Ozone occurs naturally around crashing surf, white water rapids, and lightning storms. At ground level there is more oxygen than ozone, and as we rise up in our atmosphere the oxygen decreases and the ozone increases - hence, the beautiful blue sky we enjoy when we gaze up from planet Earth. It is the ozone that makes it blue.

So why, you may ask, is there a negative twist on ozone and air pollution? In order to measure hydrocarbon air pollution, an index is required. High levels of hydrocarbons have a corresponding ozone level measured in hundredths of a ppm, so by measuring the ozone, we know how bad the pollution is. The TV weather reporter doesn't tell you that ozone as a molecule only last 20 minutes maximum at ground level where it is busy cleaning up that pollution. Carbon monoxide (hemoglobin has a greater affinity for it than for oxygen), when contacted by ozone, is changed to carbon dioxide and oxygen. Benzene, chlorides, sulfur and 40 other compounds are also oxidized by ozone contact.

Charts are available that show safe non-symptomatic and symptomatic irritant exposure levels for humans, so yes, there are dangers with high levels of ozone (too much of anything can be dangerous) but that is not to say that ozone is dangerous per se.

Ozone has long been internationally recognized as the most powerful oxidant known to chemical science. Well known as an industrial oxidizer and sterilant, it has uses in over 30 different industries. Existing applications include: production of chemicals, synthetic fibers, jet lubricants, and pharmaceuticals; clean rooms for manufacturing computer chips, circuit boards, and bio-medical products; treatment of industrial liquid wastes such as cyanides and phenols; water treatment, performing as a bactericide, viricide, and flocculant, used to handle organically dissolved metals, odor and taste producing hydrocarbons, sewage effluent, aqua culture and fish farms, and sanitizing both fresh and salt water aquariums such as Seaworld at Orlando, FL; food preservation uses such as fruit, vegetable, egg, cheese, and meat storage, cold storage and plant preservation; sterilization of containers for aseptic packaging; deodorization of gases and exhausts from industrial processes; replacing chlorine for bleaching woodpulp for paper; mining extraction of metals and minerals; and sanitation in water, soft drinks, and beer bottling plants.

Ozone's most well known use is in water treatment as a primary stage disinfectant because of its bactericidal and viricidal efficacy. EPA and FDA acknowledge ozone's ability to kill

99.9992% of all pathogenic life in water. Although accepted for use in European health clinics for 25 years or so, health applications of ozone remain controversial in the United States.

There are, at present, three technologies utilized for the generation of ozone; ultra-violet light, cold plasma, and cold corona arc. Ultra-violet light in the 180-90 nanometer frequency generates ozone from ambient air without producing nitrous oxide compounds. UV cannot generate the high levels that are required for industrial or health applications even with oxygen feed; it cannot generate more than 1-3 micrograms of ozone per milliliter of oxygen. Cold plasma is a lost engineering technique of inert rarefied gas mixtures in a vacuum tube with no filament. To my knowledge, three companies are working with it now. This is where the future lies, this same technology that was utilized in the Teslaire medical machines of the 1920's and '30's. Cold corona arc is the most maligned of the technologies, yet it generates the serious ozone needed for industrial and health applications and is useful for general air purification. When engineered properly, ambient air feed cold corona arc produces no appreciable increase in nitrous oxides. Cold corona remains the most cost effective means by which medical and industrial concentrations are achieved.

Different uses of ozone require different concentrations to obtain desired results. For instance, ultra-violet-light generated ozone is adequate for hot tub and pool disinfection, but large pools, water parks, and municipal water treatment require cold corona ozone to generate serious ozone.

All studies on benefits of ozone in health sciences utilize and oxygen tank and regulator for productions of an ozone/oxygen mixture. The oxygen feed rate from the tank is measured in micrograms of ozone per milliliter of oxygen, noted as mog/ml or ug/L. The protocols and specific doses have been established by over 40 years of documented uses in Germany.

In order to achieve a desired result with ozone, one must work within the range (ug/L) specified and proven by use on 10 million German patients over those 40 years. Use too little ozone and it will not work, or too much and it has a detrimental effect. The required concentrations and quantities have all been established and published. If someone tells you that you will get over an illness by bag aeration with an air feed UV ozone system, you had better turn and walk away.

As it is in all engineering, math tells us that specific results require specific amounts to attain specified effects. Ask questions, be an informed buyer!

Note: The FDA has not approved any ozone device for medical use within the United States, yet they were in existence prior to the FDA. Same or like devices were grandfathered in and are used by N.D.'s. Seek the advise of knowledgeable health professionals.

(Brad Hunter is a licensed engineer and a member of the International Ozone Association)

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# Physicochemical and Pharmacological Aspects of Ozone Therapy

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Paper presented at the Sixth World Ozone Conference, May 22~~5~~, 1983 in Washington D.C.

Numerous wrong ways have been followed up, before a scientifically substantiated medical ozone therapy gained the appreciation that it now has in many countries.

It may be surprising to learn that ozone has already been mentioned during the Greek antiquity by Homer who referred to it in his famous Odyssey.

In 1783, VAN MARUM realised a strange odor when experimenting with a big electrostatic machine. He observed that upon leading electric sparks through oxygen a gaseous substance developed which reacted to mercury.

In 1840, SCHONBEIN submitted a paper to the Munich Academy which stated that the oxygen freed in the electrolytic disintegration of water was accompanied by a strange smelling substance.

In 1853, ANDREWS declared to the Royal Society in London that ozone is not a compounded substance, but an altered or allotropic condition of oxygen.

It still took many more years before some doctors tried to make use of ozone for medical purposes.

First, let us take a look at the natural occurrence of ozone.

Since quite some time, in news releases, the term "ozone" shows up in connection with a certain layer of our atmosphere called "ozonosphere". It is part of the stratosphere and surrounds the earth in an altitude of approx. 12 miles. It develops from oxygen under the influence of high energy ultraviolet radiation from the sun.

To mankind, this ozonosphere is an essential shield against the solar radiation and thus plays an important part in maintaining the biological balance on our planet. Due to increasing air and soil pollution this shield is, nowadays, menaced by destruction. Diminishing its ozone concentration, however, would cause a higher translucence for UV-B radiation, and consequently an increase of - partly malignant - skin diseases with man. As based on several studies, it is to be expected that a decrease ozone concentration of the ozonosphere of only 1% would lead to a higher frequency of skin diseases among the white population.

In the lab, ozone can be produced by silent electric discharges or spark-overs through air or pure oxygen. Therefore, it may be perceived by its odor during heavy thunderstorms as well as upon operation of electrostatic machines or UV lamps. It also develops under the influence of cathode rays, canal rays, and radioactive emissions.

In mere chemical reactions ozone is produced from peroxides, permanganates, or persulfates upon addition of strong sulfuric acid. The oxidation of phosphorus also leads to the formation of ozone.

Ozone can be smelled in such low concentrations as .05 ppm in air. The feature led to its name which has been derived from the Greek word "ozein", i.e. to smell.

Since SCHONBEIN discovered the ozone in 1840, it was still very complicated to produce

sufficient quantities for further experimental studies.

When, however, WERNER v. SIEMENS the founder of German electrical engineering, developed a discharge tube which was henceforth named after him, it became possible to produce larger ozone quantities in a rather convenient way. Thus, scientists were enabled to study the qualities of this substance, more thoroughly.

Below its boiling point, ozone is a dark-blue liquid which upon further refrigeration to below its freezing point solidifies to form a black crystalline mass. Pure ozone is highly explosive when brought into contact with any oxidizable organic matter at high ozone concentration.

	Oxygen	Ozone	Air
<b>Molecular Weight</b>	32	48	
<b>Density (air = 1)</b>	1.658		
<b>Density (water = 1)</b>	0.002		
<b>Weight of 1 litre</b>	1.429 g	2.114 g	
<b>Boiling point</b>	-182.96 C	-111.9C	-194.4C
<b>Freezing point</b>	-218.4C	-192.7C	

Decisive findings as to the chemical reactions of ozone to organic compounds have been reported by CRIEGEE in 1953 and RIECHE in 1958. Besides the mere oxidizing reactions, the most important feature of ozone is its interaction with unsaturated organic compounds. This process is called 'ozonolysis'.

The reactivity of ozone to organic matter is due to the polarized molecular structure which indicates the likeliness of ionic process.

[Chemical equation omitted]

As may be seen from the graphic formula, the molecule is rather stabilized by mesomerism. This explains its special affinity towards other polarized substances, while saturated hydrocarbons and aromatic ring systems hardly react at all.

The ozonolysis means addition of ozone to double bonds in unsaturated molecular structures. The first step is a 1,3 - dipolarized addition causing the formation of a primary ozonide. This latter, however, is relatively unstable, thus evading any analytical identification.

[Chemical equation omitted]

The primary ozonide disintegrates by opening the double bond and forming carbonyl compounds as well as peroxidic dipolar ions. The existence of the latter must be assumed because of a variety of secondary reactions.

[Chemical equation omitted]

The peroxidic polar ion which may be termed carbonyl oxide is to some extent stabilized by mesomerism as may be shown by two limiting configurations. Despite of its short life span, it is the keystone in all secondary reaction mechanisms.

[Chemical equation omitted]

In 1960, STAUDINGER succeeded in the spectroscopic identification of a primary ozonide of trans-di-tertiary butylethylene, as this compound is stable up to -60 C because of the steric impediment due to the tertiary butyl groups.

[Chemical equation omitted]

Most of the primary ozonides disintegrate spontaneously, due to the high energetic -O-O-O-bond. They form isomeric compounds with a molecular structure shown below.

[Chemical equation omitted]



It is most important to mention that this disintegration does not lead to the formation of any radicals as usually observed with peroxides. Based on several investigations an ionic type of reaction must be assumed.

The reason why I emphasize this fact, is that according to recent findings in the research of rheumatism aggressive toxic superoxide radicals are produced in inflamed tissues. Primarily, these are part of a vital defence process. They are formed in activated phagocyte membranes and kill bacteria. As helpful as this process may be, in the first place, it can lead to an ominous autoaggressive chain reaction in the course of which even phagocytes themselves are destroyed. Within the cells an enzyme system of so-called superoxide dismutases controls the activity of toxic superoxide radicals. The activity of these enzymes, however, does not cover the interstitium. Superoxide radicals depolymerize hyaluronic acid which is part of the synovial liquid. Hence, friction in joints will increase and slide faces are destroyed, in due course. In this connection, it is essential to know that in the course of ozonolysis no such superoxide radicals occur.

Temporarily, it was assumed that the disintegration of ozone in water involved the formation of radicals in the same way as it had been observed upon the influence of gamma or X radiation on blood or water.

According to V. ROTHMUND in 1913 and E. ABEL in 1955, however, no such intermediates could be identified. So far, the disintegration mechanism of the system O<sub>3</sub>/H<sub>2</sub>O has not been satisfactorily revealed.

What we know exactly is the half-life of ozone in water of different purity. Naturally, the different impurities have their effects on the reaction velocity. Alkaline pH values, too, speed-up the disintegration, whereas ozone is relatively stable in strong acidic aqueous media. Of some therapeutical relevance is the disintegration of ozone in its gaseous state. Two different reaction mechanisms have to be differentiated:

1. The autocatalysis. In this case the half-life is about 3 days.

2. The heterocatalysis which strongly depends on temperature.  
It follows the equation

$$c_t = c_o \times e^{-kt} \quad c_o = \text{initial concentration}$$

$c_o$  = initial concentration       $c_t$  = conc. at time t (sec<sup>-1</sup>)

k = disintegration constant (sec<sup>-1</sup>)

The disintegration constant depends on temperature as shown by the equation

$$\log k = \log H - \frac{E}{4,575 T} \quad \begin{array}{l} E = \text{activating energy} \\ H = \text{frequency factor} \\ t = \text{abs. temperature (K)} \end{array}$$

The knowledge of the catalyzed disintegration is always then important when ozone is to be transported in glass syringes or kept in plastic bags for external ozone gas treatment.

The basic question concerning any therapeutical application of ozone is what happens if this

highly reactive agent gets into contact with blood.

The sequence of ozone reactions to the different blood constituents may be deduced from model experiments in the lab. These showed that unsaturated fatty acids most quickly form ozone adducts resulting in the formation of ozonides. Due to the instability of these compounds the double bond will readily be broken up and only a peroxide link will remain in the molecule. This peroxide link may be further disintegrated by hydrolysis or similar processes, as may be understood from the formation of an oleic acid acetalperoxide.

[Chemical equation omitted]

By any of these reaction mechanisms the long chain molecule will be divided into half length parts which can be more quickly metabolized.

Further, the peroxide link in ozonized oleic acid contains a certain amount of linkage energy which upon disintegration will be set free and may serve as activating energy for other metabolic processes. Such activating effects on metabolism have been experimentally proved by ALBERS in 1958.

Multiple unsaturated fatty acids are even more reactive to ozone, especially if they contain conjugated double bonds.

In order to study the behaviour of unsaturated blood constituents, the oxidation of linseed oil by oxygen was investigated, using human blood or plasma as catalyst.

During the first 2-3 hours no oxygen susception was observed. Neither untreated human blood nor plasma induced any oxidation. Even preozonized plasma failed. The latter, however, showed a significant oxidizing power when hemolyzed erythrocytes were added. In this case the hemoglobin iron acted as catalyst. The reaction velocity was considerably accelerated when preozonized red blood cells were used. Under these conditions a linear curve resulted with nearly no latency time.

These results clearly prove the catalytic effect of ozonized or hemolyzed erythrocytes. They further prove that in any case the iron containing hemoglobin is essential to trigger the effect of ozone produced peroxides no matter whether they were formed in blood plasma or in erythrocyte cytoplasm.

Unsaturated fatty acids which can react to ozone are only contained in blood plasma or in the cytoplasm of red blood cells. So, it might have been expected that pure crystalline hemoglobin is not in any way activated by ozone treatment. In fact, only a slight alteration could be observed in spectrophotometric comparison.

Above all, the double valent iron in the hemoglobin molecule is not oxidized to the triple valent form. It may be taken for granted that neither in native blood nor in intact red blood cells the hemoglobin is inactivated by ozone. We must assume, however, that there exist certain affinities between ozone produced peroxides and hemoglobin or oxyhemoglobin, respectively, dependent on some adsorptive linkage. The so produced adducts may lead to the formation of active intermediates.

Other investigations on linseed oil indicated that blood plasma contains certain oxidation inhibitors which must be eliminated before the normal oxidation process can start. These inhibitors cause a certain period of latency before any therapeutical effect will be recognizable.

Several observations indicate that ozone produced peroxides may have electron configurations different from those formed of normal oxygen. This different configuration may be due to certain double bond shiftings within the molecule. Anyway, it must be assumed that these so-called 'ozone peroxides' have certain catalytic activities besides their direct oxidizing effect.

The next group of blood components which are attacked by ozone are the free amino acids. The amino group is very readily oxidized. This has especially been investigated on tryptophane.

This compound belongs to the 8 amino acids which are essential for the human organism. It is the base material for the synthesis of nicotinic acidamide, Vitamin B6, and of NAD, NADH, NADP. It also plays an important part in the formation of DNS, the genetic material.

The oxidation products of tryptophane are rather complex and have not yet been clearly identified.

Similar experiments with methionine, a sulfur containing essential amino acid, showed that the oxidation always leads to methionine sulfoxide. Methionine is an important methyl group donor, and it was found that the methyl group is activated by ozonation.

In mixtures with NADH the oxidation starts on this compound, first. Only if the NADH has been consumed, the oxidation of tryptophane and methionine follows.

Next in the sequence of oxidation processes are amino acids in peptide-linkages. Out of this group, glutathion which belongs to the biological redox systems, has been tested. Its sulfur group is very readily oxidized by ozone. This reaction is to be understood as a withdrawal of electrons which is reversible. The presence of glutathion impedes the oxidation of NADH.

[Chemical equation omitted]

Another important group of blood constituents which have been tested are the nicotinic acidamide coenzymes. Experiments have been performed on 1,4-dihydro-1-methyl-nicotinamide (DMN). The following course of reaction was found by MUDD at the department of biochemistry of the University of California, in the early seventies.

[Chemical equation omitted]

Results obtained by CORNFORTH et. al. in England showed two possible products of ozonolysis:

[Chemical equation omitted]

Nicotinic acidamide coenzymes play an important part in the breathing chain, the citric acid cycle, and in  $\beta$ -oxidation of fatty acids. It was found that ozone causes better electron susceptibility in all breathing enzymes.

Several other compounds which are normally contained in native human blood were investigated as to their reactions to ozone.

All these quantitative determinations showed that the effects of ozone primarily depend upon concentration, rather than on the total amount. The following table shows the influence of different ozone concentrations in comparison with a pure oxygen treatment. It is significant that the total protein level is practically not affected, whereas uric acid is almost completely eliminated.

A decrease of cholesterol has been reported by WENNING, in 1956.

In 1977, WASHUTTL observed a 20 to 30% decrease of the initial vitamin levels in blood under the influence of ozone. This fact indicates the necessity to give the patient an appropriate amount of vitamins during ozone therapy.

Considering the results of these investigations as a whole, it can be said that ozone reacts selectively to blood constituents, and not at all unspecifically as might be expected of an oxidizing agent of such high activity. The reason is its polarized structure and hence its electrical affinity towards other polarized molecules.

Substance	Initial quantity	Substance in mg/100 ml serum			
		Oxygen	6 mcg O <sub>3</sub> per ml blood	12 mcg O <sub>3</sub> per ml blood	30 mcg O <sub>3</sub> per ml blood
Urea	66,0	64,5	60,0	59,2	52,5
Galactose	9,7	8,8	8,2	7,5	7,0

l-Lactate	20,8	19,6	18,3	18,5	17,3
Vitamin B1	3,89	3,72	3,33	3,13	3,27
Vitamin C	0,50	0,44	0,46	0,38	0,35
Vitamin E	1,10	1,00	0,90	0,95	0,90

If we assume that ozone or ozone peroxides, respectively, promote oxidizing processes in the organism, we may gather that ozone treatment supports detoxification of a great many substances, part of which may even be cancerogenic.

As early as in 1879 BAUMANN & PREUSSE reported on oxidizing detoxication processes in the liver. They had fed brombenzene to a dog and recovered it in the urine, afterwards. But now, it was linked to the amino acid cystein. The same thing happened when they used naphthalene. This, however, had been metabolized into a dihydroxy compound followed by the linkage to cystein.

[Chemical equation omitted]

Almost a century later, GROVE, HEWER & SIMS made similar experiments with benzophenantrene, a hydrocarbon which is closely related to the well-known cancerogenic substances. They, too, found that a previous oxidation has altered the initial structure by breaking-up one of the condensed ring systems. It had then been linked to glutathion before elimination.

[Chemical equation omitted]

These examples prove that oxidizing process take place in the liver which protect the organism against cancerogenic substances. They, further, back-up the theory by WARBURG, in the 1960s, that peroxides contribute to the impediment of cancer growth.

In 1956, results obtained by WENNING answered the question whether or not the membranes of red blood cells are ruptured under the influence of ozone as they are by UV, X, radioactive radiation, hypersonic wave or electric current.

Citrate containing venous blood was treated with increasing ozone concentrations, and then inspected under dark field illumination. The normal accumulation of erythrocytes in the form of coin rolls was dissolved, and the following observations recorded:

1. The light corona of the erythrocytes was very distinct after treatment with 20 mcg/ml blood.
2. The plasma got cleaner with increasing ozone concentrations. Brehmer or Scheller corpuscles disappeared.
3. Even at ozone concentrations as high as 80 mcg/ml blood the red blood cells are not destructed, neither are the white cells affected in any way.
4. At 120 mcg/ml blood the first alterations on erythrocytes were observed.

These results have been confirmed by WOLFF, in 1976.

In cooperation with the Batelle Institute at Frankfurt, W. Germany, experiments under a scanning electron microscope were performed. The pictures show that the flexibility of the erythrocytes is increased by ozone treatment. This flexibility in tissue capillaries and the so-called single file flow are pre-conditions for the oxygen exchange between red blood cells and body tissues.

It seems that ozone treatment supports the erythrocytes in performing their biological functions. This may be one of the reasons for a better oxygen supply after an ozone treatment.

A 15000-fold magnification shows tiny warts on the surface of the erythrocytes. These, however, could not yet be satisfactorily interpreted.

MENZEL, SLAUCHTER et al. found in 1975 that ozonides of oleic, linoleic, and arachidonic acid methylesters induced the formation of Heinz corpuscles in red blood cells. Simultaneously, they observed that vitamin E inhibits the appearance of these inclusions. Consequently, it should be proposed to combine any ozone treatment with appropriate doses of tocopherole

acetate.

Shortly after the discovery of ozone, the first publications appeared stating that it be a lethal poison. REDFERN submitted a paper, in 185? which said that an inhalation of ozone in the proportion of 1:240 in air would be lethal for all animals, even if it were inhaled for a very short period of time only. Death would be caused by lung compression with emphysema and dilation of the right hart.

According to a paper submitted by BARLOW, in 1879, rabbits will die after one hour of continuous inhalation of 1% ozone in the breathing air. He considered the reason as a caustic damage of ramifications of the smaller bronchi followed by edema and bronchitis.

In 1882, BINZ observed only sleepiness with humans after inhalation of ozone.

This, however, was denied by FILIPOV, in 1884, who had not observed this symptom either with humans nor with animals.

BOHR & MAAR tested, in 1903, the blood of ozone breathing animals. There was no sign of any toxic alterations detectable.

Under the direction of the Kaiser-Wilhelm Academy of the University in Berlin, KONRICH investigated during the years of 1908 to 1913, the suitability of ozone in air conditioning. All his experiments lead to the conclusion that ozone is a poisonous gas and not suitable for this purpose.

During the following years, several series of experiments were performed on animals which clearly showed the sequence of symptoms caused by ozone inhalation.

First, the laboratory animals showed sleepiness and then the breathing rhythm was altered. It became deeper and intermitted. At the end, longer periods of breathing cessation occurred, and it seemed that death was caused by respiratory paralysis.

The effects were sometimes different, not only with different species but also with different individuals. The average ozone concentration in the breathing air was 10 mg/cbm. But also with lower concentrations symptoms of intoxication were observed, dependent on exposure time. The historical inspection of lung tissue samples showed a multiple thrombotic hyperemia and pigmented indurations similar to those experienced with intoxication by chlorine, bromine, and sulfur dioxide.

The resume of all these investigations in which institutes like the Armour Research Foundation of Illinois and the Aerospace Medical Association participated, was that ozone is a toxic gas when brought into the respiratory tract. It causes alterations of the lung tissue density, irritations of the epithelium in trachea and bronchi, emphysema, peribronchial cell infiltration's, and desquamation of the epithelium.

But, obviously, there was a difference in the effects depending upon the origin of the ozone. The symptoms were much less serious if the ozone had been prepared from pure oxygen than from air. The reason is that the nitrogen content in the air leads to the formation of several nitrogen oxides, especially the di-nitrogen pentoxide which has three times the toxicity of ozone.

Based upon this fact, the postulation was established that ozone for medical purposes has to be prepared from pure oxygen under strict exclusion of air or nitrogen, respectively.

Further, it may be stated that the pure medical ozone is definitely neither a protoplasma poison nor a mutagenic substance.

As a matter of fact, in European countries where the application of medical ozone is quite usual very good and sometimes surprising results have been reported, whereby the most important field of application is that of circulatory disturbances of all kinds.

# **NEGATIVE IONS & MOOD/SLEEP/COGNITIVE ABILITY ETC.**

by Daniels

Dear Net friends,

My interest in negative ions has taken me on quite a journey. I have sifted through many abstracts and quite a bit of information and following is what I learned.

I am particularly excited about negative ions because I, personally, have had good success using the generator. After only 2 or 3 days I was sleeping much better. I have had insomnia problems for years, and before this, nothing other than sleeping pills has ever worked for me. About 3 weeks after plugging it in, I find that my mood is elevated. I ordered a small machine for my car, and another desk machine for my office. I have always suffered from the side effects of the anti-depressant medication, so finding relief without those side effects is very exciting. I am not offering this as a therapy, just sharing some research. Since everyone reading this information is in front of a computer, the last article showing that cathode ray tubes emit POSITIVE ions (which are the opposite of negative ions) should be of interest. I called my local Computer City where a tech told me that all computers, other than lap tops with liquid crystal displays) use cathode ray tubes.

I received a large number of email letters from members of groups that I posted to. Many of you have asked different questions. Quite a few asked where I bought my high density negative ion generator. I bought it from NSMI 1-800-706-3724. I paid \$109.95 plus \$5.00 shipping for mine. Also, it came with a "try it, get your money back if you don't like it" guarantee. It gave me the confidence to order it.

This is not a new area of research. Just one that appears not to have been publicized well, for reasons that I do not know.

The benefits of exposure to relatively high concentrations of negative ions produced by high density negative ion generators have been well documented over decades. Literally dozens of studies published in respected journals have concluded that negative ions can have a profoundly beneficial effect on both the mind and body. Listed here are some excerpts from just a few of the scientific studies on the subject of negative ions.

The most recent and exciting study was published in the February, 1995 issue of "Journal of Alternative and Comparative Medicine", a journal of the Columbia Presbyterian Medical Center. The results of this study were also reported on CBS News with Connie Chung.

Researchers Dr. Michael Terman (head of Columbia's Winter depression dept.) and Dr. Juan Su Terman conducted a study of the impact of negative ion therapy on people suffering from seasonal affective disorder (winter depression)--an illness that is often symptomatically indistinguishable from "all-year" depression; researchers believe that the biology of seasonal affective disorder (SAD) is very similar to that of "all-year" depression, hence, the same antidepressant drugs (such as Prozac) are used to treat both.

The study was conducted in double blind fashion and divided clinically depressed subjects into two groups. The subjects in the first group were treated for 30 minutes a day for 20 days with a low density ion generator that produced only 10,000 ions/cubic centimeter (the control group). The subjects in the second group were treated for 30 minutes a day for 20 days with a high density ion generator that produced 2,700,000 ions/cubic centimeter (the experimental group). The remission or "cure" criterion used was a 50% or greater reduction in symptom frequency and severity using the SAD version of the Hamilton Depression Rating Scale. The

results of this study shocked the medical community: While a low density negative ion generator provided little benefit, a high density negative ion generator gave relief from depression comparable to that given by Prozac and other antidepressants, without drug side effects.

The following is a transcript from CBS News 2/14/95 6:30-7:00 PM, Connie Chung. To order your own "official" copy call Burrell's Transcripts at 1-800-777-8398.

Connie Chung, co-anchor: This is the age of wonder drugs and high-tech cures, but alternative treatments, from herbs to acupuncture, have true believers, too, even among some mainstream doctors and researchers. Latest case in point: the wintertime blues. Is it possible that changing the air you breathe can treat those negative vibes and actually relieve depression? Dr. Bob Arnot has the story.

Dr. Bob Arnot: If the blustery winds of winter blowing across the nation this week are bringing you down, there's good reason. Researchers now believe that the ill winds strip away highly charged subatomic particles called Negative Ions from the air around us, contributing to a seasonal form of depression.

Ms Mahala Holmes (patient): As far back as I can recall, I had feelings, of dreading the winter and ... and went through this kind depression.

Dr. Arnot: Doctors at Columbia demonstrated the use of this machine to pump high-density negative ions into the air surrounding Mahala Holmes to treat her depression, known as seasonal affective disorder.

Ms Mahala Holmes: While I was on treatment, I felt excited, I felt energized. I felt alive.

Dr. Arnot: Here's why. Level of brain chemical responsible for mood, called serotonin, are often lower in cases of seasonal depression. Serotonin levels can be elevated by increased exposure to light or by antidepressants like Prozac. Researchers say negative ions may also increase brain levels of serotonin.

Dr. Michael Terman: (Columbia Presbyterian Medical Center): People noticed that daytime energy was returning to normal levels. They lost that pressure for increased sleep, the difficulty awakening in time to get to work.

Dr. Arnot: A study in the current "Journal of Alternative and Complementary Medicine" concluded that 58 percent of patients treated with high-density negative ions had significant relief of their symptoms, almost identical to the number improved with drugs, but without drug side effects.

Dr. Norman Rosenthal (National Institute of Mental Health): From a scientific point of view, it's very exciting. It needs to be replicated.

Dr. Arnot: The whole idea of using negative ions as a legitimate medical treatment may seem just a little bit odd. But while many doctors are still highly skeptical about alternative medicines, more and more Americans are turning to them because they haven't found the satisfaction they want from mainstream medicine.

This is not the first study to prove the benefits of negative ion generators. About 15 years ago, a double-blind study was conducted at the Air Force Aerospace Medical Research Laboratory at Wright-Patterson Air Force Base in Ohio. The study was published in the August, 1982 issue of the prominent medical journal "Aviation, Space, and Environmental Medicine" in an article entitled "Subjective Response to Negative Air Ion Exposure." The study was conducted as follows, quoting from page 822 of the journal:

"Procedure: One group of subjects served as controls and was confined to the test chamber for a 6 hour period under air ion conditions typical of an energy efficient building. The second group was similarly confined, but ion generators began operating 2 hours before occupancy

and continued all 6 hours of confinement. Generators were masked for all indications of operation, and were also present under control conditions but not turned on. Data from both groups were collected under double-blind conditions."

The results of the study were encouraging, as stated on page 823 of the journal:

"Subjective perceptions of psychological state, using individual 'normalcy' as standard, reflected significant differences between control and negative ion exposure groups. Prominent perceptions reported were reductions in irritability, depression, and tenseness, and increases in calmness and stimulation associated with ion exposure...For psychological state, negative ion exposure appeared associated with feeling better about self, less sensitive, and more responsive or innervated [energized]."

In October, 1981, a journal article entitled "The Influence of Negative Air Ions on Human Performance and Mood," appeared in the respected journal, *Human Factors*. On page 633 of the journal, the abstract of the article reads:

"44 female and 12 male 17-61 year olds were tested either in a normal- ion environment (control group) or in a predominantly negative ion environment (experimental group). After a 15-minute acclimation period, subjects asserted their psychological state and completed 2 performance tasks.

Results indicate that subjects had faster reaction times and reported feeling significantly more energetic under negative-air-ion conditions than under normal-air conditions."

Later that year, in December of 1981, a study conducted at California State University, Sacramento entitled, "The Influence of Air Ions, Temperature, and Humidity on Subjective Wellbeing and Comfort," was published in the "*Journal of Environmental Psychology*". The findings were encouraging. On page 279 of the journal, the abstract of the article states:

"106 employees kept daily assessment records of their office environment and health over a 12-week period. Temperatures about 23 degrees Celsius were associated with increased sensations of stuffiness, discomfort, and unpleasantness, but appeared to produce a decrease in the number of complaints of headaches. The office environment was found to be depleted of small air ions. The introduction of a negative ion generator increased the subjective rating of alertness, atmospheric freshness, and environmental and personal warmth. Ions reduced the complaint rate for headache by 50% and significantly reduced the number of complaints of nausea and dizziness."

Of course, much of the early research concerning negative ions has been conducted on animals. One of the earliest studies of the effects of negative ions was published in 1935 in the "*Journal of Industrial Hygiene*" in an article, "The Effect of High Concentrations of Light Negative Atmospheric Ions on the Growth and Activity of the Albino Rat." In it, researchers Herrington and Smith evaluate the effects of negatively ionized air on the activity of rats as measured by means of an activity wheel. They found that activity increased significantly with rats subjected to a reported negative ion concentration of 1.2 million ions/cc.

In 1956, a researcher named J.V. Brady published a study in "*Annals of New York Academic Science*" which showed that the strength of the conditioned emotional responses of fear and anxiety in animals can be dramatically reduced by the daily administration of the psychoactive drug reserpine.

Years later, in 1967, a similar study was conducted by Allan H. Frey at the Institute for Research, Pennsylvania State University, and published in the "*Journal of Comparative and Physiological Psychology*". The major difference was that this time, the effect of reserpine was compared to that of negative ion treatment. The study concluded:

"Results of 2 experiments, the 2nd essentially a replication of the 1st, are in accordance with



prediction. The inhibition of response in the animal was reduced by treatment with small negative air ions, as it was with reserpine."

In other words, when the animals were treated with negative ions, the animals were less inhibited--less likely to experience fear and anxiety. These results are similar to the results of experiments studying the anti-anxiety effects of tranquilizers such as Valium and Xanax.

It has also been shown that in addition to possibly having a profound effect on mood and energy, negative ions may have a strong impact on cognitive functioning. In 1965, in the journal "Psychophysiology", a study, "Behavioral Effects of Ionized Air on Rats", was published. In this study, the effects of negatively ionized air on the mental functioning of rats was tested. Researchers Duffee and Koontz reported on page 358 of the journal: "the water-maze performance improved by 350%," showing a dramatic improvement in cognitive functioning.

To support that negative ions also improve the cognitive functioning of humans as well, in April of 1978, in the science journal "Ergonomics", a study was conducted at the University of Surrey, England, and published in an article entitled, "Air Ions and Human Performance". Once again, the results were encouraging. On page 273, the article reads:

"Studied the effects of artificial negative or positive ionization of the air on the performance of psychomotor tasks with 45 18-26 year-old healthy males...Three testing environments were used: natural, negative, and positive ionizations. Negative ionization was associated with a significant increment in performance as compared to controls."

In 1984, a study was published in the "Journal of Abnormal Child Psychology" named, "Negative Air Ionization Improves Memory and Attention in Learning-Disabled and Mentally Retarded Children." The effectiveness of negative ions on mental performance was put to a test by researching the power of negative ions to improve the cognitive abilities of mentally handicapped children, as well as the abilities of normal children. Fourth graders were divided into three groups: normal, learning-disabled, and mildly mentally retarded. The results were encouraging--on page 353 of the journal, the article reads as follows:

"Half in each group were assigned randomly to an unmodified air- placebo condition under double-blind testing procedures. All of the children breathing negatively ionized air were superior in incidental memory...The action of negative ions on the neurotransmitter, serotonin, may be the mechanism by which negative ions produce such behavioral effects."

On page 358, the article states:

"Table I shows enhanced performance on the order of 8.4% for the normals, 23.6% for the learning-disabled, and 54.8% for the mildly retarded."

Obviously, there is research supporting the effectiveness of negative ions on mood, energy, and performance. But, what are negative ions, and how do they benefit us?

In the magazine, "Whole Self", Spring 1991, an article appeared entitled "Ions and Consciousness". It states, "Ions are charged particles in the air that are formed when enough energy acts upon a molecule, such as carbon dioxide, oxygen, water, or nitrogen--to eject an electron. The displaced electron attaches itself to a nearby molecule, which then becomes a negative ion. It is the negative ion of oxygen that affects us most. Remember that feeling you've experienced near a waterfall or high in the mountains? Those are two such places where thousand of negative ions occur. They create an effect on human biochemistry."

"The normal ion count in fresh country air is 2,000 to 4,000 negative ions per cubic centimeter (about the size of a sugar cube). At Yosemite Falls, you'll experience over 100,000 negative ions per cubic centimeter. On the other hand, the level is far below 100 per cubic centimeter of Los Angeles freeways during rush hour.

Research on ions began in the 1950s with Dr. Albert Kreuger, professor emeritus of the

University of California at Berkeley, and Dr. Felix Sulman, professor of pharmacology at the Hebrew University in Israel.

Dr. Kreuger excited the scientific world when he discovered ions to be biologically active, stimulated production of the powerful chemical serotonin, 5-HT. Serotonin is a very active neuro-hormone which causes profound neural, glandular, and digestive effects throughout the body."

"Dr. Sulman corroborated Kreuger's findings while studying positive ion victims of the hot, dry Sharav winds in Jerusalem. He demonstrated three effects of positive ion excess: irritation and tension, exhaustion, and hyperthyroid response. Most of these conditions, along with symptoms of depression, anxiety, headaches, and low-energy physical and mental functions, were shown to be alleviated or totally eliminated by increasing the negative ion count in the air."

"While ionization of the air is mandatory in many European and Russian hospitals and workplaces, it has only recently come to light in our country with the growing problem of toxic air in our urban environments."

Unfortunately, positive ions are the opposite of negative ions and our computers appear to emit them. In the Palo Alto, California newspaper, "The Peninsula Times Tribune", the following article appeared:

"Beating a case of the VODS: Negative ions maybe an answer to the video blahs By William Johnson Times Tribune Staff

REDWOOD CITY - A case for the blahs at work may really be a case of the VODS VODS stands for Video Operator Distress Syndrome, and the troublesome malady is not uncommon of the millions of workers who use computer video display terminals. Charles Wallach, consultant to the Federal Drug Administration on the effects of working with electronic video equipment, told reporters in the San Mateo County Hall of Justice and Records pressroom how to beat a case of the VODS. Wallch, 64, works in Washington D.C. He has served as a consultant to may government agencies and industries to create a more healty indoor working environment. The cause of the VODS, Wallach said, is a high electrostatic charge generated on the face of a video screen's cathode ray tube. Government standards protect the intrinsic safety of cathode ray tubes, Wallach said, but the VODS nevertheless still can do bodily harm. The charge, which may quickly reach many thousands of volts when the tube is energized, is not in itself a hazard. The tube merely creates the hazard within the foot or so of air space between itself and the operator's face," Wallach said. Those who work too close to the face of a cathode ray tube or who work before a terminal for too long a time typically experience increased fatigue levels, eye strain, blurred vision, skin rash, headaches, back pains, irritability, anxiety, depression and general apathy. While the cause of these symptoms may also be a depleted bank account, domestic troubles or a tyrannical boss, they can be caused by the computer terminal, Wallach said. The culprits that cause the VODS are positive ions or charged molecules of air, created at the face of the video display terminal. What are needed in the workplace, Wallach explained, are negative ions. In contrast to positive ions, negatively charged molecules of air, or negative ions, promote a sense of well-being for people. Negative ions are typically found in the natural environment at the seashor, near waterfalls and in pine forests, Wallach explained. "Every place people like to be is rich in negative ions," Wallach said. Video display terminal operators need their negative ions. "In weighing the evidence, I am convinced that the aero- electrostatic qualities of an indoor environment are the most significant single factor in the control of unavoidable air pollution," Wallach said. Mosty

comonly, offices need to install equipment to generate negative ions in the air above the video terminal operators. The devices typically look like small bristle brushed used to clean glasses or test tubes. They are suspended for the celeing at the end of long rods. At the northern Santa Clara County Communications Center in Palo Alto City Hall, negative ion generators were installed on the ceiling over the dispatchers about a year and a half ago. Cliff Almeida, operations manager at the communications center, said Monday that the ionizers have definitely filtered out pipe and cigarette smoke. But he declined to speculate whether the ionizers created a better working environment with less stress."

As I said earlier, the negative ion generator helped me, therefore I personally am very excited about it. The company that I bought mine from is NSMI 1-800-706-3724. They can be reached online at [nsminegion@aol.com](mailto:nsminegion@aol.com).

If you have any information about negative or positive ions to share, send it to me at [daniels333@aol.com](mailto:daniels333@aol.com).

# **Air Ionization and its Effects on Well Being and Stress and its Biological Effects (The Third Wave).**

Paper presented to The International Academy of Preventive Medicine  
Fairmont Hotel, Dallas, Texas  
March 10, 1979

by George W. K. King, P.E.  
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In this activity, it is our job to keep abreast of all the latest state-of-the-art developments for our client accounts in many disciplines. Only a few clients have ever been interested in ionization and only on the industrial side. This subject matter, therefore, is strictly an expensive hobby for me for the past 20 years. My only contribution is as a catalyst. Many of the statements made here are extractions from papers of various investigators and I apologize in advance for the plagiarism.

The history of the subject goes back several hundred years when atmospheric electricity was first observed. There were suspicions of biological effects then. I became interested in the subject in the 1950's during the Second wave when I met Dr. Clarence Hansell of the RCA Laboratories in Princeton, New Jersey. His findings in 1930 were perhaps most responsible for the First and Second wave of interest. I had a high respect for his work and for years have accumulated a similar high respect for many other investigators. Many will be mentioned.

## **WHAT IS AN ION**

A. According to Webster, an ion is an electrically charged atom or group of atoms in a liquid solution or in a gas. B. To ionize - is to separate into ions or disassociate. C. A. vapor in a radioactive electrical field becomes a conductor and is said to be "ionized." An example of this is a neon light. D. In normal atmospheres there many cases, including Nitrogen, Oxygen, Water Vapor, Carbon Dioxide.

These are the important gases relative to this subject. Molecules fly about and have a velocity due to temperature. In the normal-state, a molecule is electrically neutral. However, various forces will unbalance the molecule. Passing high energy particles pull electrons away from the molecule leaving positive molecules or ions. In nature this occurs about 10 per second per cubic centimeter and they do not re-combine easily. Ion generation is accomplished in many ways, both naturally and man made. Examples are thunderstorms, lightning, snow storms, waterfalls, waterspray on the shoreline. and various wind conditions around the world, rapidly moving dust, radio active materials in the earth surface and sun radiation. Then you have a number of man made means: nuclear tests, combustion, electrical equipment, high voltage discharge. thermionic emission, X-rays, radioisotopes, ultra violet and charge separation. An example of charge separation occurs in air ducts in Air Conditioning Systems, when a fine dust in the air duct contacts the duct wall it loses electrons and becomes positive. Air Conditioning then tends to strip out negative ions and pass positive ones. Another common method of

generation is high voltage discharge from a high voltage source, which is the method that most ion generators use on the market these days. Many factors influence an ion field. Space charge or an electrical field such as a charged wire or various materials affect it. A moving car produces a space charge effect. Materials influence the ion field, such as cotton, which is a conductor. PVC tends to carry negative charges. Wool and silk tend to carry positive charges. These are known as space charge effects. Pollutants affect ionization. Dirt, dust and moisture reduce the ion level and are called condensation nuclei. Smoke cuts ion level and the air is biased on the positive side. Regarding measurement, I won't touch on measurement technology, however, keep in mind that it is extremely important. All equipment on the market and all experimental tests should have known measured outputs in their specifications of the subject distance. Negative ionisers inject electrons and positive-ionizers remove them from the air. If high voltage type ionizers are designed and operated to produce excessive current densities, they can produce contaminants such as ozone, and oxides of nitrogen. If negative ionizers produce enough ozone to smell. they may produce more ozone than ions. Thus, when we speak of biological effects of air ionization, we must be aware of these many conditions. The atmosphere, in addition to its gaseous constituents, contains particulate which are condensation nuclei and often are more numerous than ions. These are sub- microscopic and microscopic dusts, salts, smokes, droplets and the like. They also have the ability to collect clusters of water molecules and to condense water vapor into water drops. That is, why they are called Condensation Nuclei. They can become electrically charged with either polarity as they capture ions from the surrounding air. When they are charged they're sometimes called large ions or Langevin ions. These ions are effective air de-ionizing agents. Consequently, as their density increases in the atmosphere, the effective small ions decrease.

As humidity increases, the condensation nuclei make effective de- ionizers. Cigarette smoke can add greatly to the densities of the condensation nuclei., Mechanical air circulating systems with their blowers, coolers, washers. filters, ducts, grills. etc.. can cause large losses of air ions. This provides the real basis for the complaint of many sensitive persons that "perfectly" conditioned air is still is depressing to them. I want to review considerable history in time increments, cut short only by the limits of this session. The first time frame is 1930 to 1955.

In 1932 at the Rock Point Long Island Laboratory of RCA Laboratories. Dr. Hansell observed that an electrostatic generator produces powerful effects upon a sensitive individual an engineer, who was working in the room. Positively charged air produced physical, mental and emotional depression, where as negatively charged air produced physical, mental, emotional uplift. The effects were so powerful that they could not pass unnoticed so that an investigation of the cause was made. This resulted in more care being taken in the operation of the machine and in the carrying out of a number of experiments relating to ionization. A short time later, Koller's paper reviewing work in Europe was published., in which he described the observed effects of air ionization. He also described the effect of falling barometric pressure in producing positive air ionization when there is respiration of air out of the ground. This seemed to provide an explanation for observation of Hansell who observed that farm animals, as well as people, responded to some stimulus, in advance of storms and bad weather. C. A. Mills, in his writings about effects of weather and climate, reported that he also observed similar phenomena. The farm animals had a strong tendency to anticipate the storms and bad weather by becoming nervous, irritable, quarrelsome and hard to control. The discovery of powerful air ionization effects upon the engineer, Koller's paper reviewing European research on air ionization and its biological effects, and the explanation it seemed to provide for many

previously observed phenomena, provoked great interest at that time. This was the first wave. They led to further experiments and to the collection by Hansell of all available information concerning air ionization and its effects. He assembled a large collection of published records, originating over a total time period of about six thousand years. He attributed much of the early Biblical phenomena to atmosphere changes and climate. In the period 1930-1950, a number of papers were published. Dr. Schorer, doing medical research in Switzerland, published a series of papers reporting important therapeutic results by use of ionized air. Unfortunately he was mistaken in his designation of polarity so that his results seemed to be directly opposed to those of many others. His work was of great importance. It had to be established that he had reversed his polarity designation. Hansell contacted Schorer in April 1955, calling attention to the inconsistency and suggesting a careful check. There followed exchanges of letters between him, Hansell and Wesley Hick. Finally, in 1956, Hicks provided Dr. Schorer with ionizers having polarity reversing switches. The polarity of ionization produced by the two switch positions were given in a sealed communication which Dr. Schorer did not open until he had found by trials which switch positions produced the beneficial and the harmful results in his patients. After the correct positions were determined by trial on the patients, the sealed papers were opened and revealed to him that his beneficial results were obtained with what the Americans had designated as negative air ionization. Although the error was thus discovered, there is no easy or effective means to bring it to the attention of all those who may have occasion to read Dr. Schorer's papers. The confusing effect may last for a long time. This points up the very large technical gap between engineering and medicine that unfortunately exists today. (by the way, one of the objectives of our institute is to close that gap)

1932. During this period. Franke at Hall, Germany made a study over 46 months on 174 patients having normal or high blood pressure. He found that all had fluctuations in blood pressure which apparently synchronized to within about plus or minus one day, apparently being controlled by meteorological factors, such as the passage of air masses. He pointed out particularly that patients often responded by changes in blood pressure in advance of arrival of the new air masses and likened it to the responses in advance of arrival of the Fohn winds, and effect attributable to falling barometric pressure causing positively ionized air to breathe upward out of the ground.

1932-1944. The engineer I mentioned at the Rocky Point Laboratory was strongly affected by operation of the electrostatic generator in his laboratory room. The generator caused the air in the room to be strongly ionized and charged either positively or negatively. depending upon the polarity of the high potential developed. Positive ionization produced in him an extreme physical, mental and emotional depression, while negative ionization gave him a powerful physical, mental and emotional uplift. The effects were so pronounced as to be very apparent each evening both to himself and to associates, who shared a car pool to and from the laboratory with him. At that time the engineer was in a chronic state of subnormal health, the most apparent symptoms being catarrh, shortness of breath, overweight, and lack of physical energy. As to habits, he was then accustomed to generous eating of rich food, took little physical exercise and kept late hours so that he had only a few hours of sleep each. It is interesting that some years later he contracted pneumonia, for which he was given aureomycin, after which his general state of health and physical energy noticeably improved. At that time his sensitivity to the indoor climate of air ionization diminished noticeably. At the same time,

Hansell, who was the Engineer-in-charge of the Laboratory, began a search for reference material relating to biological effects of air ionization. an activity which continued for 30 years, up to the time he died. He accumulated 769 references on the subject. I then decided that his massive effort was too valuable to let drop, so since then I have continued the Bibliography. The new version has now 350 additional references since 1980, most of them annotated.

In 1956, a Philadelphia news release came out citing Dr. Piersol. Dean of the Graduate School of Medicine, University of Pennsylvania as reporting on negative air ionization studies. Research was performed by Dr. Kornbluh. Piersol and Speicher on a total of 53 hay fever patients treated at the North-eastern Hospital. Of these 33 received partial to complete relief. Of 19 with severe symptoms, 11 obtained marked relief, 7 became free of all symptoms and only one patient failed to show any response. Relief was not permanent, in that symptoms usually returned in about two hours after returning to the normal atmosphere. Positive ions failed to produce any relief, but in many instances increased irritation and discomfort. This news, release was the first step in introducing a negative ionizing attachment now used for home air conditioners. The research program continued by Kornbluh tended to confirm the initial conclusion that treatment with negatively ionized air gives temporary relief to hay fever patients. In 1957, Dr. Theodore David, a Northeastern hospital and Kornbluh used negatively ionized air on about 75 burned patients, over a period of about two years. It was stated that, after two- twenty minute exposures, in a room containing a negative ionizer, the patients seldom needed any more narcotics and recovery seemed to be more rapid. From the same source it was reported that treatment with negatively ionized air also produced reductions in pain and more rapid healing in patients following surgery.

Krueger and Smith (University of California. Berkley), experimented with the effects of ionization upon the survival of staphylococci microorganisms in fine water droplets. These experiments suggested that the spread of air borne infectious diseases may be strongly affected by atmospheric humidity and pollution and that the presence, as well as the effects, of atmospheric ionization may be strongly dependent upon these factors. In 1957-1960, Krueger and Smith reported on a series of very important experiments, in which they observed effects of positively and negatively ionized air upon the trachea (wind pipe)-of animals and people. Trachea, in addition to providing conduits for passage of air to and from the lungs also are designed by nature to clean the air and to dispose of collected dirt. They are provided with a lining of cilia, which are short hair like protuberances. Each one of the cilia vibrates to and fro in the direction of the length of the trachea, and the timing or phase relations between vibrations of successive cilia is such as to provide a wave motion, tending to transport particles of dust, pollen, etc. away from the lungs toward areas from which they may be removed or eliminated. By direct observation, first of sections of rabbit trachea, taken from the animals, but still temporarily living and active, Krueger observed that the cilia vibration rate, and secretion of mucus both responded to variations in the polarity and degree of ionization of the air within the vessel-used for observation. Negative ions increased the rates of cilia vibration and mucus discharge, but positive ions decreased them, the effects being reversible by reversing the ionization. The response time constant appeared to be on the order of 15 to 20 minutes. Other responses were observed. Krueger and Smith found that responses similar to those produced by positively ionized air could be produced in animals by intravenous administration of 5-hydroxytryptamine (5-HT). while responses similar to those produced by negatively ionized air could be produced by administration of resperine. From these results they concluded that positive air ions release free 5-HT while negative air ions accelerate enzymatic oxidation of

5-HT. In general terms, this is interpreted to mean that positive and negative air ions act by respectively poisoning or activating enzyme catalysts which, in turn, control the rates of metabolic processes. Thus, the effects are amplified very greatly in about the same way that small amounts of catalytic poisons, and their antidotes, may control relatively enormous volumes and energies of reactions in industrial catalytic chemical processes.

In 1959, Ludvil: Erbar of Czechoslovakia reported positive ion effects on blood pressure; a decrease in blood albumin and increase in globulin; a drop in total and free cholesterol; and increase in 17- ketosteroid. Other effects were noted.

1960 - In making tests on several varieties of negative air ionizers. Hansell and his associate observed some interesting effects upon themselves. For example, during several hours in a room with negative ion densities averaging perhaps 20,000 ions per cubic centimeter. Hansell experienced a strong diuretic effect. It was assumed that the negative ions had increased his metabolism and that the principal resulting waste product was water. The result suggested at least a doubling of the rate of oxidation of food and body materials. As another example, an associate engineer was exposed to negative ion densities of a few thousand ions per cubic centimeter for about seven hours per day, five days per week. He was not conscious of much effect during exposure, but afterward each day he felt an increased need for sleep, in the evening and at night, so that he slept more soundly and for a few extra hours. This was attributed to the body's need for recuperation after exposure to negative ions which had raised his metabolism. These experiences suggested that exposures to negatively ionized air might help in reducing body weight and in overcoming insomnia. 1960-1965 - Johannson in Sweden studies negative ion effects on burns, and found a decrease in the total amount of 5-HT in blood on animals after burn injuries. In five human patients he found an increase in the total urinary excretion of the five HT metabolite which is 5-hydroxyindole-aceticacid (5-HIA)-which seems to indicate an increase in the metabolism of 5-HT; this confirming work by others. Kornblueh and others have found a sedative and analgesic influence on burn patients.

In the 1960-65 period, Jaan Reinet at the USSR Academy of Science, published a compendium of air-ionization investigations in the USSR, touching on much of the physics. Kornblueh amplified the work previously done on post-operative discomfort of 187 burn patients at Northeastern Hospital, Philadelphia. Hamburger, in London, studied the uptake of oxygen during exercise and indicated that it IS highest when the air is positively ionized. This indicates that all of the favorable effects are not necessarily due to negative ionization.

Sulman conducted a considerable experiment on the effect of hot desert winds in Israel on the metabolism of hormones. Musseilman conducted negatively ionized air tests on post-operative treatment - amplifying earlier work by Kornblueh and others. Bullatov, Leningrad investigated ionization treatment on bronchial asthma and cardio-vascular disorders.

Fihchtev, Leningrad. Investigated the treatment of occupational poisoning with negative ions, and the effect of negative ions on the blood of persons suffering from manganese, carbon-disulphite, or benzene poisoning. Other Russians also investigated effects of air ionization on animals poisoned with carbon monoxide with favorable results.

Boiko and others (USSR) reported on the use of ionization to disinfect the air. Skorobogatova, Russia. Showed that the site of application of aerions is a receptor field of the mucosa of the upper respiratory tract. Earlier studies of negative ions versus sleep were confirmed. Tromp, Amsterdam, reported high density of positive ions produced symptoms of dryness, burning and



itching of the nose, nasal obstruction, headache, dry scratching throat, dizziness, difficulty in breathing and itching of the eyes. He further reported that exposure of human subject to positive ions resulted in a rise of blood pressure, decrease of blood albumin and increase in 17 ketosteroids. Minkh, Russia, reported on negatively ionized air, significantly improving the state of health, appetite, and sleep of male subjects exposed for 15 minutes ,daily, for 25 days. No significant effects were noted in blood pressure, pulse and respiration rates. It was noted that for the first nine days there was no change in physical performance capacity. Thereafter the capacity for static work increased 46% for dynamic work 59.5% and was further augmented by 87% by the 25th day. He also reported motor reaction time was continually shortened during the exposure and was reduced by 22 milliseconds at the end of the experiment. He noticed significant changes in urine chemistry. It was his conclusion that negatively ionized air enhances the metabolism of water soluble vitamins.

Krueger experimented with mice inhaling positively ionized air which exhibited a significant rise in blood level of 5-HT. About this time, he developed the "serotonin hypothesis" with considerable foundation. Gualtierotti confirmed findings on the sedating and analgesic effects of negative ionization. He recommended employment of negative ionization indoors at times of smog typical in Milan. Further work was also done on bronchial asthma. Work has been done in the Soviet Union to confirm the effectiveness of air ions in reducing the viable cell count of bacterial aerosols. Boyko reported that an aerosolized culture of *M pyogenes* had no survivors after treatment of the air for 60 minutes with high concentration of negative ions. Yaroshenko found that concentration's of negative ions ranging from 5.2 times 10 to the fourth to 9.5 times 10 to the fourth cubic centimeter reduced the viable population to values averaging 7-15% of the control population. Another investigator confirmed the same trend.

In 1970, analogous, but more dramatic lethal effects were obtained by Biro who studied the action of negative air ions on aerosols of *M pyogenes*, the same as the Russians. 1965-1970 - Deleanue, Romania, reported on the inducement, as well as treatment of ulcers in animals and humans using ionization. Pain and other symptoms were diminished or abolished after 66 patients with peptic ulcers were exposed from 12 to 15 days to negative ions. Wehner treated 214 patients for various respiratory disorders with electroaerosols. The patients were subjected to 2,930 treatments, roughly 13.7% per patient. 72% of all the patients had good to excellent results. 20% responded fair, and 8% no improvement. Otarova, at the University of Leningrad, studied the influence of ions on blood coagulation of cats. He found that ion levels, as well as the polarity influence blood coagulation, positive ions increase the calcium levels of the blood and decrease the average time of coagulation and recalcification of the plasma. Negative ions had the opposite effect.

In 1966, Balti at Hadassah Medical School, Israel, reported 41 experiments with ionization on 19 children of whom 13 were suffering asthmatic asphastic bronchitis. The results of the experiments were very significant. Wofford, University of Southern Mississippi, conducted 100 experimental tests on undergraduate psychology classes with regards to reaction time and manipulative dexterity tasks. Later ions had a significant effect on reaction time, but not dexterity. Others during this period confirmed both. In general, during the period of the 1960's and into the early 1970's most research in the USA came to a halt due to the trough effect of the FDA action on commercial hardware companies. The field of study at that time was badly bent and few research funds were available in the USA. However, research work continued as usual in Eastern and Western Europe. It appears that we Americans must have an immediate

commercial result out of any research, in order for research to be sponsored. As you know, this simply doesn't happen. No doubt this reflects considerably on the materialistic attitude of American society. Caused by, no doubt, such incidious things as taxes and inflation effects on qualified experimenters. What it amounts to is that if there is no fast result, there is no interest on the part of the investigator, and similarly no interest in research grants. The lack of research funding has been extremely devastating in this area of study, more so than in others. One of the objectives of our Institute is to encourage research funding, but it is extremely important that we have good experimental protocols prepared in advance.

In the 1970-1978 period, Sulman continued very substantial studies on weather sensitive patients relative to serotonin hypersecretion, catecholamine deficiency and histamine over-production in addition, he conducted studies on migraine. Blakemore and others at the Graduate Hospital, Philadelphia, reported on the need for control of airborne contaminants in post-operative care the pollution problem. Kornbleuh reported on the relationship between hospital visits and air pollution and weather. Sulman reported on ionization effects with EKG and EEG, Eiter reported on a problem of atmospheric electricity and space climate in buildings, ventilation and air conditioning technology. Deleanu reported the influence of negative air ion therapy on the physical effort in young sportsmen. Straus - Rumania followed Deleanu's earlier experiments upon 4 month to 15 years children in the hospital for bronchial asthma or asthmatic bronchitis. Favorable results were reported.

Sulman, 1975 conducted clinical and biochemical studies of Sharav patients in designated a cluster of signs and symptoms such as migraine, nausea, irritability, etc. as belonging to the serotonin syndrome, The complaints were successfully treated by inhalation of air containing large numbers of small negative ions and by administration of serotonin containing drugs.

Rim of Israel, 1977- 440 subjects were tested on a micro-climate with small negative ions. 225 subjects were tested on Sharav days; whereas 215 tested on regular days as controls. It was hypothesized:

A. That test performance on Sharav days could be similar to that controlled group due to the ionized climate and

B. That the improved performance would be different for subjects high or low on neuroticism and extroversion.

The results showed that the performance of the Sharav groups was considerably similar to that of the controls. It was further found that Sharav days subjects high on neuroticism scored worse on controls on non-verbal intelligence, whereas extroverts scored worse on substitution tests. Around the world there are certain weather fronts that develop abnormally high concentration of positive ions. On Sharav in the Near East is one example. One of the most striking features of the Sharav are the sudden rise in temperature, a drop in humidity and an accompanying wind. The Sharav produces illness in about 30% of the exposed population. Robinson and Dirnfeld studied the phenomenon and noted that weather sensitive individuals began to suffer just at the time that total air ion count rose with a disproportionate increase in the number of positive ions. This was 24-48 hours before any other changes occurred in environmental parameters, such as wind velocity, direction, solar radiation, temperature and humidity. Sulman confirmed these observations and also conducted intensive clinical and biochemical studies of the Sharav patients. After considerable sorting out, it was concluded that the only physical factor that had changed is the number of positive ions in the air. They designated a cluster of signs and symptoms, such as migraine, nausea, vomiting, irritability,

edema, conjunctivitis, congestion of the respiratory tract, etc. - this was called the serotonin irritation syndrome. The sequence is elevated density of positive ions, increased production of serotonin in the exposed subject, resulting in evolution of the clinical syndrome, and rise in renal excretion of serotonin. The probability that this series of events was connected in a meaningful way was corroborated in two further observations. The diseases were successfully treated by air containing small numbers of negative ions and by administration of serotonin blocking drugs. The serotonin hypotheses is based on a considerable body of experimental data and perhaps is most relevant because it bridges the gap between pure laboratory observation and the possible role of ions in the natural environment. Serotonin (5 HT) is a very powerful and versatile neurohormone. For example, it is capable of inducing profound neurovascular, endocrinal and metabolic effects throughout the body. It is concerned with the transmission of nervous impulses. It occurs in considerable quantities in the lower mid brain - where it plays important roles in such basic patterns of life as sleep and are an evolution of mood. It has the further advantage of being subject to assay in microgram amounts by a sensitive and accurate methods. Dr. Krueger found that negative air ions reduce the amount of free 5 HT normally present in the trachea of mice and rabbits. When he exposed the guinea pigs to negative ions and collected all the urine, he observed a considerable increment in the amount of 5 HIAA, an inactive end product of the oxidation of 5 HT. The data suggested that negative ions lowered tissue level of 5 HT by accelerating the enzymatic oxidation process. He advanced the hypothesis that small negative ions stimulate, while small positive ions block monoaminoxidase action, thus producing, respectively, a drop or rise in the concentration of free HT present in certain tissues and eliciting a corresponding physiological response. This hypothesis was established in extensive experiments conducted in a period of over 16 years on animals. High concentration of positive ions raised blood levels of 5 HT while high negative concentrations had the opposite effect. Krueger also found that the brain content of free HT was responsive to the concentration of air ions in air. In the course of this work, they performed spectrofluorometric analysis of more than 12,000 brain and 36,000 blood samples from controls and ion treated mice. This general mechanism of air ion action has been confirmed by other investigators such as Gilbert and Olivereau.

Olivereau concluded that air ion induced alteration in blood levels of 5 HT account for very significant physiological changes in the endocrine glands and central nervous system. These, in turn, substantially alter basic physiological processes. He also observed that negative ions exert immeasurable anxiety reducing effect on mice and rats exposed to stressful situations. This same phenomena was noted by several other investigators. This same response parallels that which follows administration to animals or humans of reserpine and other methods used in treating hypertension. Reserpine and negative ions have in common the ability to reduce the amount of serotonin in the brain and apparently this accounts for this tranquilizing effect.

### **TODAY'S SITUATION**

Regarding the situation today, some comments are in order. After one pours over hundreds of papers in the subject area, one must be convinced that there is substantial measurable evidence of viability of the effect of air ions in biology. An observer of the literature may find that one experiment is directly contradicted by another, tend to be rather arbitrary and unfairly so, by saying that perhaps one of the major reasons for the claims and counter claims in the early days is due to the fact that the measurement technology in detecting huge orders of magnitude was not possible compared to the present state of the measuring art. I refer specifically to the advent of solid state physics that permit measurements down near molecular level. One of the

most damaging elements in the air ion dispute is the very uneven quality of the research that has been reported. Sometimes faulty experimental design permitted the impact of elements other than air ions and the results were erroneously attributed to ions. There are occasions when no air ions at all reach the subject because of improper procedure and meaningless results were reported. Major factors contributing to errors of observation were:

1. Neglect of various gaseous contaminants such as ozone and oxides of nitrogen that can be produced by corona discharge ion sources of bad design.
2. Failure to control ion densities, failure to monitor temperature, humidity and barometric pressure.
3. Use of air containing particulates combined with air ions that lead to widely fluctuating small ion densities.
4. Failure to hold the experimental subjects at ground potential so that their surfaces developed high electrostatic charges and repelled or disbursed approaching air ions. In effect, a Faraday cage. which is a shield around the subject.

Many of these simple observations in the early history were neglected and these, in combination with the poor measurement technology, seemed to cause a high order of reporting errors in early history. Therefore, I arbitrarily look critically at any measurements prior to 1960 as probably fraught with considerable error. This I am sure is an unfair evaluation, and certainly arbitrary, but one of concern. Nevertheless, in recent years there has been substantial improvement in experimental design such that one can have considerably higher confidence in the level of reporting. Changing the subject a bit: The FDA today so far has not taken any action that I know of against the proliferation of advertising claims flying from coast to coast in the media. There have been rumors of passing the effort over to the EPA. Can you imagine what will happen when the Environmental Protection Agency starts to rule on medical problems - but stranger things have happened. Do we need some bureaucrat to tell us to clean up the third wave of interest? I say no. Let the equipment manufacturers follow existing FTC labeling rules - and when the advertising alludes to therapeutic claims, they had better be in a position to prove it. In my opinion, the "ion controversy" no longer exists. The state-of-the-art in ion and particulate physics is well known. Equally well studied are pollution and electrostatics if we take the time to do so. The state-of-the-art in some of the cause-effect chemical changes has definitely turned the corner. There is no doubt in my mind that you can make chemical changes in the body by biasing the environment around you. The scientific preponderance of study makes it clear the serotonin hypotheses, as only one example, no longer is a hypotheses... It is a fact. The major problem now is to more fully understand what are the effects of the chemical changes in the body. In reviewing hundreds of papers, a number of effects appear repetitively :

1. Ions have an analgesic effect - they appear to reduce or eliminate the need for drugs in post operative cases.
2. There is an influence on unhealthy people.
3. More of an influence on unhealthy people - less influence on healthy people.
4. They cause definite chemical changes to take place in the body. Serotonin, MAO, catecholamines and many others are noted. The effect of the chemical changes apparently is known only to a degree.
5. Regarding pollution: Ionization will precipitate particulate, but should not be relied upon exclusively for practical reasons. Electrostatic precipitation and mechanical precipitation are also necessary. A controlled ozone environment within a precipitator

will cancel odors by the strong oxidation that takes place. Obviously, if the particulate in the air is too small for virus to ride upon, there is less possibility of contamination in a doctor's office, hospital, school, hotel, home, etc.

6. Gaseous ions influence coagulation time of the blood.
7. Ion fields effect metabolic rate.
8. Ions change the ciliary rate in the trachea.
9. Ions change reaction time.
10. Ions and serotonin appear to be pain related.
11. Ions inhibit growth of bacteria and fungi on solid media.
12. They reduce the viable count of bacterial aerosols.

There are many more. Regarding study approaches - In the past many years, there have been predominantly two approaches to study. A. The simple cause and physical effect relationship and B. The cause and chemical relationship.

The first approach was predominant prior to the 1960's. Since then there have been increasing studies to determine what the chemical changes are in the body. Once these chemical changes are determined and several of them have been then the end results can be more predictable.

I presume many people here are medical practitioners. It would be extremely helpful if I could hand you the complete state of the science, such that you could apply it tomorrow. It will take some time and involvement to accomplish this, but you are the key. We need your feedback.

In 50 years, air ionization has perhaps 100 times the scientific documentation of acupuncture. Are we so slow to adapt? Why? I leave these answers to you.

Some comments on conducting experiments - If you are interested in conducting treatment, do so only under the close supervision of a qualified medical person and a technician familiar with electro- statistics. This is not for experimentation by laymen.

### **SOME GUIDELINES**

1. Study your subject literature thoroughly. Nobody will hand it to you - you will have to dig it out yourself.
2. Prepare a written protocol in advance to keep yourself on track.
3. If unfamiliar, use negative fields for the first try. Positive can be tried later with close supervision. Each field has special effects.
4. Get an ion generator where the manufacturer will specify the free space ion field at the working distance under standard conditions. The manufacturer must guarantee the output and freedom from contaminants such as ozone and the oxides of nitrogen's. The manufacturer's specification should clearly say so.
5. From your data, watch for anomalies caused by barometric pressure, humidity, air temperature, as well as medical, drug and psychological parameters. As usual in any experiment - isolate the variables as best possible.
6. There is no clear answer relative to the strength of the ion field - anywhere from 5 to 20 times normal outside environment should be considered. Outside environment under favorable conditions can vary from 400 to 3,000 ions/cc.
7. Permit no synthetic materials in the working area.
8. Ground the subject at earth potential.

### **WHAT IS NEEDED NOW?**

1. We need cautious and well informed medical and scientific investigators. I am hopeful

- that many of you have the will and the way to investigate and practice.
2. We also need research grants. Much work must be funded.
  3. But first a well prepared protocol is a must in order to get funding, and funding is very tight.
  4. We need the open-minded practitioner with an experimental attitude along with considerable intestinal fortitude. It is better to let the patient suffer rather than run the risk of a liability suit. I am sure some of the answers will come back like ..."next patient", and I can't say that I would blame you.
  5. We need practitioners who will apply what is known. The Europeans have no reservations about practicing the science - but, then again, they don't have much of the "thou-done-it" bureaucrats that we have.
  6. Last and not least, we need your feedback - documentation of any - I mean any results, good or bad. Send me your findings - formal or not.

### **LAST STATEMENT**

If you hear words about a "so called" Air Ion Controversy - let it be known - the controversy no longer exists. I must apologize for a rough attempt to convey electro-chemical-medical technology. I am sure that I have over-simplified the subject in many areas. Keep in mind that an engineer looks at the human body as complex electrochemical-machine - certainly an over simplified approach. What remains to be done now is Just plain hard work to bring a well documented technology into every day practice and make sure the Third wave sustains itself without that devastating trough that could follow.

# Ozone in Medicine: Overview and Future Directions

by Gerard V. Sunnen, MD

## Abstract

Ozone, an allotropic form of oxygen possesses unique properties which are being defined and applied to biological systems as well as to clinical practice. As a molecule containing a large excess of energy, ozone, through incompletely understood mechanisms, manifests bactericidal, virucidal and fungicidal actions which may make it a treatment of choice in certain conditions and an adjunctive treatment in others.

## Introduction

Ozone, best known for its protective role in the earth's ecological harmony, and for its interaction at ground level with industrial pollutants, has unique biological properties which are being investigated for applications in various medical fields.

As early as the First World War, ozone's bactericidal properties were used to treat infected wounds, mustard gas burns and fistulas. These first treatment attempts, however, were hampered by technological difficulties. Medical ozone generators have since been developed and refined. They differ from industrial generators in their capacity to deliver the purest ozone-oxygen mixtures in precise dosages. A critical advance in medical ozone technology was the development, in the early 60's, of plastics which can adequately conduit this mixture and permit proper interfacing with patients. In the last few years ozone treatment has seen growing interest from diverse medical disciplines, and research is in progress to delineate its effects on biological systems and to define its clinical applications.

## Historical Perspectives

The history of ozone's discovery is intrinsically entwined in the evolution of the earliest concepts in chemistry. Priestly and Cavendish noted that electrical sparks fired in a closed volume of air resulted in volume compression.[1,2] In 1785, Martinus Van Marum, subjecting oxygen to electrical discharges, noted "the odor of electrical matter" and the accelerated oxidation of mercury. In 1840, Schonbein repeated these experiments, concluded that this odor was due to a gas which he named ozone, from the Greek ozein (odorant), and described several of its properties.[3] Numerous researchers since that time have worked to elucidate the nature and actions of ozone. Still today, theoretical issues remain regarding its electron structure, the varieties of its molecular configurations and its kinetics. Mariniak and Delarive showed that it is an allotropic form of oxygen, and Mulliken and Dewar clarified its molecular architecture.[4]

In the latter part of the 19th century, ozone was found to oxidize a spectrum of organic compounds and to interact with double bonds. Chemists made use of these properties to study complex molecules by cleaving them into smaller fragments. Harries, by such methods, discovered the structure of natural rubber.[4]

The ability of ozone to destroy toxic or noxious industrial impurities (phenols, cyanides, tetraethyl lead among others) and to inactivate bacterial contaminants in sewage has made it an attractive alternative to chlorination. Wiesbaden, Germany became the first city to use ozonation for purification of its drinking water (1901), followed by Zurich, Florence, Brussels, Marseille, Singapore and Moscow (the largest installation in the world), among others. The

history of ozone's medical applications has nebulous and anecdotal beginnings. Kleinmann is said to have carried out the first bacteriological studies on pathogenic organisms using the Siemens tube, shortly after its invention.[5] Payr,[6] and Fisch and Wolff[7] were clinician pioneers, and J. Hansler developed one of the first reliable models of medical ozone generators.[5,8]

### **Physico-Chemical and Biochemical Properties**

The oxygen atom exists in nature in several forms: (1) as a free atomic particle (O), it is highly reactive and unstable; (2) oxygen (O<sub>2</sub>) its most common and stable form, is colorless as a gas and pale blue as a liquid; (3) ozone (O<sub>3</sub>), has a molecular weight of 48, a density one and a half times that of oxygen and contains a large excess of energy in its molecule (P3--) $3/2 O_2 + 143$  KJ/mole. It has a bond angle of 127 [3], which resonates among several forms, is distinctly blue as a gas and dark blue as a solid; (4) O<sub>4</sub> is a very unstable, rare, nonmagnetic pale blue gas which readily breaks down into two molecules of oxygen.

Ozone is a powerful oxidant, surpassed in this regard only by fluorine. Shonbein,3 in 1855, discovered that it reacts with ethylene. Exposing ozone to organic molecules containing double or triple bonds yields many complex and as yet incompletely configured ephemeral transitional compounds (zwitterions, molozonides, cyclic ozonides), which may be hydrolyzed, oxidized, reduced or thermally decomposed to a variety of substances, chiefly aldehydes, ketones, acids or alcohols. Ozone reacts with saturated hydrocarbons, amines, sulfhydryl groups and aromatic compounds.

Of importance to biological systems is ozone's interaction with tissue (especially blood) constituents. The most studied is lipid peroxidation although interactions have yet to be more fully investigated with complex carbohydrates, protein, glycoproteins and sphingolipids. These dynamics are especially relevant for medical applications because some of the most practiced methods in ozone therapy involve the mixing of a small volume of whole blood with a pure oxygen ozone mixture and subsequently returning it to the patient. In this manner, it is calculated that the dose of ozone administered will perform its therapeutic functions without disrupting blood constituents.

Since there are a variety of lipid components in whole blood, it is of more than theoretical interest to determine the end products of ozone per oxidation and their effects, not only on physiological systems but on the integrity of ambient pathogenic organisms, since one of the mechanisms of viral inactivation is thought to be through this modality. Cholesterol accounts for 120 to 220 mg/100 ml, of which 60% to 75% are cholesterol esters; phospholipids 9 to 16 mg/100 ml; triglycerides 40 to 150 mg/100 ml, and free fatty acids 6 to 16 mg/100 ml. Given a total lipid concentration of 450 to 1000 mg/100 ml and the large variety of lipid constituents, the possible end products of ozonation are bountiful.[9,10]

This question is further complicated by the presence of systems to buffer lipid peroxidation, including vitamin E, uric acid,[11] and enzymes such as superoxide dismutase, catalase, and the glutathione peroxidase system which has gathered the most experimental attention.[12]

Several agents derived from lipid peroxidation include free radical, singlet oxygen, hydrogen peroxide, hydroperoxide, ozonides, carbonyls, alkanes and alkenes. Of these, lipid hydroperoxides, the most extensively studied, are known in sufficient concentrations to manifest their toxicity by altering cell membranes. Acted upon by glutathione peroxidase, they are reduced to their corresponding alcohols.

### **Method of Manufacture and Precautions**



The production of ozone-oxygen mixtures for human and veterinary applications is subject to important technical consideration and standards. Clinical ozone generators which regulate the flow of medical grade oxygen through high voltage tubes with outputs ranging from 4000 V to 14000 V are capable of producing precise ozone-oxygen mixtures within concentration ranges extending to 5%, predicated on three variables: (1) the voltage applied; (2) the oxygen flow rate; and (3) the electrode separation distance. The purity of the oxygen source is especially emphasized since nitrogen, in the presence of high energy fields, forms toxic nitric oxides. Since the half life of ozone is 45 minutes at 20C (68F), losing its concentration to 16% of its initial value in two hours, it must be freshly generated for immediate use at the treatment site. The maximum dose generated, 5% ozone to 95% oxygen, is well below the explosive limit (15 to 20%). Caution is needed not to appose ether and an ozone, an especially reactive mixture. Listed contraindications to ozone treatment[5] include acute alcohol intoxication, recent myocardial infarction, hemorrhage from any organ, pregnancy, hyperthyroidism, thrombocytopenia and ozone allergy.

### **Methods of Administration, Dosage, and Clinical Applications External Ozone Gas Application**

Historically, ozone was first administered by application to external body surfaces to determine its effects on a variety of lesions, A. Wolff,[13] in 1915, is credited for using local ozone treatments for wounds, fistulas, decubitus ulcers and osteomyelitis. Like natural rubber which cracks and fritters when exposed to oxygen-ozone mixtures, early materials caused ozone to "bag" around skin surfaces and met with early oxidation disuse. Today, specially designed plastics (Teflon) enable extremities or portions of the head or torso to be comfortably encased in a space where a determined dosage ratio of oxygen to ozone is administered at a chosen flow rate. In this way, the walls of the transparent bags do not touch the patient, an important consideration in burn treatment.

Indication for external ozone application include poorly healing wounds, burns,[14] staphylococcal infections, fungal and radiation lesions, herpes simplex and zoster, and gangrene (diabetic or Clostridium). Dosage is adjusted to the condition treated. Gas perfusions may last from 3 to 20 minutes, ozone concentrations varying from 10 to 80 ug/ml (maximum five parts of ozone to 95 parts of oxygen). High ozone concentrations are used for disinfection and cleaning (or debridement), while low concentrations promote epithelialization and healing.[6,15]

### **Ozone Insufflation**

Payr in 1935[6] and Aubourg in 1936[16] first used ozone-oxygen mixtures in rectal insufflation to treat ulcerative colitis and fistulae. The list of indications has expanded to include proctitis and hemorrhoids. It is reported that in inflammatory diseases of the bowel, ozone promotes healing and restores the flora balance disturbed by pathogenic organisms. In a typical treatment for ulcerative colitis, daily insufflations are applied starting with 50 ml in severe cases, increasing as tolerated in increments (till 500 ml), high concentrations administered initially (75 ug/ml) to achieve hemostasis, followed by low concentrations to promote resolution.[5] This technique may have some promise in the treatment of bowel infections associated with AIDS.

Microsporidia, a tiny, rarely detected parasite may be responsible for many cases of AIDS wasting illness,[17] and studies await determination of its susceptibility to ozone treatment.

### **Major Autohemotherapy (AHT)**

Whereas it can be readily understood that external ozone applications produce local effects such as disinfection, wound healing or local circulatory enhancement, the technique of introducing ozone into the circulation poses more complex theoretical issues. In the technique of major autohemotherapy, 50 to 100 ml of blood is drawn from the patient, mixed with a dose of ozone-oxygen of a predetermined concentration, then returned via the same intravenous catheter (butterfly). Returned to the patient, the ozonated blood is rapidly distributed to all tissues.

In the treatment aliquot of blood, it is gauged that the dose of ozone given not only will exert therapeutic actions locally (virucidal activity, oxygenation, increased red cell fluidity), but will determine beneficial systemic actions.[18]

The duration of time that ozone remains in solution and its effects on endocrine, neurological, and immunological systems are not known. Clinically, some patients, upon receiving their own ozonated blood, report a faint background taste of ozone, which may be an indication of its survivability in solution for at least a few seconds.

Major autohemotherapy has been applied to the treatment of several conditions, including acute and chronic viral infections (hepatitis), some carcinomas, circulatory disturbances (diabetes, arteriosclerosis), and hyperlipidemia.[8,19-21] Added to a standard pharmacotherapeutic regimen for postmenopausal osteoporosis, this technique enhanced remineralization of bone.[22] Clinical reports however, need to be substantiated by properly designed studies. Of interest are the reports of some patients, who after receiving this treatment experience feelings of well-being lasting for a few minutes to several hours. Whether this represents a placebo effect, a metabolic alteration or possibly a neuro-psychiatric mechanism remains to be determined.

### **Miscellaneous Applications**

Although the above techniques of ozone administration represent the majority of hospital or office-based procedures, others deserve mention.

### **Minor Autohemotherapy**

In this technique, 10 ml of venous blood is drawn from the patient, mixed with ozone-oxygen, then injected intramuscularly. Listed indications include asthma, acne, some allergic conditions and some carcinomas.[18,23,24]

#### **Direct Intra-arterial or Intravenous Administration**

Mostly of historical interest, this method was first used by Iacoste in 1951[25] for circulatory compromise and its possible sequelae (gangrene). Up to 10 ml of pure ozone-oxygen may be slowly injected directly into the artery (usually femoral), or into a vein, without incurring embolization since both gases are readily soluble in blood.[20] Indications include intermittent claudication, leg ulcers and cerebral vascular insufficiency. Due to accidents produced by too rapid introduction of the gas mixture into the circulation, this technique is now rarely used.

#### **Intramuscular Injection**

Up to 10 ml of pure ozone-oxygen mixture is injected into the gluteus maximus muscle or the deltoid. This treatment along with major autohemotherapy is invoked as an adjunct to cancer therapy.[15,18,26,27]

### **Ozonated Water**

Ozone is approximately 10 times more soluble in water than oxygen. Mixed into aqua

bidestillata (pyrogen free) water, the half life of ozone is nine to ten hours (at pH 7 and 20C); and at 0C, it is doubled. Ozonated water finds applications in dental surgery where it is reported to promote hemostasis, enhance local oxygen supply and inhibit bacterial proliferation. Applied following tooth extraction or during dental surgery,[28] it may also be rinsed in conditions such as thrush and periodontal disease, swallowed in cases of gastritis or gastric carcinoma, or irrigated in chronic intestinal or bladder inflammation.

### **Ozone Ointments**

Ozonated olive oil provides long term, low dose exposure of ozone and lipid peroxides to tissues. Decubitus ulcers and mycoses are indications for its use.[29,30]

### **Balneotherapy**

Ozonated water bubbled in warm baths, provides stimulation of local circulation and disinfectant action to varicosities, peripheral circulatory disorders and dermatological conditions (eczema, ulcers).[5]

### **Blood Purification**

The possibility of using ozone to sterilize blood supplies has been investigated by several authors.[7,31] The treatment of 500 ml of whole blood with 100ml of O<sub>3</sub>/O<sub>2</sub> mixture (40 to 50 ug/ml) is reported to render it virus-free without injuring any cellular elements. One study [31] examined 10,000 samples and found no cases of hepatitis transmission. This technique may extend its efficacy to the HIV virus as one preliminary unpublished study indicates although once ensconced in the genetic cellular material, it is unclear how any agent could inactivate it without compromising cellular integrity.

### **Metabolic and Physiological Effects of Ozone**

Most research on ozone's biological effects have concentrated on pulmonary responses with emphasis on its toxicity. Interest has been keen on ozone's role in ground level atmospheric pollution. Produced as a result of interactions between industrial gases, oxygen and ultraviolet rays, there is evidence of synergistic action on pulmonary compromise. The effects of pure ozone, however, need to be differentiated from those of smog.

The majority of studies have been performed on animals who show great interspecies variability in their response to inhaled ozone. Extrapolation to humans is difficult due to differences in pulmonary anatomy and physiology. Mice[32] seem to be the most sensitive (LD50, 22 ppm for 3 hrs) and birds[33] the least (turkeys survived 417 ppm ozone for 3 hrs). While overdose is marked by pulmonary edema and hemorrhage, long term, low level exposure produces poorly understood, sometimes contradictory findings.

Reported effects[34] include enhanced enzyme activity, as evidenced by increase in glucose utilization, lactate and CO<sub>2</sub> formation and elevated glucose-6-phosphate dehydrogenase; an increase in the NADPH-cytochrome P-450 content in rat lung pointing to enhancement of metabolizing enzymes; increased lung fibroblast glucose uptake, and production of lactate and pyruvate.

Humans exposed to ambient ozone (0.24 ppm in room air for two hours) typically develop mild accelerated breathing in the context of symptoms such as tracheal or laryngeal irritation and chest tightness on inspiration. Large intersubject response differences are notable.[35] Athletes[36] performing moderate intermittent exercise show a 7% drop in Forced Vital Capacity (FVC) and a 15% reduction in Forced Expiratory Volume (FEV). The threshold for

significant changes in respiratory compromise ranges from 0.15 ppm[37] to 0.25 ppm,[38] increasing ozone concentrations yield corresponding airway hyper-responsiveness through bronchoconstriction. Histological findings extrapolated from primate research points to ciliated cell inhibition and type 2 cell proliferation, increased membrane permeability and variable inflammatory response.[12] Reported biochemical alterations[39] include increased oxygen consumption and glucose utilization; activation of NADPH, superoxide dismutase, GSH peroxidase, GSH reductase and glutathione peroxidase. Pulmonary effects from ozone in low doses appear to include metabolic activation of lung cells while higher doses produce evidence of cellular metabolic compromise.

In the methodology of ozone treatment, care is given to avoid the escape of ozone into the treatment area and modern machines are equipped to catalytically convert excess ozone to oxygen during administration. Interestingly some studies point to possible beneficial effects of low dose ambient ozone.[40,41] The phenomenon of ozone tolerance or adaptation the response to ozone exposure decreasing with time and finally evolving to a plateau occurs in both humans and animals.[38] Its significance remains obscure.

For the reason that below 0.30 ppm the probability of ozone traversing the respiratory epithelium and entering the systemic circulation is so low, very few studies have attempted to measure these effects.[39] In the technique of major autohemotherapy and others that involve the direct introduction of ozone into the circulation, however, this question is of special relevance. Studies of human blood in young adult males exposed to 0.50 ppm ozone for 2-3/4 hours[42] show significant changes in erythrocytes (RBC) as well as in the serum. RBC membrane fragility, glucose-6-phosphate dehydrogenase and lactate dehydrogenase enzyme activities were increased, while RBC acetyl cholinesterase and reduced glutathione reductase were not significantly changed. Serum vitamin E and lipid peroxidation levels were significantly increased. These findings indicate that ozone exposure increases metabolic activation parameters in red blood cells.

According to other researchers,[20,24,43] the direct intravascular injection of pure oxygen-ozone mixtures results in the following responses: (1) an activation of enzymes involved in peroxide or erythrocytes, an outgrowth of which is (2) stimulation of the [2,3] Bisphosphoglycerate cycle, shifting the oxyhemoglobin dissociation curve to the right thus releasing oxygen to the tissues. Further physiological effects include (3) an enhanced oxidative decarboxylation of pyruvate with the formation of Acetyl-CoA, and consequent citric acid cycle activation, (4) a direct influence on the mitochondrial transport system with reduction of NADH and oxidation of cytochromes, and (5) an increase in RBC pliability, blood fluidity, and arterial PO<sub>2</sub>.

### **Mechanisms of Bactericidal, Virucidal and Fungicidal Action**

Although the inhibitory and lethal effects of ozone on pathogenic organisms have been observed since the latter part of the 19th century, the mechanisms for these actions have not yet been satisfactorily elucidated. Ozone is a strong germicide needing only a few micrograms per liter for measurable action. At a concentration of 1 g/m<sup>3</sup> H<sub>2</sub>O at 1C, ozone rapidly inactivates coliform bacteria, staphylococcus aureus and Aeromonas hydrophilia.[44]

The inactivation rate of enteroviruses[45] is more rapid than for E. coli, takes place in relatively small concentrations of ozone, and is influenced by pH, temperature, and the presence of ambient organic compounds.

Viruses differ in their susceptibility to destruction by ozone. The resistance of polio virus type 2 was 40 times that of coxsackie AS,[46,47] and in an experiment using a continuous flow

mixed reactor under controlled laboratory conditions, relative resistance in descending order was found to be: polio virus type 2, echovirus type 1, polio virus type 1, coxsackie virus type B5, echovirus type 5, coxsackie virus type A9. In pure water, at maximal solubility of ozone and room temperature, Echovirus type 29 is inactivated in one minute, polio virus type 1 in two, type 3 in three and type 2 in seven minutes.

The cell envelope of Gram negative microorganisms such as *E. coli* is a complex multilayer system composed of an inner cytoplasmic membrane made of phospholipids and proteins invaginating into the cytoplasm, a peptidoglycan layer, and an outer membrane of poly polymers such as polysaccharides. Gram positive cells have a less complex, three layer envelope with a thick peptidoglycan middle layer.

The most cited explanation for ozone's bactericidal effects centers on disruption of envelope integrity through peroxidation of phospholipids and lipoproteins. There is evidence for interaction with proteins as well.[48] In one study[49] exploring the effect of ozone on *E. coli*, evidence was found for ozone's penetration of the cell membrane, reacting with cytoplasmic substances and converting the closed circular plasmid DNA to open circular DNA, which would presumably lessen the efficiency of bacterial proliferation. It is notable that higher organisms have enzymatic mechanisms to restabilize disrupted DNA and RNA, which could provide a partial explanation for why, in clinical treatment with ozone at doses prescribed, ozone appears to be toxic to infecting organisms and not to the patient.[50]

Ozone possesses fungicidal effects, through poorly understood mechanisms. In one study, *Candida utilis* cell growth inhibition with ozone was greatly dependent on phases of their growth, budding cells exhibiting the most sensitivity to its presence.[51] Interestingly, in another study,[52] low doses of ozone stimulated the growth and development of *Monilia fructigena* and *Phytophthora infestans*, while higher doses were inhibitory.

Viruses are parasites at the genetic level, separated into families based on their structure, type of nucleic genome and mode of replication. Many virions contain a phospholipid envelope with glycoprotein spikes, encasing the nucleocapsid which contains nucleic acids (DNA or RNA), and structural proteins (including enzymes).

Lipid-containing viruses are sensitive to treatment with ether, assorted organic solvents, and ozone, indicating that disruption or loss of lipids results in impaired or destroyed infectivity. Viruses containing lipid envelopes include the Herpesviridae a large family grouping the Simplex, Varicella-Zoster, Cytomegalovirus and Epstein-Barr viruses; the Paramyxoviridae (mumps, measles); the Orthomyxoviridae (influenza); the Rhabdoviridae (rabies); and the Retroviridae (HIV). The HIV virus has an outer envelope made of a double layer of lipids penetrated by proteins of several types encasing two molecules of RNA.[53]

Many of the above viruses have complex, sometimes baffling life cycles and replicative strategies with progressions from host cell attachment of the virus particle, to penetration, uncoating of the viral envelope, synthesis of molecular components, and release of new generations of virions to the surrounding medium, most often through cell lysis. Many chronic viruses have eclipse phases alternating with phases of viremia, when waves of viral particles flood the bloodstream.

In view of the above considerations, what part can ozone play as an antiviral agent? In one study,[46] polio virus 1 was exposed to 0.21 mg/liter of ozone at pH 7.2. After 30 seconds 99% of the viruses were inactivated (lost their ability to replicate within host cells), but appeared to maintain their structural integrity. Analysis of viral components showed damage to polypeptide chains and envelope proteins, which could result in attachment capability compromise, and breakage of the single-stranded RNA into two parts, producing replicating

dysfunction at its root level. Other researchers[54] in similar experiments concluded that in ozonation, it is the viral capsid which sustains damage. It is to be noted however, that the polioviridae (Picornavirus family) contain four structural proteins encapsulating a single RNA strand and are devoid of lipids.

In those clinical applications which make use of external (or body cavity) application of ozone, it can be appreciated that in view of the fact that a direct ozone-organism contact exists, inactivation of micro-organisms, bacteria, viruses or fungi, proceeds by any one of a variety of different mechanisms. The treatment of burns, superficial mycotic infection, decubitus ulcers and abscesses is applied by this method. Theoretical issues present themselves, however, when examining treatment strategies aimed at systemic infections, notably viral afflictions which make use of introducing ozone-oxygen mixtures into the bloodstream (usually major AHT). The ozone-treated aliquot of blood which is reported to be rendered viral-free through direct contact with ozone and ozone peroxides,[5] is reintroduced into the circulation. Since very little free ozone remains in solution due to its high reactivity, it is its products mainly lipid compounds, possibly others which are thought to interact with circulating as well as tissue-bound virions, thus inactivating them.

Within the dose ranges prescribed (up to 10 mg (O<sub>3</sub>/100 ml of blood), we may be curious to measure this overflow antiviral capacity. Although unproven to be outright curative for any viral illness, ozone blood treatment, as reported in several studies[21,31,55] may lessen clinical severity or duration. Thus therapeutic benefits have been noted in hepatitis, acute and chronic, and herpes.[55] In chronic viral infections Cytomegalic, Epstein-Barr and Retroviridae (AIDS) among others blood ozonation performed in viremic cycles or in periods of clinical exacerbation may, through direct action, through the production of cofactors inhibitory to viral replication, or through modification of immune function, be used in inducing viral quiescence. Ozone is reported to be an immuno-stimulant in low doses and immuno-inhibitory at higher levels.[15,26,27]

It is not inconceivable, in view of the possibilities given to ozone's antiviral properties that new generations of machines may be developed to test the therapeutic potential of the extra-corporeal treatment of circulating blood.

### **Ozone Treatment in Cancer**

The logic sustaining the use of oxygen-ozone application to the treatment of carcinomas rests on the strategy of capitalizing on the disturbed metabolism of cancer cells. Since the first bio-chemical hypothesis of cancer was proposed by Warburg[56] in 1925; that all tumors have higher rates of glycolysis under aerobic conditions than do nontumor cells, efforts have been made to find the variations which could best affect treatment strategy. Although his statement has subsequently been amended considerably, there is a massive and evolving body of research centering on biochemical differences between normal and malignant cells.[57]

Some tumors have high rates of glucose use and lactic acid production in the presence of oxygen, a reflection of a number of possible mechanisms, from membrane transport differences to variations in ATP regulation. Cancer cell mitochondrial ribosomes have altered J structure and function which could diminish their oxidative energy producing abilities thus accounting for their limited aerobic potential.[57]

Some authors[5,26] report a peroxide intolerance in tumor cells. Possessing insufficient catalase and peroxidase, they are incapable of effective peroxide inactivation. Such cells exposed to ozone are said to show a significant decrease in lactate content, indicating that ozone may induce metabolic inhibition in some carcinomas.

In one study,[58] cultured cells of different carcinoma types were compared with non-cancerous human lung fibroblasts on exposure to ozonated air (0.3, 0.5, and 0.8 ppm of O<sub>3</sub> for 8 days). Alveolar (lung) adenocarcinoma, breast adenocarcinoma, uterine carcinosarcoma and endometrial carcinoma showed 40% cell growth inhibition at 0.3 ppm and 60% at 0.5 ppm. The non-cancerous lung cells were unaffected at these levels. In 0.8 ppm exposure, cancer cell growth inhibition was 90%. Interestingly, it was at this level that the control cell group started to manifest anabolic slowdown (50%). The authors postulate that cancer cells are less able to compensate for the oxidative challenge of ozone than normal cells, possibly by way of a less functional glutathione system.

There are many clinical and anecdotal reports,[21,25,27,59] of ozone major or minor autotherapy, at times prescribed on a daily basis for several weeks applied to the treatment of various carcinomatous conditions but with a paucity of controlled data. Several researchers have focused their efforts on using ozone as an adjunct to radiation or chemotherapy.[23]

### **Summary and Future Directions**

Ozone, an allotropic form of oxygen, possesses unique properties which are being defined and applied to biological systems as well as to clinical practice. As a molecule containing a large excess of energy, through incompletely understood mechanisms, it manifests bactericidal, virucidal and fungicidal action which may make it a treatment of choice in certain conditions and an adjunct to treatment in others. Although ozone's medicinal effects were discovered in the 19th century and clinically applied during World War I, equipment capable of purity and reliability of delivery of oxygen-ozone mixtures were not available until the late 1950s. Since then, experience has accumulated for the administration of ozone to humans and animals via a variety of routes, in doses that are both nontoxic and relevant to clinical problems, externally in gaseous form (or in solution) and systemically in blood ozonation.

A review of a large body of literature is presented which describes a spectrum of therapeutic indications. Of these, ozone application for superficial infection, burns, dental and intestinal conditions, and possibly circulatory problems seem to be the most promising. As regards blood ozonation, further research is indicated to delineate the nature of its dynamics and the extent of its effectiveness in (1) the identification of the galaxy of compounds formed in this process which, in view of doses administered, by all evidence, have metabolic, immunological, endocrine and possibly neurological effects; (2) the purification of blood or blood components for transfusion purposes; (3) the inhibition of carcinomas with reference to the types which may be the most susceptible and to its use as an adjunct to radiation or chemotherapy; and (4) the inactivation or the repression of viral diseases with special attention to chronic conditions of the Herpes or Retroviridae (HIV) families.

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# Comparison of effects on tissue oxygenation of hyperbaric oxygen and intravascular hydrogen peroxide

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Unfortunately figures and tables had to be omitted.

There are numerous pathologic conditions that are related to, or caused by a decrease in tissue oxygenation. These conditions include many cardiovascular and pulmonary diseases, as well as certain infectious and toxic states. During the past few years there has been considerable interest in the experimental use of both hyperbaric oxygen (OHP) and intravascular hydrogen peroxide ( $H_2O_2$ ) as techniques for improving tissue oxygenation. Although the mechanisms of action are different, both OHP and  $H_2O_2$ , are effective in increasing tissue oxygen tensions. The present study was designed to compare the effectiveness of these 2 techniques.

## METHOD

Studies were performed on New Zealand albino rabbits anesthetized with Nembutal. Tissue oxygen tensions were measured with the Beckman 160 Gas Analyzer and polarographic microelectrode. This electrode and gas analyzer system were described in previous reports.[1,2] The electrode was positioned percutaneously in the hindlimb muscle of the rabbit through an 18 gauge Riley needle. Oxygen tension determinations were read continuously during control, experimental, and postexperimental periods. Oxygen tension levels obtained by this equipment are a reflection of the flow of current through the electrode as a result of the reduction of oxygen molecules at the cathode. These levels were expressed as "arbitrary units," which represented the reading on the gas analyzer. Precise calibration of oxygen tension levels in tissues cannot be obtained by the technique used in these studies. However, ratios of the peak values obtained during the experimental periods to the control, pretreatment levels were calculated, and the effectiveness of the various experimental regimens on increasing tissue oxygen tensions were compared.

Studies were performed on 20 animals exposed to hyperbaric oxygen in a small hyperbaric chamber. The cable of the polarographic electrode was brought out through a penetration in the chamber and connected to the gas analyzer on the outside. After stabilization of the oxygen tension readings during the control period, the chamber was pressurized with 100 percent oxygen over a 10 to 15 minute period. A pressure of 15 p.s.i.g. was reached and was maintained during the experimental period with a continuous ventilation of 5 to 10 liters per minute. After 10 to 15 minutes at 15 p.s.i.g., a gradual decompression was carried out until the chamber pressure again read 0 p.s.i.g. Oxygen tension recordings were continued during a variable time span in the posttreatment period.

An additional 20 studies were performed with intravascular hydrogen peroxide. Infusions of

0.2 percent  $H_2O_2$  were maintained by a constant infusion pump at rates of 0.5 to 2.0 ml. per minute. The hydrogen peroxide was administered through polyethylene catheters in the external iliac artery or vein.

In 8 of these studies the  $H_2O_2$  was infused intra-arterially; in 7 studies, intravenously; and in 5 studies, the peroxide was infused intravenously in a retrograde direction. In all these studies, the polarographic electrode was placed in the midportion of the gastrocnemius muscle. Oxygen tensions were recorded during the control period, the infusion period, and the postinfusion period. The peroxide infusions were maintained for 25 to 138 minutes.

## RESULTS

In the hyperbaric oxygen studies, the tissue oxygen tension levels rose rapidly after starting compression (Fig. 1). In most of these studies, the oxygen tensions began to rise in less than a minute and significantly elevated levels were attained as the pressure of the chamber reached 15 p.s.i.g. (Table I). The mean ratio of peak/control levels in the 20 studies was 4.44 (Table II). Usually, the  $pO_2$  levels rose in a stepwise fashion as the pressure in the chamber was increased pound by pound. The tissue oxygen tensions remained at elevated levels during the entire experimental period, although there were some fluctuations noted. Within one minute after starting decompression, the oxygen tensions began to fall. A mean time of 27 minutes elapsed before the  $pO_2$  values again reached control levels.

The effect of hydrogen peroxide on oxygen tensions in the gastrocnemius muscle depended on the route of administration of the peroxide. A significant rise in tissue oxygen tensions occurred during the intra-arterial infusion (Fig.2), and also during retrograde intravenous infusion. Ratios of peak/control levels averaged 5.96 and 6.30, respectively (Table II), or 6.09 if the total of 13 studies was combined. In contrast, conventional intravenous administration of hydrogen peroxide did not appear to affect oxygen tension recordings in the leg muscle. Peak/control ratios in intravenous studies averaged 1.01.

Muscle oxygen tension levels were not affected by the intra-arterial and retrograde intravenous infusions of  $H_2O_2$  for the first 30 to 40 minutes of infusion (Table I). After this time, the levels rose rapidly and reached peak values during the infusion period or, in some studies after the infusion had been discontinued. Marked fluctuations in  $pO_2$  levels often occurred during the  $H_2O_2$  administration. Upon discontinuation of the peroxide infusion, the levels usually began to fall rapidly, although in several studies this was delayed for a relatively long period. A very gradual return to control levels occurred, averaging about 1 hour in time. The peroxide infusions appeared to cause a localized response in tissue oxygenation which was characterized by a gradual pink flushing of the skin. In some studies, one could follow the progress of the flushing and as it extended to the area of the electrode, the  $pO_2$  levels rose.

## DISCUSSION

The results of these studies are dependent upon the accuracy of the polarographic electrode measurements. It has been our experience with more than 500 experimental runs that this equipment cannot be used for determining precise oxygen tension levels in tissues in terms of millimeters of Hg. However, gross changes in tissue  $pO_2$  levels can be detected with the polarographic microelectrode and reproducible results can be obtained. The electrode is a delicate instrument and preparation for use and maintenance during an experimental study are difficult. A loss in sensitivity can occur with localized bleeding, fat or fibrin deposition, or precipitation of electrolytes in the vicinity of the tip of the electrode. Even a slight movement of the electrode during the experimental run can cause a change in calibration and a loss of

validity. However, this equipment is of considerable value in detecting acute changes in tissue oxygen tensions. The speed of change can also be measured since the response time of the electrode is within seconds. The effects of various conditions on tissue oxygen tensions can be compared if the electrodes are used with a uniform technique.

The mechanisms of action of hyperbaric oxygen and intravascular hydrogen peroxide are quite different. During exposure to hyperbaric oxygen, the ambient  $pO_2$  rises, resulting in an increase in alveolar and arterial  $pO_2$  levels. The arterial  $pO_2$  rises about 760 mm. Hg with each added atmosphere of pressure, and the oxygen content in the blood rises 2 volumes percent per atmosphere. Hemoglobin becomes fully saturated with oxygen, and more oxygen is physically dissolved in the plasma. The generalized increase in arterial  $pO_2$  quickly causes an increase in tissue oxygenation. The effects of  $H_2O_2$  on increasing tissue oxygenation are a result of the degradation of  $H_2O_2$  to water and oxygen by catalase and peroxidases.

These enzymes are present in excessive quantities in the blood of man and certain experimental animals, including rabbits.[9] Much of the released oxygen is dissolved in the blood, which turns bright red. However because of saturation of the blood, small oxygen bubbles can be seen, which in some circumstances can act as harmful emboli.[11]

In the present study both  $H_2O_2$ , and OHP were effective in raising tissue  $pO_2$ , levels.

The increase in tissue  $pO_2$ , due to hyperbaric oxygen occurred almost immediately and was well maintained during the pressurization period. Upon discontinuation of the pressure, the  $pO_2$ , levels rapidly fell and dropped to control values in an exponential manner. The effect from hydrogen peroxide, in contrast, appeared to take much longer in reaching the tissue under study. The increased  $pO_2$  levels were maintained during the infusion period and occasionally well beyond the discontinuation of the infusion. The ratio of peak/control levels during peroxide infusion was slightly higher than that occurring during administration of oxygen at 2 atmospheres absolute. It would be reasonable to consider that the effect of a peroxide infusion, with the use of 0.2 percent  $H_2O_2$ , at 0.5 to 2 ml. per minute, is comparable to the effects on tissue oxygenation of hyperbaric oxygen at 2 to 3 atmospheres absolute.

The first reported use of intravascular hydrogen peroxide was by Oliver and Murphy[8] who injected  $H_2O_2$  intravenously in 1920 in an effort to treat hypoxia due to pneumonia. More recently, there have been numerous reports of the use of intra-arterial  $H_2O_2$  as a means of providing regional oxygenation. [3,4,6,7,12] Recent reports by Rogers and Manguikian[10] and Germon and associates[5] demonstrated an increase in tissue oxygenation with intra-arterial peroxide, and these findings were confirmed in the present study. A more rapid response to peroxide occurred in the studies of Rogers and Manguikian. This may be explained by the fact that the polarographic electrodes in their studies appeared to be closer to the area of infusion. Germon and associates observed a slow or delayed tissue response to peroxide, or no response at all, in their experiments. The present studies indicate that the diffusion of oxygen along the full length of tissue supplied by a catheterized artery is a relatively slow process compared to the almost immediate response of the hyperbaric oxygen effects. No mention was made of the prolonged effect of peroxide after discontinuing the infusion in the reports by Rogers and Manguikian and Germon and associates.

There would appear to be potential advantages in the use of both intra-arterial hydrogen peroxide and hyperbaric oxygenation, depending on the particular circumstances. The advantages of intra-arterial  $H_2O_2$  include the facts that a localized oxygenation effect can be obtained without fear of systemic toxicity, and that expensive and complicated equipment can be avoided. On the other hand, hyperbaric oxygen can furnish a generalized increase in oxygenation when this is required and can provide oxygenation to tissues that are not supplied

by a single arterial system. Retrograde intravenous administration of peroxide appeared to improve oxygenation only in a very localized area and would probably have very little value as compared to intra-arterial administration. An ordinary intravenous infusion of  $H_2O_2$  did not cause any systemic or localized effect on tissue  $pO_2$ . The resulting increase in venous  $pO_2$  is lost by diffusion as this blood passes through the pulmonary capillaries.

## SUMMARY

Measurements of tissue  $pO_2$  by polarographic electrodes in the hind limb of rabbits have indicated that significant increases occur following the use of both hyperbaric oxygen and intra-arterial and retrograde intravenous hydrogen peroxide. The effect from the  $H_2O_2$  is delayed until the oxygen diffuses slowly into these tissues, but the effect is maintained for a longer period after discontinuation of the infusion. Hyperbaric oxygen causes an almost immediate rise in tissue  $pO_2$ , and when discontinued causes an almost immediate fall in the elevated levels. Intravenous hydrogen peroxide causes no change in the tissue  $pO_2$  levels. Ratios of peak/control tissue  $pO_2$  levels caused by OHP at 2 ATA, and 0.2 percent  $H_2O_2$  administered intra-arterially at 0.5 to 2 ml. per minute were 4.44 and 5.96, respectively, indicating that the effect of the peroxide was equivalent to the effect of hyperbaric oxygen at a pressure of at least 2 ATA.

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# Comparison of Arterial and Tissue Oxygen Measurements in Humans Receiving Regional Hydrogen Peroxide Infusions and Oxygen Inhalation

Radiology 1968; 91: 669-672

by  
Patricia A. Germon M.D., Donald S. Faust M.D.,  
and Luther W. Brady M.D.

Unfortunately figures and tables had to be omitted

Following the report of Gray that tumor sensitivity to irradiation increased in an environment containing an increased oxygen concentration (1), interest was stimulated in the possible application of this principle in the treatment of cancer patients. Churchill-Davidson first used the hyperbaric chamber to provide increased oxygen tensions within the body. Mallams, using regional intra-arterial infusion technics, reported that equally high concentrations of oxygen could be delivered to the tumor area with infusions of hydrogen peroxide solutions (2, 3).

Because of reports of the ease of Mallams' technic and the beneficial effects of this adjunct to radiation treatment (4, 5) a study was undertaken to evaluate oxygen tensions generated in arterial blood and muscles of animals and patients receiving infusions with hydrogen peroxide solutions.

## METHODS AND MATERIAL

In vivo measurements of arterial oxygen tensions have been obtained in 3 dogs and 16 patients, 20 patient studies having been performed. Patient age range was thirty-three to seventy-one years, with a median of fifty-one. The experimental design was to insert percutaneously, via the femoral or brachial arteries, an indwelling infusion catheter into the thoracic or abdominal aorta. Concomitantly, indwelling Cournand needles were inserted percutaneously into the opposite femoral artery and in several instances into the nearby thigh muscle. During the procedure all but one of the patients received only local anesthesia for the insertion of the Cournand needles; the animals received general anesthesia with pentobarbital.

This arrangement permitted the direct measurement of oxygen tensions by inserting the precalibrated Beckman micro-oxygen electrode through the indwelling Cournand needles in either the artery or the muscle at any desired interval before, during, or after hydrogen peroxide infusion. A continuous record of the observed changes in oxygen tension as measured by the microelectrode and the Beckman 160 physiologic gas analyzer was obtained on a strip-chart recorder.

In early studies, when high oxygen levels were anticipated, the oxygen electrode was calibrated in a specially constructed pressure chamber containing Ionosol solution(3) at a known temperature, through which 100 percent oxygen or air was bubbled at pressures varying from 0 to 50 p.s.i. In later experiments, calibration was obtained by bubbling 100 percent oxygen or air at atmospheric pressure through Ionosol solution at a known temperature. After correction to body temperature, a reference curve was obtained which related millimeters of deflection obtained from the strip-chart recording to the dissolved oxygen tensions. In more recent



studies, the comparative changes of the arterial oxygen levels were evaluated in vivo and in vitro following oxygen inhalation via mask or demand valve and hydrogen peroxide infusion.

## **RESULTS AND DISCUSSION**

An earlier report presented data from the initial phase of this study (6). The salient information, briefly summarized, was that in all 3 dogs studied cyanosis and respiratory distress developed when hydrogen peroxide solutions were infused at rates greater than 4 drops per minute. These conditions were not reversed with attempts at resuscitation with oxygen. (This is in direct contrast to findings in an earlier publication by the original investigators of this technic (2).) Only one of our animals survived for a prolonged period while receiving a slow infusion of hydrogen peroxide, but respiratory distress developed when the flow rate was increased. Oxygen measurements in the artery and muscle of this animal were unchanged throughout the period of slow infusion. All data from the dog experiments were considered unreliable because of the unstable physiologic status of the animals, which were receiving active resuscitative measures. Additional animal studies were not performed after it was learned that the dogs required preparation with exogenous catalase prior to study. It was considered that an animal thus prepared would have significant enzymatic imbalance and any data obtained would reflect this abnormal state.

Twenty studies were performed on patients with malignant tumors in the esophagus, abdomen, or pelvis who were receiving arterial infusions with 0.48 per cent hydrogen peroxide solution as an adjunct to radiation therapy. Four patients were evaluated on two different occasions. These early investigations demonstrated several patterns of tissue and arterial oxygen response in our patients during infusions, but none of these determinations confirmed reports of marked increases in oxygen tension resulting from in vivo decomposition of hydrogen peroxide. It was also observed that each patient varied in response to infusion in a totally unpredictable manner and that a patient could differ in response from one study to the next.

When it became evident that the infusion technic failed to provide reliable or significant oxygen increases, an effort was made to evaluate the comparative results of oxygen inhalation via face mask or demand valve versus hydrogen peroxide infusion. Simultaneously, an attempt was made to confirm the in vivo measurements obtained with the micro-oxygen electrode with in vitro measurements using the micro- oxygen electrode in the Instrumentation Laboratory gas analyzer. No tissue measurements were made during this phase of the investigation.

In this comparative study, each patient exhibited consistently elevated arterial oxygen tensions with oxygen inhalation. All patients demonstrated at least a threefold increase in the arterial oxygen level.

Figure 1 demonstrates the oxygen tensions resulting from inhalation through a plastic rebreathing mask which delivered approximately 30 percent oxygen. Oxygen levels obtained with hydrogen peroxide infusion are also shown.

TABLE 1 presents data and compares the results of in vivo and in vitro measurements in this same patient. All in vitro measurement were made in duplicate, and values within 10 mm were averaged and reported. In the second control determination a wide divergence in the oxygen readings was obtained, and therefore both readings were reported. Reasonable agreement between the two methods was found.

Figure 2 demonstrates the arterial oxygen concentrations obtained with oxygen inhalation

through a demand valve and with the use of a nose clip. This method of delivery provided essentially 100 percent oxygen to the patient. In vivo measurements showed a rapid rise of the arterial oxygen tension and approximately fourfold increase over levels obtained with hydrogen peroxide infusion. However, after infusion, with repeat oxygen inhalation, the increase in gas tension was not so great as found initially and was achieved only after a prolonged period of oxygen breathing. This finding is unexplained but may be related to altered ventilation/perfusion relationships within the lung.

Figure 3 again demonstrates the increase in arterial oxygen obtained with the inhalation of 100 per cent oxygen through a demand valve compared with hydrogen peroxide infusion.

Figure 4 reveals another interesting facet. Prior to our evaluation, the patient was heavily sedated with meperidine and hydroxyzine because of anxiety over the pending procedure. In the initial phase of this experiment, oxygen inhalation provided a threefold increase in oxygen tension. With hydrogen peroxide infusion, at 76 drops per minute for ten minutes, little increase in oxygen tension was noted. Approximately one minute before the next determination, the infusion rate was increased to 160 drops per minute, which resulted in an approximate twofold increase in oxygen tension. By this time the subject had become more alert as the effects of sedation subsided, and repeat oxygen inhalation provided arterial oxygen pressures approximately five times greater than the control. It is believed that the depressant effects of the drugs on respiration may have a direct influence on the low oxygen levels obtained early in the study.

Since no measurements of tissue oxygen tensions were obtained during the evaluation of the efficacy of oxygen inhalation, we are unable to report tissue changes that might occur in the presence of increased arterial oxygen tensions provided by this mode of delivery.

Several interesting observations were noted during this investigation. It was found that hydrogen peroxide infusion provided little significant increase in the systemic arterial oxygen tension. This was most evident in patients who had infusion catheters in the thoracic aorta, while arterial oxygen tensions were measured in the femoral areas. It was noted that the nearer the oxygen electrode was to the catheter tip and the more rapid the infusion rate, the higher the oxygen tension recorded. It is doubtful that the electrode is measuring only dissolved oxygen when it is in close proximity to the catheter tip. A more probable explanation is that the electrode is measuring both molecular and nascent oxygen produced by hydrogen peroxide decomposition on or near the electrode membrane surface. Conversely, the farther the separation between the microelectrode and the hydrogen peroxide source, the lower the readings. These readings are believed to reflect the true levels of oxygen generated by hydrogen peroxide decomposition.

While oxygen inhalation provides more reliable and consistent elevations of arterial oxygen, and is the more physiologic method of systemic oxygenation, it has inherent problems. In patients, significant cardiac and pulmonary disease can influence arterial oxygenation. Sedation can also depress respiration and hence the oxygenation of the blood. Alterations in the state of the sensorium can prevent adequate patient cooperation with this mode of oxygen administration. And lastly, the arterial oxygen levels are affected directly by the concentration of the inhaled oxygen.

From a review of the data obtained from this investigation, it appears that, if the reported benefits of hydrogen peroxide infusion are related to the elevated oxygen tensions produced,

then equally beneficial effects should be obtained by oxygen inhalation.

## **CONCLUSION**

Although regional intra-arterial infusion systems using hydrogen peroxide have been suggested as a means to increase oxygen concentrations in arterial blood and tissues data from this study fail to confirm the magnitude of changes previously reported. The magnitude of the measured changes appears related to the rapidity of infusion and the distance of the hydrogen peroxide source from the measuring electrode. It is believed that the high oxygen readings obtained while the electrode and hydrogen peroxide source are in close proximity reflect other factors besides dissolved oxygen. Comparative studies with inhalation of oxygen in high concentrations demonstrated that high arterial oxygen tensions can be produced consistently in patients in the absence of significant cardiopulmonary disease and depressant drugs.

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# **Regional Arterial and Tissue Oxygen Tensions in Man During Regional Infusion with Hydrogen Peroxide Solutions**

Radiology 1967; 88: 589591

by

P.A. Germon, D.S. Faust, A. Rosenthal, and L.W. Brady

Unfortunately figures and tables had to be omitted

Gray and his co-workers (3) demonstrated in tissue culture and in animals a general relationship between radiation sensitivity and oxygen saturation at the time of irradiation. Churchill-Davidson et al. (1) later applied this principle at the clinical level by employing the hyperbaric chamber to increase oxygen saturation of the tumor during the radiation event.

Mallams and Jay et al. adapted regional intraarterial infusion technics, evolved through experience with chemotherapeutic agents, to deliver oxygen to the tumor area, using hydrogen peroxide solutions (4, 5). Data from early reports of these methods revealed that significant increases in oxygen tensions could be achieved in arterial and venous blood, muscle, and tumor tissue.

The purpose of the present Pilot study was to evaluate the oxygen tensions generated in arterial blood and muscle in animals and patients being regionally infused with hydrogen peroxide solutions.

## **METHODS AND MATERIAL**

To date, in vivo measurements of the arterial and tissue oxygen tensions have been obtained in 3 dogs and 7 patients. The experimental design consisted of an indwelling infusion catheter inserted percutaneously via the femoral artery into the abdominal aorta and in indwelling Cournand needles inserted into the opposite femoral artery and the nearby thigh muscle. During the procedure, the animals received general anesthesia with pentobarbital. The patients received only local anesthesia for the insertion of the Cournand needles.

With this arrangement, direct oxygen tensions could be measured by inserting the precalibrated Beckman micro-oxygen electrode through the indwelling Cournand needle in either the artery or muscle at any desired interval before, during, or after hydrogen peroxide infusion. A continuous record of the observed changes in oxygen tension as measured by the micro-electrode and the Beckman 160 physiologic gas analyzer was made on a strip-chart recorder.

The oxygen electrode was calibrated prior to each experiment in a specially constructed pressure chamber which contained Ionosol solution at a known temperature through which oxygen or air was bubbled at pressures varying from 0 to 50 pounds per square inch. After correction to body temperature, a reference curve was obtained which related millimeters of deflection obtained from the strip-chart recording and the dissolved oxygen tensions.

In one experiment, arterial blood samples were obtained and evaluated in vitro with an Instrumentation Laboratory gas analyzer. Studies included the oxygen and carbon dioxide tensions and the pH of arterial blood samples taken before, during, and after infusion with hydrogen peroxide.

## **RESULTS AND DISCUSSION**

In the animal experiments, it became apparent that the dog was not an appropriate animal for the study. In direct contrast to Mallams' initial report in 1962 cyanosis and respiratory distress developed in all animals when infused with hydrogen peroxide solutions at a rate greater than 4 drops per minute. Therefore, data from the early dog experiments were not reliable because of the unstable physiologic status of the animals and the active resuscitative measures required. One animal survived for eighty-four minutes without difficulty when infused with 0.24 per cent hydrogen peroxide solution at a rate of 4 drops per minute; however, cyanosis and respiratory distress developed promptly when the infusion rate was increased to 12 drops per minute. In this animal, oxygen measurements were unchanged throughout the period of infusion prior to the onset of respiratory distress. In a personal communication with the original investigators (2), it was learned that the dog required preparation with exogenous catalase. Since it was considered that the animals would have significant enzymatic imbalance and could not provide reliable data, further dog studies were terminated.

In our 9 patient studies, 7 subjects were evaluated; 3 on two different occasions. All patients had malignant tumors in the abdomen or pelvis and were receiving infusions with 0.48 per cent hydrogen peroxide solution as a part of their radiation therapy program.

The patients demonstrated three patterns of change in arterial and tissue oxygen tensions during infusion. One showed an early increase in arterial oxygen followed by a delayed increment in the tissue oxygen (Fig.1). In these patients a four- to fivefold increase in the arterial oxygen tension developed: from an initial 1.5-3.0 pounds to a maximum of 10.0-18.0 pounds. The maximum tissue values which were obtained varied between 5.0 and 10.5 pounds of oxygen.

Another pattern was one of a slow increase in oxygen in both the artery and tissues during the period of infusion (Fig. 2). In this group of patients, one demonstrated a maximum arterial oxygen pressure of 10.0 pounds with a maximum tissue pressure of 14.0 pounds. In 2 patients maximum arterial oxygen tensions of 4.5 and 6.7 pounds developed, with a peak tissue tension of 3.0 pounds.

The last pattern found was that of an initial increase in arterial oxygen with or without similar changes in the tissues (Fig. 3). Thereafter, a plateau or steady decline in oxygen was noted during the period of infusion. In this group of patients minimal changes, if any, were found.

It was impossible to predict beforehand the type of patient response. It was also found that a patient could vary in his response from one study to the next.

Lastly, arterial blood samples were obtained from one patient before, during, and after infusion with hydrogen peroxide and were analyzed in vitro with the Instrumentation Laboratory gas analyzer (Table 1). Although concomitant studies with the micro-electrode were not obtained, the data support in vivo studies, i.e., with infusion only minimal changes in oxygen tensions could be demonstrated. It was also found that in the presence of an unchanged carbon dioxide tension, the arterial pH became more alkaline, indicating that electrolyte alterations resulted from the infusion.

Our data to date, therefore, do not confirm the work of others who have reported significant increases in arterial oxygen tensions resulting from the in vivo decomposition of hydrogen peroxide.

## **CONCLUSIONS**

Regional intra-arterial infusion systems using hydrogen peroxide have been suggested as a means to significantly increase oxygen tension in arterial anti venous blood as well as other tissues in the areas infused. Data from this pilot study to date indicate that there may be only a two- to fivefold increase in oxygen tension over normal levels and do not confirm the

magnitude of changes which have been reported by others. Contrary to original reports, rapid infusions of hydrogen peroxide solutions have been found to be lethal in the unprepared dog. The exact mechanism, however, is not understood at this time.

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# Hydrogen Peroxide/Ozone for municipal water supplies?

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If what the media is saying is true about chlorine destroying the ozone layer, then it is urgent that attention should be given to one of the largest uses of chlorine, and that is municipal water supplies. Some limited experimental studies are being done in the U. S. on the use of hydrogen peroxide and/or ozone as a disinfectant for municipal water supplies. These two substances are widely used in Europe. As an example, 3000 cities in Europe use ozone to disinfect their municipal water supplies. Paris is one of the cities that has used ozone for many years. Los Angeles, California recently installed an ozonator in their water system. Let's take a look at some of the studies that have been or are being conducted.

## **H<sub>2</sub>S WATER TREATED WITH H<sub>2</sub>O<sub>2</sub>**

Mohan V. Thampi authored the article "Water Treatment Controlled By H<sub>2</sub>S Levels", appearing in the May, 1991 issue of WATER/Engineering & Management. Thampi says that "More than 90 percent of the drinking water supply in Florida is derived from groundwater aquifers. In Central Florida water wells 500 to 1000 feet deep tap the Floridian aquifer. This raw groundwater is of excellent quality, with all contaminant levels, except for dissolved H<sub>2</sub>S (aq)." Hydrogen sulfide (H<sub>2</sub>S) is generally stripped out of the water by cascade tray aeration or mechanical forced-draft aeration. Then it is stored in elevated tanks and chlorinated prior to distribution. Population growth and widely varying water demands have resulted in current processes not being as efficient as they once were. During high demand periods, there is less stripping of H<sub>2</sub>S, use of higher quantities of chlorine, turbidity (cloudiness) and this results in poor water quality as to taste and odor. Thampi goes on to say "To find a quick and cost effective solution to the turbidity and chlorine residual problem, a pilot test was conducted using NaOH (sodium hydroxide) and H<sub>2</sub>O<sub>2</sub> (hydrogen peroxide) chemicals at the 10 million gal./day Econ Water Plant in Orange County." Finding the correct H<sub>2</sub>O<sub>2</sub> dosage proved difficult initially. "It was found the turbidity occurred despite (the) addition of H<sub>2</sub>O<sub>2</sub> and most of this H<sub>2</sub>O<sub>2</sub> was leaving the tank unreacted. Chlorine demand was unusually low. This meant there was another H<sub>2</sub>S oxidizing reaction taking place." "Inspection of the insides of the tanks showed high clusters of colloidal sulfur adhering to the tank walls. Thus, it was deduced that the oxygen dissolving during the aeration was continuing to react with the H<sub>2</sub>S in the tank the tank because of favorable equilibrium conditions. When excess H<sub>2</sub>O<sub>2</sub> was added to overcome the air oxidation, only then would the H<sub>2</sub>O<sub>2</sub> oxidation with H<sub>2</sub>S proceed. So during startups, it took about 2 days for the H<sub>2</sub>O<sub>2</sub> reaction with H<sub>2</sub>S to establish its own reaction conditions in the tank.

## **OXIDATION TREATMENT OF WELLS FOR TWO EASTERN CITIES**

The March, 1991 issue of Public Works contained an article by Dyksen et al about the experimental use of ozone and hydrogen peroxide for the clean up of two contaminated wells. One of the wells is located in New Jersey and the other at Spring Valley, New York. A grant of \$66,000 was awarded by American Water Works Research Foundation of Denver to the Ridgewood Water Department. Expertise and financial resources are also being provided by Malcolm Pirnie, Inc. of Paramus, New Jersey, for a total project cost of \$115,600. "The project's overall objective is to develop a practical and cost effective means of applying the ozone/ H<sub>2</sub>O<sub>2</sub> treatment system for use at individual public water supply wells. A pilot test unit will be designed to inject, dissolve and contact the oxidants in a pressurized line, simulating conditions in a well pump discharge line." Dyksen et al reported the importance of controlling organic contaminants in groundwater. This can be done by protecting groundwater resources and/or by reclaiming groundwater that has been affected. Chlorinated hydrocarbon solvents and gasoline- related contaminants have been detected in groundwater supply systems. Precautions have been taken at some wells affected by organic chemicals with such techniques as packed tower air stripping and granular activated carbon systems but there are limitations with each process. There is potential for air contamination around packed towers since organic substances are transferred from water to air. With activated carbon there is a need to replace the carbon on a frequent basis and a concern about using it where radon occurs, "because of the potential buildup of radioactive materials in the GAC bed." Methods considered were several Advanced Oxidation Processes (AOP's) because they ". . . have the potential for removing organics from drinking water including ozone, chlorine, chlorine dioxide, permanganate, and hydrogen peroxide." Ultraviolet light alone or in combination with other oxidants was also considered. In the end, ozone and hydrogen peroxide were chosen as having the most potential. Advantages of an in-line treatment of ozone/hydrogen peroxide are the fast destruction of many organic chemicals, adaptability for plant applications, cost-effectiveness and lack of toxic air emissions. Reports should be out soon on these tests.

### **COMPARISON STUDIES OF PEROXIDE AND OZONE**

An article by David W. Ferguson et al appeared in the April 1990 issue of the AWWA Journal and is entitled "Controlling Taste and Odor Compounds, Disinfection By products and Microorganisms." It describes the third of a five phase pilot project being conducted by the Metropolitan Water District of Southern California, ". . . in evaluating the hydrogen peroxide ozone (PEROXONE) advanced oxidation process---(followed by secondary disinfection with chloramines) for removal of taste and odor compounds, control of disinfection by- products (DPM's), and inactivation of microorganisms." The water being treated is from the California State Water Project and the Colorado- River. At the pilot plant facility, ozone is bubbled through four glass ozone contactors. Just prior to this, the raw water can be treated with hydrogen peroxide by means of a metering pump or in-line static mixer. The water depth is maintained at 16 feet and water treatment times varied up to 12 minutes, as do the levels of oxidation treatments. The article contains some plant schematics, numerous tables and charts describing the experiments and their effects on contaminants, effect of contact time, oxidation residuals, etc. Further studies will be conducted through the mid-1990's as the five phase process continues. Thus far, the study concludes that PEROXONE is significantly more effective than is ozone alone in oxidizing taste and odor compounds.

As reported in a previous newsletter, a pilot plant was being designed "to cleanse San Fernando Valley water-supply wells of industrial solvents." This was reported in the March 25, 1988 issue of the Los Angeles Times. Hydrogen peroxide and ozone were selected over



alternative processes because they remove contaminants from the water without creating hazardous waste problems. The initial design cost for the plant at North Hollywood was \$423,200, the cost of the plant that was to be built to range from \$500,000 to \$1.5 million. The plant was designed to break down trace chemicals including TCE and PCE. Wells eventually to be treated are in Los Angeles, Burbank, Glendale and in the Crescenta Valley County Water District. "More than 2 dozen wells have been shut down because of pollution."

# HYDROGEN PEROXIDE FACTS

by

Kurt W. Donsbach, D.C., N.D., Ph.D.

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ECH<sub>2</sub>O<sub>2</sub> Inc.

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There have been many incorrect statements regarding the ingestion of **hydrogen peroxide** and now, **magnesium peroxide**. I would like to address these so that you as a patient will not be misled and stop using a potentially beneficial product.

Myth #1 : Any of the peroxides destroy friendly bacteria in the gut and require that you reintroduce fresh bacteria constantly if you are using the peroxide on a regular basis. The proof offered was that when you put hydrogen peroxide into a yogurt culture, the resultant yogurt was weak and watery.

FACTS: THE FRIENDLY BACTERIA IN THE GUT ARE AEROBIC, MEANING THEY LIVE AS AN OXYGEN-USING ORGANISM. If you want the opinion of the bible of bacteriology, check this out in Bergey's Manual of Systematic Bacteriology or Clinical Diagnosis By Laboratory Methods by Todd & Sanford. The addition of extra oxygen to the yogurt culture could have altered other factors in the milk used in the culture, rather than destroying the lactobacillus. The reference used by the writer was conspicuously lacking bacteria counts before and after the addition of the hydrogen peroxide! The truth is you help, not hinder, lactobacillus with H<sub>2</sub>O<sub>2</sub>.

Myth #2 : Oral ingestion of hydrogen peroxide promotes the growth of various viruses, including what has been called the EBV virus, the HIV virus and others.

FACTS : HYDROGEN PEROXIDE IS CAPABLE OF DESTROY EACH AND EVERY ONE OF THESE VIRUSES IN LABORATORY TESTS. This does not necessarily mean that the same action occurs in the body, but it is a pretty good indicator. THE MOST IMPORTANT FACT REGARDING THIS ALLEGATION IS NOT WHETHER OR NOT HYDROGEN PEROXIDE KILLS OR STIMULATES A VIRUS, BUT HOW HYDROGEN PEROXIDE IS HANDLED BY THE BODY WHEN IT IS ABSORBED FROM THE GUT, What actually occurs is that the instant hydrogen peroxide crosses the intestinal barrier and enters the blood stream, the enzyme catalase splits the compound into water and free radical oxygen. This takes one molecule of catalase for every 10,000 molecules of hydrogen peroxide and uses up about 1/10,000 of a second. In approximately another 1/10,000 of a second you will see one free radical oxygen (O1) join another free radical oxygen to form stable oxygen (O2). Since this all takes approximately 1/5,000 of a second, when does the hydrogen peroxide have time to enter the circulatory channels and end up in the T cells where the HIV virus proliferates? Obviously it doesn't. THIS IS ALSO THE ANSWER TO THE CLAIM THAT FREE RADICAL OXYGEN WILL CAUSE CELLULAR DAMAGE. THE FREE RADICAL OXYGEN HAS AN EXTREMELY SHORT LIFE IN THE BLOOD STREAM ONLY AND NEVER GETS CLOSE TO CELLS !

# **INDOOR OZONE HEALTH CONCERN: A STATEMENT OF THE AMERICAN LUNG ASSOCIATIONS IN MINNESOTA**

Due to the hundreds of calls received questioning the health hazards of indoor ozone, the American Lung Association wishes to clarify some areas of confusion about this pollutant and warn people who are living in environments with elevated levels of ozone about possible health effects.

## **OZONE AND ITS FORMATION**

Ozone is a highly reactive, oxidizing gas that is a variant of oxygen ( $O_3$  rather than  $O_2$ ). Ozone is the most important of a class of substances known as photochemical oxidants. An oxidant is a chemical substance that can damage biological molecules by adding oxygen atoms to them with greater facility than normal atmospheric oxygen. This unstable, colorless gas with a pungent odor is a powerful respiratory irritant even at the levels frequently found in most of our nation's urban areas during summer months. Ozone is normally created in the stratosphere by the action of sunlight and ultraviolet radiation on oxygen. High above the earth, it is an important substance for absorbing ultraviolet light and heat of solar energy. While protective in the stratosphere, excess amounts in the part of the atmosphere (troposphere) which is our breathing zone can be harmful to lung tissue. With atmospheric mixing, usually no more than 0.03 parts of ozone per million parts of air (ppm) reach ground level. Our lungs need oxygen not ozone. Excess ozone at ground level is considered a pollutant. There are national standards for its outdoor levels and federal regulations through Occupational Safety and Health Administration (OSHA) to protect people at their worksite. Outdoors, excess ozone is produced when hydrocarbons [volatile organic compounds (VOC's)] and oxides of nitrogen ( $NO_x$ ) combine in the presence of sunlight. The majority of hydrocarbon production is from highway vehicles and evaporation of organic solvents such as fuel, paint, and dry-cleaning fluids. Nitrogen oxides arise primarily when fuel is burned such as in power plants and motor vehicles. Indoors, ozone production has been usually found only in negligible amounts being associated with brush type electrical motors and produced by the action of electrical discharges on oxygen in the air. Ozone is formed as a by-product at low safe levels when equipment such as sewing machines, workshop motors, electrostatic-precipitators or ion-generating air cleaners are working properly. In small offices photocopy machines may need added ventilation. Of great concern is the recent trend toward purchase of air cleaning machines designed specifically to produce ozone for use within "indoor occupied spaces". While these "ozone generating" devices may be very effective in controlling cigarette smoke, odors and some other air contaminants, the practice is highly questionable because of lung tissue irritation found to occur above 0.05-0.08 ppm of ozone.

## **OZONE STANDARDS AND GUIDELINES**

The American Lung Association would like the public to be very aware of the following standards and guidelines established to protect lungs. The Food and Drug Administration (FDA) has set a maximum level of 0.05 ppm ozone that can be emitted by any electronic device sold as medical equipment. The American Society of Heating, Refrigeration, Air

Conditioning Engineers (ASHRAE) guidelines for indoor air are that the level of ozone to which the public may be exposed should not exceed 0.05 ppm. The Occupational Safety and Health Administration standard for the worksite is 0.1 ppm averaged over an eight-hour workshift. This OSHA standard was established only considering the strong and healthy worker. The American Lung Association and many experts feel the standard should be lowered to 0.08 ppm. The goal for compliance by the nation's cities for outdoor air is the National Ambient Air Quality Standard (NAAQS) for ozone of 0.12 ppm as a one-hour maximum concentration not to be exceeded more than once per year. If ozone should reach levels of 0.275 ppm in cities with ozone problems, experts recommend all outdoor sports and games involving physical activities be suspended. Community calls indicate that many people are under the belief that there is a difference between indoor generated ozone and outdoor ozone. The health effects are no different for indoor vs. outdoor exposure. There is no "good ozone" and "bad ozone". Ozone is ozone wherever it is breathed. People who ignore established standards to buy equipment for the purpose of generating increased levels of ozone indoors with the belief they are "cleaning" their air, or who allow malfunctioning electrical equipment to produce excess amounts of the gas, are risking damage to their airways and lungs. We cannot recommend the use of such devices because of the possibility of reaching elevated levels in enclosed spaces. The concentration of ozone in the air of a room depends on many variables: distance from the source, rate of generation, ventilation and amount of particulate matter in the air to react with ozone.

### **SYMPTOMS OF OZONE EXPOSURE**

The characteristic odor is detectable as low as 0.01 to 0.05 ppm; however, as the concentration of ozone increases, the ability to smell it may decrease when a person is frequently exposed. Using the sense of smell is not a reliable method to determine strength or ozone. At levels of 0.05 ppm some ozone sensitive people begin to experience irritation to the eyes, nose, sinuses, throat and lungs leading to runny eyes and nose and coughing. Tightness of the chest, shortness of breath, pain on deep inspiration, substernal pain, and wheezing may occur as levels approach or exceed 0.12 ppm. Less common complaints are blurred vision, headache, nausea, vomiting and malaise or tiredness. Dosages at which symptoms appear vary with the sensitivity of the person and the degree of exercise or other physical exertion occurring. Air intake can increase as much as ten times average breathing and be drawn deeply into the lungs with exercise. Worrisome about ozone exposure is that many studies have demonstrated a "Tolerance" or "adaption" effect, in which one exposure might decrease symptomatic reaction to following exposures. Tolerance is not viewed as a useful protective mechanism. In fact, there is concern among health scientists that people may be further damaging their health by continuing their exposure to ozone due to moderation of symptoms after repeated exposures. Recent research in animals has shown that persistent damage to lung cells accumulates even as functional adaptation takes place.

### **HEALTH EFFECTS OF OZONE**

Tests carried out on healthy adults and children undergoing heavy exercise have found decrease in normal lung function at the federal health based outdoor air standard of 0.12 ppm. When the level of exercise was increased or when the level of ozone was increased, it took a shorter period of time to see the same lung function deficits. Recent research on longer exposures of 6 in hours at or just below 0.12 ppm found even larger reductions in lung function, biological evidence of inflammation of the lung lining and more frequent respiratory

discomfort. The lowered lung function from such short-term exposure may persist for days. Questions remain whether frequent short-term effects have long-term consequences. Recently, attention has begun to focus on the effects of long-term, repeated exposures to high levels of ozone. Although such research tends to use animals, study of a sample of long-time residents of Los Angeles, which has the highest and most frequent ozone smog problem in the nation, found that the group had a higher than expected loss of lung function over time. Long-term exposures of animals to moderate ozone levels produce changes in the structure of the lung. Damage usually occurs at points where the smallest bronchial passages (airways) merge into alveoli (air sacs). The affected tissue becomes inflamed and swollen, fluid leaks from the bloodstream into the air spaces, the rate of cell division may increase, and the most sensitive cells may be replaced by different types more resistant to ozone. Larger bronchial passages usually are not as affected, perhaps because their surfaces are better protected by a layer of mucus. These effects are most obvious at exposure concentrations of 0.5 ppm and higher, but they may occur in exposures to as little as 0.2 ppm for as little as two hours. If exposure lasts for weeks or months, either continuously or intermittently, the damage tends to remain, and may be produced by levels as low as 0.12 ppm in laboratory animals. Ozone also appears to disturb lung defenses against bacterial infections.

### **INDIVIDUALS AT GREATEST RISK**

The U.S. Environmental Protection Agency (EPA) has identified three groups of people who are at particular risk from high ozone levels: people with pre-existing respiratory disease, who may not be able to tolerate an additional reduction in lung function; a subgroup of the general public referred to as "responders" who experience greater lung function losses than the average response to ozone -- approximately 5 to 20 percent of the U.S. population; individuals who exercise or otherwise increase their respiratory rate during activity in environments with elevated ozone. The American Lung Association also wishes people to realize that children are more vulnerable to pollutants than adults. Their airways are narrower and irritation, producing only a slight response in an adult, can cause a dangerous level of swelling in the lining of their narrow airways. Children also breathe more rapidly and inhale more pollutants per pound of their body weight than does the adult. Parents should be aware that studies show that while ozone causes symptoms in adults at peak outdoor levels, there is a large set of data indicating that such symptom response does not occur in children. Lung function testing has been done at summer camps during peak ozone periods. What this suggests is that children may suffer lung irritation but not sense or complain about symptoms.

### **RECOMMENDATIONS**

The American Lung Association recommends against installing any equipment to use in occupied indoor spaces for the purpose of increasing ozone levels. (We are not talking about ozone generators used for water purification or used in special cases in unoccupied spaces to control odor problems such as after a fire.) Other unnecessary electrical equipment with brush type motors should also be avoided. Special ventilation may be needed for ozone sources such as photocopiers. Electrostatic air filters should be maintained regularly. For short-term exposure, lung irritation and decreased pulmonary function usually return to normal within a few days depending upon the dosage of ozone experienced. For long-term exposures or if one suspects they are experiencing ozone related respiratory problems, it is suggested that they make their physician aware that they have been exposed to elevated levels of ozone because one would not usually consider it as the source of a respiratory problem in this part of the

country. Respiratory examination is needed and possibly pulmonary function tests. Depending upon the situation, your family doctor may refer you to a pulmonary medicine specialist, respiratory allergist or occupational medicine physician.

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# Ozone-therapy Today

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There are several reasons explaining why autohaemotherapy after ozone treatment has remained in a scientific limbo: firstly, the biological basis have remained nebulous and have been barely studied [1,2], partly because of lack of financial support by the pharmaceutical industry, secondly the therapeutic schemes have been elaborated on personal bias rather than on the evaluation of objective parameters [3,4], thirdly clinical experience, although vast, had remained limited to private practice with the consequence that results have been reported on an anecdotal fashion and never published in peer-reviewed journals [1,3-8]; even worse, a few quacks have completely discredited ozonotherapy by claiming wonderful results and exploiting patients. Fourthly, ozone has often been used improperly without knowing exactly its physicochemical properties [9] and fifthly, the awareness that ozone is one of the worst pollutant and can generate formation of oxidizing compounds [10-14] has comprehensibly originated a strong prejudice for its use. Thus, it is not surprising that the use of ozone for medical purposes is only allowed in Germany, Austria, Switzerland, Italy, Russia, Cuba and in a few States of USA. England and France, although widely using ozone for the treatment of drinking water, refrain from using it in Medicine. This involutive state of affairs has now undergone a critical reappraisal by considering that:

- a) Of the various routes of ozone administration, the exposure of a volume of blood to a precise ozone dose offers a meaningful and reproducible delivery system.
- b) Ozone is now considered a cytokine inducer with a definite benefit/risk ratio. As a consequence, autohaemotherapy may favour immunorestitution in secondary cellular immune deficiencies.
- c) Blood cellular components display such a marked functional heterogeneity that under ozone action quite different biological responses have to be expected. This does not exclude however, that therapeutic activity in each disease has a multifactorial origin.

## **Routes of ozone administration in different pathological conditions.**

The solubility of ozone in water, is about 50% higher than oxygen and it follows Henry's law [1,15]. However when ozone dissolves in the plasma, Henry's law is no longer valid because ozone decomposes in about one second and generates a cascade of unstable and highly reactive oxygen intermediates (ROI) among which are aldehydes, ozonides, hydrogen peroxide and lipid hydroperoxides that almost instantaneously react with membranous and cytoplasmic components [1,14-17]. On the other hand, cells and body fluids contain a wealth of antioxidant compounds such as vitamins, low molecular weight compounds and proteins [18] as well as a number of enzymes able to either scavenge ROI or to rapidly regenerate reducing compounds. Both parenteral (intravenous, intra-arterial, intramuscular, subcutaneous and intra-articular) and local (nasal, tubal, oral, vaginal, vesical, colorectal and cutaneous) routes have been used [1,3] for the treatment of a number of pathological states with ozone (Table 1 [19-26]). One is

surprised to note that, with the exception of the intravenous route, only minor side-effects have been observed probably because the potential toxicity of ozone is largely quenched by the body antioxidant reservoir and because the initial irritating (burning feeling) action of ozone in tissues is within few minutes followed by analgesia.

Use of the intravenous administration route is extremely dangerous because even if the gaseous mixture of oxygen-ozone is administered very slowly with a pump, it frequently procures lung embolization and serious side effects, particularly when daily dosing is up to 120 ml. Moreover, to the best of my knowledge, this procedure does not yield clinical benefit and no data have been published.

Jacobs [27] has analysed the type of accidents and side-effects after ozonotherapy in Germany in a total of 5,579,238 applications performed in 384,775 patients up to 1982. Although the **percentage of accident due to ozone was 0.0007 %**, it nonetheless included four fatalities most likely due to lung embolization while the remaining were minor accidents due to technical mistakes. During the last decade the administration of ozone via the intravenous route has been prohibited in Europe but regrettably someone still uses it in USA.

Intraarterial administration of O<sub>2</sub>-O<sub>3</sub>, useful for treating chronic limb ischemia, is far less risky probably because only a small volume of gas is injected and because there is rapid gas solubilization and absorption at the capillary level [3,4,6,8].

Administration of up to 150 ml of O<sub>2</sub>-O<sub>3</sub>, via intramuscular and subcutaneous routes is painful for a few minutes, and although therapeutic efficacy is claimed to be good, convincing clinical data are lacking [3]. My prejudice against these routes, particularly when used for immunomodulatory purposes, is that ozone dosing is totally empirical because no stoichiometric relationship can be defined between the ozone dose and the unknown volume of blood exposed in an internal cavity or tissue.

Of the local treatments, the cutaneous one (for torpid ulcers or necrotic lesions due to vascular limb disorders), is free of side effects and effective particularly when combined to autohaemotherapy [3,6,8,15].

Colorectal insufflation over a period of one minute of up to 800 ml of O<sub>2</sub>-O<sub>3</sub> (ozone concentration 20 ug/ml) is reported to be free of side-effects and effective in AIDS patients with intractable diarrhoea and in hepatitis patients [28-30]. This route ought to be borne in mind because the procedure of execution is simple, it can be done by the patient at home and it is a practical alternative when there is not a venous access. However, so far neither endpoints are available for establishing an optimal dosage for this route, nor do we know how ozone insufflated into the colon lumen works. While there will occur an improved oxygenation of portal and peripheral blood [29] and possibly of intestinal lymph, we can only speculate on the activation of the colon-associated lymphoid system. It remains also unknown whether the bactericidal activity of ozone enhances absorption of bacterial compounds, similar to muramyl/peptides, with immunoenhancing properties.

In conclusion, all of these routes have the disadvantage that ozone dosing has to be defined on a trial and error basis which is difficult and time-consuming to assess. Thus, at present time,



ozonated autohaemotherapy, first described by Wehrli and Steinbart [31], represents the best option because it implies an almost stoichiometric relationship between a known dose of ozone versus a volume of blood measured by weight (about 105 g correspond to 100 ml) and because we can correlate several biochemical and immunological parameters with ozone dosing. These are crucial advantages that associated with the simplicity of the procedure, portray ozonated autohaemotherapy as a very important therapeutic possibility. After the discovery [32] that endothelial and other cells synthesize NO, that is an inorganic free radical gas and use it as a mediator and immune modulator, we ought to examine without any bias the biological activity of ozone.

### **Induction of cytokines from blood mononuclear cells (BMC) during ozonation.**

Autohaemotherapy represents an almost ideal model because there is a reasonable stoichiometric relationship between ozone and blood. However, even in this case, among blood samples there are unavoidable uncertainties such as a variable amount of antioxidant compounds [18,33], of intracellular reducing enzymes [33,34], as well as quantitative and qualitative differences in cell components. As we have found [35,36] already great variability among normal donors, we expect an even greater variability among patients and for this reason, rather than suggesting an optimal ozone concentration (around 70 mcg/ml ozone per ml of blood at normal barometric pressure), we propose that effective ozone concentrations range between 50 and 80 mcg/ml without any evident toxicity when erythrocyte counts range between  $3.5-5.0 \times 10(6) / \text{mm}^3$ . Within these concentrations there is no formation of metahaemoglobin, either haemolysis or intraerythrocytic reduced glutathione levels remain below 3.0 or 10%, respectively [35,36], cell viability is normal and no morphologic cell damage is evident by electron microscopic analysis (Bocci et al., manuscript in preparation).

The new result which has confirmed the hypothesis that ozone can act as a cytokine's inducer [37] is that blood, after being exposed for a few minutes to concentrations of ozone ranging from 10 up to 90 mcg/ml (per ml of blood) at normal barometric pressure, upon the usual incubation in air/CO<sub>2</sub> (95/5%) for up to 72 hours, progressively releases small amounts of cytokines such as interferon (IFN) B and  $\gamma$ , tumor necrosis factor (TNF $\alpha$ ), interleukins (IL) 1B, 2, 4, 6, 8 and 10, granulocyte-macrophage, colony-stimulating factor (GM-CSF) and activated transforming growth factor (TGF) B1 [35,36,38-40]. IFN $\alpha$  has been barely detectable and other cytokines will be measured as soon as we have suitable reagents. At least for IFNs B/ $\gamma$  and TNF $\alpha$  there is correspondence between biological and immunoenzymatic activities. In spite of great variability among normal blood samples, that is a normal fact due to the existence of either low or high responders [41], there is an ozone dose/cytokine response effect that tends to level off when ozone concentration reaches the 70 ug/ml mark. At the 105 ug/ml level, that is the maximum ozone concentration delivered by the generator, we have often noted a depressed cytokine production suggesting a possible cytotoxic effect [40]. Cytokine production is markedly depressed when blood is collected in the usual Ca<sup>2+</sup> chelating solution (citrate-phosphate-dextrose) and incubated in the absence of extracellular Ca<sup>2+</sup>. This finding led us to test the physiological anticoagulant, i.e., heparin (25 U/ml of blood) additioned with CaCl<sub>2</sub>, to a final concentration of 5mM [35]. Thus, a five-fold surplus of extracellular Ca<sup>2+</sup> (physiological Ca<sup>2+</sup> level is about 1 mM) displays a superinducing effect [2] but it must be noted that further Ca<sup>++</sup> addition up to 50 mM, although modestly increasing cytokine's production, yields a prohibitive haemolysis [35]. However, heparin occasionally presents the problem of excessive anticoagulation as it has recently occurred in two hepatitis

patients leading us to re-evaluate whether CPD treated blood, once heparinized and recalcified at physiological levels, is sufficiently activated. Data to be reported soon have shown that, after  $\text{Ca}^{2+}$  addition, the production of cytokine is partially restored whereas blood sample incubated without  $\text{Ca}^{2+}$  are consistently inhibited. These results have practical importance because they indicate that either CPD<sup>-</sup> or heparin-treated blood after ozonation and reinfusion will release similar amounts of cytokines in vivo. As a rule now, for patients under anticoagulant therapy, or aspirin, or prone to the haemorrhagic syndrome, or thrombocytopenia or hepatic dysfunction, we collect blood in CPD only thus avoiding any risk of dyscoagulation.

How ozone acts at the cellular level remains uncertain and for the time being, it is a matter of speculation. Probably ozone may oxidize unspecifically some carbohydrates, probably galactose [42,43], present on the cell membrane lectins leading to a coupling with transducer proteins and to an enhanced  $\text{Ca}^{2+}$  influx. Moreover ROI can passively diffuse through the cell membrane and activate the gene-regulatory Nuclear Factor-Kappa B (NF-Kappa B) that appears to play many roles in the immune cells and certainly causes gene activation for several cytokines [44,45]. At the present our working hypothesis is that ozone acts unspecifically: the bulk of generated ROI is consumed by antioxidant substances in plasma and by the huge amounts of phospholipids present in erythrocytes because their membranous surface is as large as  $70 \text{ m}^2$  per 100 ml of blood. As there is about 1 BMC every 3000 erythrocytes, there should occur a transient overproduction of ROI, for them to reach the trans-activating factor in the cytoplasm and release the inhibitory subunit I Kappa B. Schreck et al [44] have indicated a threshold of about 30  $\mu\text{M}$  of hydrogen peroxide to be effective in their system, implying that if ROI are not homogeneously distributed, BMC will not be activated. We do not envisage and actually we do not notice cell damage because intracellular catalase, superoxide dismutase as well as other reducing enzymes and chainbreaking compounds [14,17,18,33], are capable of quickly neutralizing or scavenging residual ROI terminating the ozone action. In conclusion it would seem that ozone dosing is critical in the sense that if it is too low it is probably ineffective while if it is excessive, it may induce oxidative stress and eventually cell apoptosis [46].

Another interesting characteristic of this approach is that blood, after being thoroughly exposed to  $\text{O}_2/\text{O}_3$  ex vivo for 5 minutes can be reinfused in the donor without practically any trace of ozone. Only the  $\text{pO}_2$  level, from a baseline value of 33-40 mmHg reaches in a few minutes a plateau level of about 400 presumably returning to the original value after gas exchange in the capillaries. Lipid hydroperoxide levels in plasma increase about 3-fold immediately after ozonation and return to baseline values within 3-4 hours when blood is incubated in vitro. However it is most important to note that in vivo, even 5 min after reinfusion, peroxides in the plasma remain at baseline value.

Both CPD- and heparin-treated blood are occasionally mixed to minimize erythrocyte sedimentation and reinfused fairly rapidly without any vascular or respiratory distress. In order to stabilize the plasma levels of antioxidants and to make sure that patients receive a normal vitaminic support we have always described a daily multivitamin (including vitamin C and E) supplement.

### **Mechanisms of action of ozonated autohaemotherapy.**

Until recently it was thought that in chronic viral diseases, the virucidal properties of ozone were of paramount importance [1,3,7,21,47-49] for the therapeutic effect, neglecting the fact that the viral reservoirs are the internal organs (liver for hepatitis, lymph nodes and spleen for HIV infection, neuronal ganglia for herpes viruses etc) and that less viral particles are free in the plasma, implying a minimal direct effect during exposure of a small aliquot of plasma to ozone [50]. Moreover it was reported that after ozonation, leukocytes improved their phagocytic activity and that immunoglobulin levels could increase without underlying the causes of these biological effects [51]. The breakthrough has come with the demonstration that ozone acts as an inducer of cytokine's production [35,36,38-40]. Since then the approach of ozonized autohaemotherapy has gained a rational basis and one can understand why synthesis of antibodies can be stimulated by IL-6. enhanced phagocytic functions and leukocytosis can be due to IL-8 and GM-CSF and how both direct and indirect antiviral activities can be stimulated by IFN $\beta$ ,  $\gamma$  and TNF $\alpha$ . In viral diseases, however, it cannot be excluded that small amounts of free virus inactivated in the plasma during ozonation may act either as an endogenous immunogen or/and an activator of cell-mediated immunity. It is worth while mentioning that autohaemotherapy has been surprisingly used also for the treatment of autoimmune diseases such as rheumatoid arthritis [52] and it would be desirable to investigate whether particular ozone concentrations may enhance the release of inhibitory cytokines leading either to the suppression of autoreactive cytotoxic T cell clones or/and to the blocking of inflammatory cytokines by the release of either soluble receptors or/and cytokine antagonists. It is possible that the release of IL-10 [53] and TGF $\beta$ 1 [54,55] can serve the useful purpose of quenching an excessive immune stimulation, thus leading to an orderly reprogramming of immune responses.

#### **Distribution and fate of ozonated blood cells after reinfusion.**

With the exception of the most aged erythrocytes that, being more susceptible to ozone, are likely to be taken up by the reticulo-endothelial system [56], it is reasonable to speculate that most erythrocytes will continue to circulate in the vascular system. On the other hand, activated BMC may home in various lymphoid and non-lymphoid organs and we plan to verify this possibility with Indium-111 labelled cells as soon as possible. If this happens, as we have shown during in vitro incubation [35,36], BMC will release around the pericellular environment various cytokines which can bind to the appropriate receptors on neighbouring stationary or in transit cells. In comparison to classical mitogens, which can easily activate 10-20% of the isolated BMC causing the synthesis of large amounts of cytokines, depending upon the fairly critical ozone dosing, a smaller percentage of BMC appears activated so that the minute amount of released cytokines is consumed in cellular microenvironments and does not emerge in the general circulation via the lymphatic system. This tentative explanation is supported by two pieces of evidence: firstly, we have never detected any significant change in cytokine's levels in the plasma of healthy volunteers at 1, 3, 6, 9 and 24 hours after reinfusion of ozonated blood [57]. In contrast, after injection of as little as 4 ng/Kg body weight of endotoxin in patients, there is a massive release of pyrogenic cytokines with IL-1, IL-6 and TNF $\alpha$  peaking a few hours after endotoxin administration [58]. The second point is that although autohaemotherapy does not allow the release of endogenous cytokines in the circulation, which is an important advantage. it has a real biological effect because 48-72 hours after reinfusion we have measured [57] in BMC an increase of the Mx protein that is one of the best indicators of IFN release [59]. The progressive enlargement of the area under curve of Mx protein versus time throughout autohaemotherapeutic treatments suggests that in vivo there

occurs a progressive amplification of the priming and IFN production [57]. Thus, ozonated autohaemotherapy may be assimilated to a slightly enhanced physiological response [41,60] due to a gaseous inducer which acts rapidly and disappears. Further support to this interpretation is that typical side effects such as chills, fever, fatigue and nausea never occur after autohaemotherapy and actually the patients often report a sense of well-being and euphoria that may be due to improved oxygenation or/and release of hormonal factors not yet identified. As far as the number of treatments to be carried out is concerned, one treatment only can be hardly effective as the number of ozonated BMC present in 300 ml of blood is probably less than 0.1% of the total BMC mass [61]. If this calculation is correct, only the prolonged repetition of autohaemotherapy (two treatments weekly for several months) can allow a progressively amplified activation of the immune system via numerous pathways such as activation of either major histocompatibility complex-restricted cytotoxicity, or unspecific killing and removal of viral-infected and metastatic cells. Table I reports a list of chronic viral diseases or pathological situations accompanied by either immune deficiency or immune dysregulation, where ozonated autohaemotherapy has and could play a beneficial role.

Autohaemotherapy may prove to be very useful as an adjuvant treatment particularly if either chemotherapy or/and radiotherapy have been effective in reducing the tumor mass. Several immunotherapeutic approaches such as: a) therapy with monospecific or bispecific antibodies [62]; b) adoptive immunotherapy with more or less genetically engineered cells [63]; c) exogenous administration of either an array of immunostimulants [64] or/and d) of recombinant cytokines such as IFNs, IL-1, 2, 3, 6 and 12, TNF $\alpha$  and leukopoietins are being actively pursued. Approaches a to c are in a more or less advanced experimental phase while therapy with cytokines has dominated the scene in the last decade. Unfortunately pharmacological administration of cytokines, that physiologically are not present in the circulation, causes a substantial increase of their plasma levels which correlate well with fairly severe toxicity [65]. Clinical results in solid neoplasms have been far below expectations and the cost/benefit ratio is very high [66].

### **The variety of biological effects depends upon the heterogeneity of blood cells.**

While immunomodulatory effects are due to BMC activation, the beneficial effect of autohaemotherapy in chronic limb ischemia, in cardiac, ophthalmologic and cerebral vasculopathies [3,4,6,8,22] in infections and in burns [1,3,4,6,8,15,19,20] can be explained by improved transport of oxygen due either to increased oxygen availability, or oxygen delivery to hypoxic tissues due to an increase of 2-3 diphosphoglycerate in erythrocytes. The rapid healing of torpid ulcers in ischemic disorders is becoming particularly interesting since the demonstration that transforming growth factors (TGF) B1 accelerates the healing process [67-69] and that levels of activated TGF B1 increase substantially after ozonation of blood, probably due to partial degranulation of platelets [40]. There is no doubt that improved oxygenation enhances cell metabolism and proliferation and that the local application of ozone inhibits bacterial infections but, until now, the crucial role of proteins such as TGF B1, vascular endothelial growth factor (VEGF) for enhancing neovascularization [70] and healing has not been taken into account. Thus it appears that clinical benefits possibly derive from the activation of erythrocyte function, the release of either TGF B1, other growth factors and by improved leukocytic functions in terms of removal of necrotic tissue and bactericidal activities.

### **Final remarks**

It has been pointed out that ozonated autohaemotherapy performed with an optimized procedure represents a powerful therapeutic approach. Its main advantages are the lack of toxicity, often a feeling of well-being and the equilibrated, although slow, stimulation of cytokine production accompanied by improved oxygenation and metabolism. Both in the treatment of neoplasia, particularly after chemotherapy, and of chronic viral diseases the frequent report of well-being after treatment is relevant because the quality of life of these patients is generally poor. We are planning to investigate the reason of euphoria and we believe that it may be due to an immune-neuroendocrine response elicited by the ozonated blood. On clinical ground there is also the need to carry out extensive and well-controlled clinical trials in several diseases including HIV infection [50]. The treatment is simple to execute, safe, far less expensive than comparable procedures and could be carried out easily also in Third-World Countries where it could be applied also to several parasitic diseases.

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# Ozone in Preventive Medicine

by E.G. BECK

Unfortunately the tables had to be omitted

The spreading of contagious diseases via drinking water has played a tragic part in history. It was not until the end of the 19th century, after Pettenhofer and Koch had established a basis for effectively combating epidemics and preventing infections, that they concentrated on disinfecting drinking water supplies. Even if, as early as 1900, the monitoring of water supply systems had been legally enforced by the Imperial Law on Contagious Diseases [Reichsseuchengesetz], it was not until 1976 that a Regulation on Drinking Water [Trinkwasserverordnung, TrinkwV] ensuring health maintenance and consumer protection came into force based on the enactment of the Federal Law on Contagious Diseases [Bundesseuchengesetz]. In addition to this, in 1980, the "Guideline on the Quality of Water for Human Consumption" [Richtlinie über die Qualität von Wasser für den menschlichen Gebrauch] was announced and thus enforced by the European Community. In 1991, an amendment was made to the German Regulation on Drinking Water [TrinkwV] which included the "treatment of drinking water" [Trinkwasseraufbereitung] in its provisions. In this way all demands on the quality of drinking water were comprised within a single regulation for the first time.

Nowadays, on the basis of the Federal Law on Contagious Diseases [Bundesseuchengesetz] (p 11, Section 2) and the Foods and Utilities Law [Lebensmittel- und Bedarfsgegenstandegesetz] ( 9 and 10), the fact now applies that drinking water must constitute so that no damage to human health, in particular through pathogens, as a result of its consumption or use.

Naturally, this legal principle is also valid for the drinking water used in medical practices and hospitals, i.e. for "medically used drinking water" (Tab. 1), also including the medical field of balneology.

## **Drinking water for medical use**

Hospitals are generally supplied by drinking water from the main system (public utilities), where it is being used for for risk patients with an increasingly weakened resistance, in the care and treatment of patients, for diagnostic and therapeutic measures as well as in the operation of technical medical equipment, where additional quality criteria play a part. Microbiological and chemical contaminations in drinking water generally originate, not from the drinking water supplied, but in a secondary fashion through technically required or necessary subsequent treatment in the hospital or practice.

In fact, where "medically used drinking water" is involved, populations of microorganisms far above the legal limits and guidelines found in regulations [here the Regulation on Drinking Water, Trinkwasserverordnung] are counted at the outlets or pick-up points of dental units.

The main reason for this is direct and indirect contamination of drinking water with problem microorganisms at the practice or clinic involved, possibly caused by bad maintenance of ion exchangers as well as in a retrograde manner on contact with the patient via germs which have been transferred from the his/her mouth up into the tube systems via suction valves, where they are able to proliferate due to the frequent stagnation of the water in the narrow tubes involved as well as due to the plastic material used. Such pathogenic organisms are modest in their needs, frequently using the plastic as a source of the carbon basic to their metabolism

(*Pseudomonas*, *Staphylococcus*) and changing their surface to form a slimy coating which is generally resistant to the active constituents of disinfectants.

Particularly where invasive dental treatment is concerned, the risk of infection is increased due to a break in the integrity of the buccal mucosa, or when hemorrhages occur. As regards the infections thus caused, the immune status of the patient concerned plays a decisive part. It must here be remembered that, in future, due to the rising percentage of elderly persons in the population, as well as due to the effects of environmental pollutants, a continuously increasing number of patients with immune deficiencies will have to be accounted for. Resultant infections or infectious diseases occurring later due to their long incubation periods, such as hepatitis B or C, are generally absent from patient histories and thus avoid infection control by the dentist involved (Tab. 3)

This can all be prevented to a considerable extent if the medically used drinking water is continuously disinfected with ozone during treatment. Due to the special demands made of medically used drinking water in practices and hospitals, a constant quality control must be ensured. In § 13 (1) No. 4 of the Regulation on Drinking Water [TrinkwV], the relevant authority is provided with the possibility, over and beyond the indicator group of pathogens, to have tests carried out for *Pseudomonas aeruginosa*, pathogenic *Staphylococcus aureus*, atypical mycobacteria as well as for fecal bacteriophages or enteropathogenic viruses. Due to the frequent contamination, for example of dental treatment units with *Pseudomonas aeruginosa* and *Legionella pneumophila*, an extension of the microbiological testing of drinking water on the basis of § 13 (1) No. 4 of the Regulation [TrinkwV] in this field is expedient.

This is also the aim of the Guideline on Hospital Hygiene and Infection Control [Richtlinie für Krankenhaushygiene und Infektionskontrolle (RKI Annex to Paragraph 5.6 under 2.7)], according to which the hygienic tests must be carried out on water at specified sample-taking points. This correspondingly includes the Annex to Paragraphs 4.4.6 and 6.7 of the Guideline entitled: demands for hygiene made on the water supply "among other factors, particularly in dental units (e.g. for the number of colonies of *Pseudomonas aeruginosa*, *Legionella* spp.) at half-yearly intervals" in order to "recognize and combat infections acquired in medical installations" (Annex to Paragraph 5.6.3).

This is one of the reasons why we recommend and use ozonized water for the continuous sterilization of dental treatment units. As early as the turn of the century, ozone was being used as a disinfectant. We are here dealing with one of the most powerful disinfectants in existence, which has bactericidal, fungicidal and virus-inactivating properties (Tab. 4).

Thus, all obligatory pathogens (classical infectious pathogens) as well as the facultative pathogens (hospital-specific, problematic pathogens) are included whose presence can be demonstrated where the contamination of drinking and swimming pool water as well as of "medically used water" occurs (Tab. 5).

This equally applies to viruses which can be transmitted via water such as, for example, the pathogens of hepatitis A, B, C in addition to viruses causing conjunctivitis, echo-, rota- and adenoviruses. An ozone concentration of 0.4 mg/L, which must, however, be maintained for longer than four minutes is considered to be necessary for effective disinfection (WHO) (Tab. 6)

The ozone concentrations given and their time of effect on microorganisms and viruses produced the definition of the "CT value" which is the product of the ozone concentration in water at mg/L and the time in minutes during which this ozone concentration is maintained. This means that, independently of the microorganisms involved, shorter exposure times at higher ozone concentrations and/or longer exposure times at lower concentrations can also

obtain the required degree of success.

A quality control of "medically used drinking water", i.e. with a minimum quality corresponding to the requirements of the German Regulation on Drinking Water [Trinkwasserverordnung, TrinkwV] and the European Community's Guideline on the Quality of Drinking Water, the addition of ozone is also safely provided for where the continuous disinfection of a quantity of water necessary for treatment passing through a dental unit is required. In addition to this, the ozonized water can be therapeutically effective, i.e. acting as a disinfectant, oxygen-releasing and granulation-accelerating agent in the tissue. Furthermore, the use of chemical additives in the rinsing and cooling water the dental units, a factor often considered when other sterilizing agents are required, is not necessary when using ozone due to its comparatively wider range of action and its toxicological safety due to its rapid disintegration.

The oxidizing and thus microbicidal and virus-inactivating effect of ozone is more than just in the foreground for preventive medicine; its preventive and therapeutic effect in the context of oxygen release and/or circulatory improvement, immunostimulation, infection prevention and therapy means that it will find for itself an increasingly justified place in medical science (geriatrics, environmental medicine).

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## SWIMMING POOLS AND HOT TUBS

The following information on the use of hydrogen peroxide for swimming pools/hot tubs is considered experimental. Check with your swimming pool or hot tub manufacturer about the compatibility of hydrogen peroxide to your system.

### Swimming Pools

It has been found for start up that 1 pint of 35% food or technical grade hydrogen peroxide should be added for each 1000 gallons in the pool system. Let stand for one day with the circulation pump running intermittently. (Dr. Donsbach indicates from his experience that an average size pool takes about eight gallons to begin with and then one-half to one gallon must be added per week.) The pool should be maintained at 40 parts per million. This can be determined by peroxide test strips or by use of a titration kit.

It is extremely important to keep the filters clean. The addition of an ultra violet light or an ozonator will reduce the amount of hydrogen peroxide that you will need to add.

Sunlight will dissipate hydrogen peroxide just as it dissipates chlorine, so regular additions of  $H_2O_2$  will have to be made. The number of people using the pool or frequency of pool use determines the amount of  $H_2O_2$  that must be added.

Most water from municipal water supplies contains chlorine. This is why the original "shock" of a large amount of hydrogen peroxide is necessary for start up. Hydrogen peroxide forces chlorine out of the water in the pool or hot tub.

One incident where  $H_2O_2$  did not work in the pool was because of the mineral content of the water. A diatomaceous filter will require more attention than a sand filter because a diatomaceous earth system will filter out smaller particles than a sand filter. If you have a diatomaceous earth filter, the addition of a paper filter ahead of the filter will keep it from clogging up as frequently.

Just a note as to what may happen with extreme amounts of hydrogen peroxide. I swam in a pool with one hundred parts per million and noted on getting out of the pool the dead skin flakes that floated on top of the water. It was very refreshing.

### Hot Tubs

Check with the hot tub manufacturer to determine the compatibility of your system with  $H_2O_2$ . The average size hot tub could be started up with one quart or more of 35%  $H_2O_2$  until it tests 40 ppm. Turn the circulation pump on to distribute it evenly, then intermittently during the next 24 hours. Add enough hydrogen peroxide from time to time to maintain it at approximately 40 parts per million.

Peroxide test strips can be ordered from:

Lab Safety Supply  
P.O. Box 1368  
Janesville, WI 53437  
1-800-356-0783

H<sub>2</sub>O<sub>2</sub>, Inc.  
2560 Muhlenhardt Road  
Shakopee, MN 55379  
612-496-1417

Jerry Freeman  
4853 Joyce Drive  
Dayton, OH 45439  
513-299-4283

Titration test kits for hydrogen peroxide are available from:  
Hach World Headquarters  
P.O. Box 389  
Loveland, CO 80539  
1-800-227-4224

CHEMetrics, Inc.  
Rt. 28  
Calverton, VA 22016  
1-800-356-3072

*"Many feel it to be the most promising, safe and effective treatment for major degenerative diseases, from cancer and arthritis to AIDS and chronic fatigue. It's ozone-medical ozone-considered the most dynamic of the many oxygen therapies. -Gary Null*

## **WHAT IS MEDICAL OZONE**

The ozone layer on high keeps the planet and us from sizzling like kebobs on a barbecue. Closer to home, ozone has a bad name-it creates smog. But unlike its atmospheric cousins, ozone in its pure form-O<sub>3</sub>, or medical ozone-is a potent cleanser and detoxifier. Ozone frees oxygen in the system like wildfire, disabling troublemakers like bacteria, viruses, parasites, fungi and cancer cells, which thrive in low oxygen environments at the cellular level. At the same time, ozone strengthens our healthy cells which normally thrive in high oxygen environments.

### **OZONE FIGHTS CANCER**

Three decades ago, Dr Otto Warburg, Nobel prize winner and director of the Max Planck Institute in Berlin, made an important discovery. He confirmed that the key precondition for the development of cancer is a lack of oxygen at the cellular level. Since we know that ozone increases oxygen to the cells, ozone is considered an anti-cancer agent. Low concentrations of ozone have been proven to produce two potent anti-cancer agents, alpha interferon and interleukin-2, which activate the immune system.

### **PROSTATE CANCER**

Naturopathic physician Dr Stanley Beyerle treats prostate cancer with an ozone protocol that he reports yields phenomenal results. He performs five treatments over the course of 20 days, and the program helps prostatic tumors shrink dramatically. Beyerle states that most prostatic cancer is contained within a capsule until it is biopsied and he attributes the overuse of biopsies to the spread of cancer within the body. He feels that a big advantage of ozone is that it successfully treats this cancer while it is encapsulated.

### **BREAST & OTHER CANCERS**

Dr Beyerle reports major improvement using ozone with other types of cancer too, including tonsil, throat, ovarian, colon and breast cancer. "I have had three breast cancer patients now who were supposed to be dead a year ago," he said.

Also, he is seeing improvement in breast cancer patients where there is metastasis to the bones, liver and spinal column. "We are seeing patients who were bedridden two years ago and sent home to die...They are becoming ambulatory. Their energy level is coming up. They are gaining weight. And we see these spontaneous fractures in the spine are gradually disappearing. Strength is returning to the musculature. There is no spinal pain," says Beyerle.

### **OZONE FIGHTS AIDS**

Research by Dr Horst Kief, the first physician to successfully treat HIV-positive patients, reports that ozone is "highly effective against viruses." The study noted an "astonishing improvement" in AIDS patients where the disease has not severely progressed and partial remission in 30% of cases of complete manifestation of AIDS.

HIV is no small matter. Nathaniel Altman, author of Oxygen Healing Therapies explains: "When I was in Cuba, I interviewed one of the chemists doing research on the subject. She said if a person infected with HIV receives ozone before it gets into the lymphatic and bone systems, HIV can be killed and stopped right on the spot."

### **OZONE HEALS HEPATITIS & OTHER DISORDERS**

"In treating hepatitis, direct AHT (a type of ozone treatment) has been demonstrated countless times as being effective. By doing this procedure, at least 15-21 days, we've been able to see hepatitis completely wiped out," claims pioneering physician Dr John Pittman. Besides ozone's success treating different types of hepatitis, cancers, and AIDS, physicians report particular success treating candida, allergies and bladder infections. Other disorders treated with ozone therapy include: herpes, arthritis, respiratory conditions, multiple sclerosis, sexually transmuted diseases, parasitic infections, gastrointestinal disorders and problems with wound healing. In some countries, there is an ozone generator in the emergency room of every major hospital, particularly benefiting heart patients and stroke victims.

### **THE SAFETY OF OZONE**

Over the past 40 years, an estimated ten million ozone treatments have been given to over one million patients in Germany alone. According to scientific research, ozone therapy is amazingly safe and nontoxic. Adverse reactions are astonishingly low-one data review reported fewer than six thousandths of one percent. The reactions include mild muscle pain and occasional fever. Compare that to the toxic side effects of many pharmaceuticals and surgical procedures. Ozone therapy has been benefiting clinical practice since WWI, but primarily in Europe. While there are fifteen thousand ozone practitioners in Europe alone, the U.S. has been slow to recognize ozone's wide-spectrum healing abilities. When will mainstream medicine and regulatory agencies acknowledge and deliver this potent healing therapy? How much longer must the American Public wait?"

## OZONE: A WIDE-SPECTRUM HEALER

Article by Gary Null, Ph.D.

*"It is my belief that the use of ozone in association with other complementary therapies can convert AIDS from a uniformly terminal illness to something that is chronically manageable, which is better than what anyone else can offer at this point."*

- Dr. John Pittman, Medical Director, The Caroline Center for Bio-Oxidative Medicine.

Many feel it to be the most promising, safe, and generally efficacious treatment for major degenerative diseases, from AIDS and chronic fatigue to cancer and arthritis. It's ozone--medical ozone. Medical ozone differs from atmospheric ozone in that it is pure and concentrated. This is an important distinction because atmospheric ozone, produced from ultraviolet radiation, is combined with different nitrous-oxide and sulfur-dioxide products and is harmful. It's not used in medical practice.

Ozone (O<sub>3</sub>) is produced by the reaction of oxygen (O) atoms with molecular oxygen (O<sub>2</sub>). This allotrope (different form) of oxygen possesses unique properties that, while they have yet to be completely defined and understood, have been benefiting clinical practice for years--albeit mostly in Europe. Most of the states in this country (USA) have yet to legalize use of the healing powers of this nontoxic molecule.

Of course, lack of official acknowledgment in no way negates the properties of any natural substance. Ozone manifests bactericidal, virucidal, and fungicidal action, which may make it a treatment of choice under certain conditions and an adjunct to treatment in others. Some of its characteristics and applications are described by Dr. Stanley Beyerle, a naturopathic physician who trained with some of the pioneers of ozone research and treatment.

"Systematically," Beyerle says, "it oxidizes organic compounds. Topically, it can be used to treat burns. Ozone has hemostatic effects that stop bleeding. It accelerates wound healing, induces enzyme production, and activates immune-system response. It is also believed that ozone may have the ability to peroxidize lipids [break up fats]."

As early as World War 1, ozone's bactericidal properties were used to treat infected wounds, mustard-gas burns, and fistulas, although these treatments were limited by the technology at the time. Current ozone therapy uses a mixture of ozone and pure oxygen, and with today's medical ozone generators, the ability now exists to deliver pure ozone-oxygen mixtures in precise dosages. The Medical Society for Ozone, based in Europe, and the National Center for Scientific Research, in Havana, currently use the treatment for a wide variety of conditions, including wound problems, gastrointestinal disorders, cancer, and AIDS. Doctors report particular success with the different types of hepatitis, as well as candida, allergies, and bladder infections. Other disorders treated with ozone therapy include herpes, arthritis, respiratory conditions, multiple sclerosis, other sexually transmitted diseases, and parasitic conditions. And this is just a partial list.

What's more, while ozone can be used to treat a wide spectrum of conditions, it can also be used prophylactically to combat harmful viruses, bacteria, and free radicals before degeneration



and disease occur. Additionally, healthy people can use ozone to rejuvenate cells to stay younger longer. As science reporter Nathaniel Altman, author of *Oxygen Healing Therapies* (Health Arts Press), observes, it is unusual that one substance can treat such a tremendous range of conditions.

"First of all," Altman begins, "it stimulates the production of white blood cells and increases the production of interferon, interleukin-2, and tumor necrosis factor, which the body uses to fight infections and cancer. It is anti-neoplastic, which means that it inhibits the growth of tumors. One study performed at Baylor University in Texas, in 1962, determined that ozone can help to kill tumors and enhance the effect of different types of antitumor drugs.

Ozone kills bacteria and viruses. In addition, it increases the amount of oxygen in the blood and helps deliver oxygen to all of the cells in the body. It also helps degrade petrochemicals. This includes different toxins that one might have in the body due to the environment or food eaten. It helps dissolve and eliminate them from the body, and hence lightens the body's toxic load. It also increases red-blood-cell membrane distensibility, making it more flexible. This is one way it is used in the treatment of heart disease. The administration of ozone changes the blood formation and helps the blood flow more effectively. In Cuba, for example, there's an ozone generator in every major hospital emergency room. It helps heart patients and stroke victims recover much quicker. It also increases the effectiveness of the antioxidant enzyme system, which scavenges excess free radicals in the body. These are just some of the things that it does.

## **HOW IS OZONE USED**

There are several ways to dispense ozone for therapeutic purposes. One is to introduce the ozone mixture into a fixed volume of the patient's blood *ex vivo* (outside the body). This method is known as autohemotherapy, and is performed mainly in central Europe. A.H.T. is claimed to have therapeutic value in circulatory disorders, viral diseases, and cancer.

With A.H.T., 50 to 100 milliliters of blood are drawn from the patient, mixed with a dose of ozone and oxygen of a predetermined concentration, and then returned via the same intravenous catheter. Once it's returned to the patient, the ozonized blood is rapidly distributed to all tissues. While it is not known how long the ozone remains in solution, its therapeutic effects have been seen to include virucidal activity, oxygenation, and increased red-cell fluidity. Some patients, upon receiving their own ozonized blood, report a faint background taste of ozone, which may be a sign of the ozone surviving in the solution for at least a few seconds. Of interest, notes Dr. Gerard V. Sunnen, of New York University- Bellevue Hospital Medical Center, in *The Journal of Advancement in Medicine*, are reports of A.H.T. patients who experience feelings of well-being lasting for a few minutes to several hours after treatment. Sunnen does not know if these feelings constitute a placebo effect, a metabolic alteration, or a neuropsychiatric phenomenon.

Another commonly used form of administration is rectal insufflation. Essentially, a catheter is put into the colon and gas from an ozone machine is allowed in at a determined concentration and flow rate. The ozone can also be self-administered this way, with a Teflon bag.

Beyerle, who is certified by the German Medical Ozone Society, studied rectal-insufflation method of delivering ozone therapy in Germany with Dr. Klaus Rilling, one of the pioneers in the field. Beyerle explains, "The blood vessels in the colon, small intestine, and bladder are the mesenteric veins, which deposit into the portal vein and go straight to the liver. The simple introduction of the catheter into the colon, at a low flow rate to increase concentration, gets ozone into the systemic venous system. Rilling says that if nothing else is done but rectal

insufflation, which does not really require a physician at all, you see dramatic results." Positive therapeutic effects on diseases of the rectum and colon have been noted with this method since 1936. Beyerle has seen people recover from irritable-bowel syndrome, colitis, and Crohn's disease, almost immediately. "There may be some initial discomfort," Beyerle says, "some bloating and gas on occasion, but as far as irritations, we have yet to see any contraindications. If you've got colitis or irritable-bowel syndrome, when ozone is administered properly, there are no negative side effects, only positive ones. It renews the mucous lining and gets to the bacterial infestation that has infiltrated the tissues of the colon." Although ozone gas can be directly injected into veins or muscles--a process known as intra-articular or intravenous application--this method can be dangerous and is not recommended. Safer therapies involve drinking ozonized water or introducing ozone to the skin in a sauna bag, after a hot shower and a brisk rubdown.

### **OZONE AGAINST CANCER**

Low concentrations of ozone have been proven to increase alpha interferon, an anticancer substance that laboratories all over the country are trying to reproduce. With ozone, the body will make its own. Beyerle elaborates on how he uses ozone in treating cancer, saying, "When I treat cancer, I want the body's immune response to take care of it and activate the immunological properties." Beyerle treats prostate cancer with an ozone protocol that he reports has yielded phenomenal results. His treatment includes taking five c.c.s. of the patient's blood, mixing it with five c.c.s. of ozone at a low concentration, shaking it up, aerating it, making sure it is saturated, and reinjecting it into the prostate. He performs five treatments over the course of 20 days, and the program shrinks prostatic tumors dramatically.

Beyerle states that most prostate cancer is contained until it is biopsied, and claims that often the spread of cancer within the body is due to overuse of biopsies. He prefers to check the prostate with ultrasound, and he feels that a big advantage of ozone is that it successfully treats this cancer while it is still encapsulated.

Beyerle reports major improvement using ozone for other types of cancers as well, including tonsillar, throat, ovarian, colon, and breast. "I have three breast-cancer patients now who were supposed to be dead a year ago," he says. Also, he is seeing improvement in breast-cancer patients where there is metastasis to the bodes, liver, and spinal column. "We are seeing patients who were bedridden two years ago and sent home to die. They are becoming ambulatory. Their energy level is coming up. They are gaining weight. And we see these spontaneous fractures in the spine are gradually disappearing. Strength is returning to the musculature. There is no spinal pain."

### **H.I.V. AND AIDS**

Recent studies support the use of ozone therapy for people who are H.I.V. positive or have AIDS. In one study, Dr. Michael Carpendale treated two male H.I.V. positive asymptomatic patients with colonic insufflations of an ozone-oxygen mixture intermittently for 180 weeks. Both patients increased their CD4 (T4) cell counts and one, after the 160th week, became polymerase-chain-reaction-negative. According to the doctor, both patients have remained in the best of health, with no infections and no adverse symptoms or malaise.

Carpendale's program consisted of insufflating ozone produced from a portable medical ozone generator through a Teflon catheter into the patient's colon. For two years the patients treated themselves daily, then weekly, with a booster does. CD4 cell counts were monitored about every two months. Studies showed that low doses of ozone in serum stimulated cell growth,

and larger doses began to suppress it. Furthermore, ozone was shown to reduce H.I.V. in serum, and did not adversely affect healthy cells.

In another study, Carpendale and other researchers used colonic insufflations of medical ozone to treat five AIDS or AIDS-related-complex patients with intractable diarrhea. Treatments were given daily for 21 to 28 days, with doses of ozone ranging from 2.7 to three milligrams. Three patients, whose diarrhea was of unknown cause, experienced complete resolution; the fourth improved markedly. The fifth patient, whose diarrhea was due to cryptosporidium, experienced no change. No adverse systemic effects were noted during treatment. Carpendale and his colleagues feel that the results of the study reinforce the findings of previous research on colonic-insufflation ozone therapy--i.e., that it is simple, safe, and effective. Further, they assert that the treatment should be used routinely to treat chronic intractable A.R.C.-AIDS diarrhea.

H.I.V. reversal is no small matter. Altman explains, "When I was in Cuba, I interviewed one of the chemists doing research on the subject. She said if a person infected with H.I.V. receives ozone before it gets into the lymphatic and bode systems, H.I.V. can be killed and stopped right on the spot."

In Germany, H. Vetter, a naturopathic practitioner, studied the results of ozone therapy with 100 patients in different stages of AIDS. He concluded, "None of the patients developed any new opportunistic infections or deteriorated, compared to their initial condition. Other infections occurred and were overcome, as in the H.I.V. negative population." Vetter reported that H.I.V. positive patients need high concentrations of ozone, and that added vitamin C enables a patient to tolerate this without the risk of hemolysis (the breakdown of red blood cells). Success was also attributed to uninterrupted ozone administration, and low reinfusion of ozonized blood.

Various protocols have been developed for treating AIDS patients with ozone. One doctor recommends 12 treatments on 12 consecutive days. "Virtually all the people I have treated--and I have treated over 170--have reversed their condition within days," he reports. "People come in on a stretcher, and within days their general condition dramatically improves." This doctor strongly believes that with AIDS, ozone is the most important modality of all, because it removes infections and that, at least in Western countries, AIDS is a conglomerate of 30 or more infectious diseases--the result of drug use or malnutrition.

## **ANTI-AGING**

An important benefit of ozone is that it increases the effectiveness of the antioxidant enzyme system, which scavenges excess free radicals in the body. Free radicals are molecules with unpaired electrons in their outer ring. Their structure enables them to latch on to other molecules and damage cells, tissues, and organs. Once this occurs, they weaken physical vitality and can damage body systems, including the neurological, cardiovascular, and immune systems.

Unlike bacteria, viruses, and parasites, which can co-exist with the body, free radicals only damage the system, causing a variety of symptoms and degenerative conditions. According to Dr. Lamar Rosquist, free radicals contribute to more than 60 diseases or health-related symptoms, ranging from aging of the skin to chronic fatigue to damage of cell membranes, leading to cell destruction, which leads to damage to D.N.A., which can cause precancerous conditions.

Some doctors envision ozone being used by the general population for its rejuvenating effects. One doctor, from a state in which ozone use is not approved, says, in fact, "This is the main

application I would like to use it for the future."

This doctor goes on to explain his enthusiasm for ozone as an anti-aging factor, saying, "Ozone, first of all, has what I have called the homeopathic ozone effect. This reverses most latent overt aging factors and disease processes that happen in the body that you don't even know about. In a six month period, after just one ozone application, virtually every single person tells me of dramatic improvements.

"The second thing is the immune-modulating effect of ozone and the reduction of allergic factors. An allergy is an accumulation of fluid. It prevents you from absorbing nutrients, and causes other symptoms. Any person who has significant allergies is in a constant state of nutritional deficiency.

"Third, it reverses the cross-linking of the collagen and reduces the aging pigment. ...By reversing those things, it will restore the elasticity in all tissues.

"It removes the arterial plaque the same way it removes plaque in the pipes of heating and air-conditioning systems. It also removes the fibrin in the veins by breaking it down to pieces that are recognized by the macrophages and then scavenged away. Indirectly, it works like a Roto-Rooter by changing unnecessary fibrin deposits or arterial plaque to a point from which both the arteries and veins are cleaned out. Obviously, if you have more circulation to all parts of your body, all toxins can be removed and every cell of the body functions better.

"As far as immune modulation is concerned...many researchers say that a person is as old as the immune system. If you can have a perfectly young immune system, the rest of the body will follow suit, and you will be as young as your immune system again."

### **ONE PART OF THE PICTURE**

Clinicians usually recommend ozone as part of a larger holistic protocol in the treatment of seriously ill patients. Thus, it is a supplemental therapy used in conjunction with other treatment modalities. As Dr. John Pittman explains, "I rarely give ozone treatments unless they are combined with some other supportive therapy. Admittedly, the shortcoming of doing this is that you don't always know which component is most beneficial. But I certainly know from experience which things generally help the most. Combining ozone with proper dietary therapies and addressing other cofactors, particularly in the G.I. [gastrointestinal] tract, you can see tremendous changes in a person's constitution. Their blood work can turn around, and it definitely can improve the quality of life of an individual, as well as the length of their life."

It's Pittman's observation that the best benefits occur when ozone is taken on a daily basis. "The half-life of ozone is 45 minutes," he says. "After that time, it breaks down into oxygen. In the meantime, what it's really doing is transferring its high-energy electron to other elements in the blood and producing various peroxide formations that are continuing this oxidative effect. The powerful oxidative effect appears to last 24 hours, making a daily treatment the most effective way of using ozone."

### **OBSTACLES TO OZONE'S USE**

While ozone is without a doubt a wide-spectrum healing modality, in this country (USA) it is also widely ignored and even suppressed. Altman surmises that "because these elements are very available and also non-patented, the pharmaceutical industry has not been very happy with them." Because it isn't as easy to make money with ozone as with patented drugs, there has been no impetus for private companies to do expensive studies of its effectiveness. The unfortunate result: The general public is simply unaware of medical ozone as an option. In fact, most states prohibit the use of ozone therapy, the rationale being that researchers must first

prove that the process will not harm people. The fact that it has been used safely in Europe for decades doesn't seem to count.

Funding for research is continually denied by the National Institutes of Health, while exorbitant sums are earmarked for less effective, but more conventional, treatments. The situation doesn't seem to make sense. For instance, State University of New York virologist Bernard Poiesz has found that ozone could be used for "almost seemingly complete destruction" of H.I.V. without affecting blood protein, yet the N.I.H. has refused funding, saying it was not a priority. Dr. Kwaku Ohene-Frempon, head of the Children's Hospital Sickle-Cell Center, in Philadelphia, says that "ozone kills bacteria" and "supplies a lot of oxygen to tissues that need to be repaired." In the United States alone, 72,000 people suffer from sickle-cell anemia, and the N.I.H. spends about \$70 million a year to try to alleviate the disease. However, it will not fund ozone research, even though Cuban doctors find that ozone cuts the length and severity of painful sickle-cell episodes in half. Nor will research on ozone for diabetic conditions be funded, despite the fact that Germany has been healing diabetic wounds with ozone for quite some time.

Beyerle expresses the sentiments of the frustrated practitioners. "Extensive studies have been done in other countries," he points out. "It amazes me to see the literature that is being published and utilized in Germany and Europe but has failed to appear in literature or clinics in this country.

"In my opinion, it's all politics," he continues. "It starts at the beginning with our F.D.A., which is tremendously influenced by our drug companies. Drug companies give almost 80 to 90 percent of funding for medical schools. That's a fact. If drug companies have an influence on medical schools and medical research, then this information will never get there. Ozone's cheap. All you need is pure oxygen, an ozone generator, and the proper training. I just recently met with two professors from Frankfurt [who have been] using ozone with cancer for over 15 years, and have spectacular results. Why isn't it here? We have a medical mafia. There's too much money being made in medicine for certain companies to allow something so inexpensive and so worthwhile to be introduced."

Overseas, the picture is different. Medical ozone is used in Germany, Austria, Switzerland, Italy, Russia, and Cuba. In England and France, while they don't use ozone medically, they do treat drinking water with it.

Not long ago, at the 12th World Congress of the International Ozone Association, in Lille, France, research papers were presented that covered many areas in which medical ozone has proven of value.

Heart disease was one; ozone treatment was shown to improve the status of patients with ischemic cardiopathy, fostering diminution or disappearance of irregular heart rhythms, decreases in coronary failure, and increased fitness levels. When used in the treatment of early-stage stroke, ozone also demonstrated benefits, according to a German study. Glaucoma was another condition for which scientists reported ozone's benefits, and central-nervous-system disorders were shown to be helped as well.

In orthopedics, ozone has a significant contribution to make, as reported by C. H. Siemsen, of Buxtehude, Germany. He stated, "The application of medical ozone in acute and chronic painful diseases of the joints in an alternative method of treatment for obtaining rapid pain relief, decongestion, subsidence of effusion, a reduction in temperature, and an increase in motility." Siemsen reported that a number of therapy-resistant painful joint conditions were recently treated with ozone for the first time, noting that the treatment is a low-risk one.

The Cubans, in particular, seem to be keeping abreast of ozone's possibilities. The Ozone

Research Center at the Cuban National Center for Scientific Research recently investigated the cholesterol-lowering effect of the substance. Cuban researchers reported ozone's positive effect found on cholesterol metabolism, as well as in the stimulation of the antioxidative defense system. Other researchers from Cuba reported on clinical improvements in humoral immunity for children who received ozone treatments.

Children with hearing loss benefited from ozone, too, according to Cuban researchers. In a double-blind study with 34 children, hearing loss was reduced in the ozone-treated group. Ozonized oils were used in still other Cuban studies to successfully treat candidiasis, a fungal infection, and giardiasis, a parasitic condition.

Other reports at Lille concerned ozone's use in dermatology, and its disinfectant uses in oral surgery.

But ozone's problems with the medical establishment were not ignored at the Lille symposium. V. Bocci, of the University of Siena Institute of General Physiology, suggested that the biological basis for ozone's therapeutic effectiveness needs to be further clarified.

Bocci acknowledged, too, that reports of ozone's benefits have at times tended toward the subjective and anecdotal; this is a consequence of the fact that clinical experience with ozone, although vast, has remained limited to private practice. He also acknowledges two other factors that have not worked in medical ozone's favor--unfortunately, some practitioners have used this modality improperly; and people are prejudiced against ozone because they confuse it with the pollutant type.

Despite these problems, Bocci's assessment of ozone therapy today was upbeat. The sense of his presentation was that this is a therapy that has already contributed much, and in the future it will benefit people even more. As the century draws to a close, the public is growing disenchanted with toxic and problematic "magic bullet" remedies, and more interested in holistic and natural approaches to health care. It's only a matter of time before ozone comes into its own.

**Penthouse Editors note:**

Please consult your physician before considering any ozone treatment. For more information on alternative treatments for AIDS and the uses of ozone, please contact: Dolores Perri, The Healing Center, 175 West 72nd Street, New York, N.Y. 10024; (212)787-2404.

# WHAT IS OXIDATIVE THERAPY?

Reproduced article from :  
International Biooxidative  
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Most biochemical reactions in the body are 'Balanced' through 'Redox' mechanisms. Redox means (Red)uction (Ox)idation. Chemically, anytime a substance is reduced (chemically changed) something else must be oxidized (chemically changed the other way) for your body to stay in balance. Oxidation, as an example, is the process which causes 'rust' on metals (slow oxidation) or fire (rapid oxidation). In the body, some types of oxidation is thought to be harmful (produces Free Radicals). We even suggest people take Vitamin E (anti-oxidant) to help reduce Free Radical formation. We know however, there could be no life if certain types of oxidation did not occur. The body uses oxidation as its first line of defense against bacteria, virus, yeast and parasites. Even breathing OXYGEN is an oxidative process. Without oxidation we die very quickly. Without OXYGEN for more than a few seconds, serious consequences follow. Natural chemicals, found in the body, are used in 'OXIDATIVE THERAPY' to encourage healthy oxidation in the cells and tissue.

## WHAT CHEMICALS ARE USED IN OXIDATIVE THERAPY?

A number of substances are known to cause oxidation in the body but the most important of these is Hydrogen Peroxide. Hydrogen Peroxide, when exposed to your blood or other body fluids, containing the enzyme 'Catalase', is chemically split into OXYGEN and water. Remember how Hydrogen Peroxide foams when you put it on a wound? The foam is OXYGEN being produced by the action of catalase on the Hydrogen Peroxide. A small amount of Hydrogen Peroxide can supply large amounts of OXYGEN to the tissue.

## IS THIS A NEW FORM OF THERAPY?

Injections of Hydrogen Peroxide are nothing new. It was first reported by Dr.T.H.Oliver in the British Medical Journal (Lancet) in 1920. Patients with influenzal pneumonia were treated with Hydrogen Peroxide infusions with very good results. The use of Hydrogen Peroxide injections, to generate OXYGEN in the body, have been studied at many major medical research centers throughout the world. Research reports have come from Baylor, Yale, Harvard, UCLA, Boston, England, Japan, Germany, Sweden, Russia, Canada, Nova Scotia and others. Today, between 20 and 50 scientific articles are published each month about the chemical and biological effects of Hydrogen Peroxide. More recently the "Therapeutic Use of Intravenous Hydrogen Peroxide" was reported by Dr. C.H. Farr at an International Medical Symposium in Czechoslovakia attended by representatives from 26 different countries. Oxidative Therapy, introduced by Dr. Farr, is the rediscovery of an old treatment first reported almost 70 years ago.

## HOW DOES IT WORK IN THE BODY?

There are many theories about the function of Hydrogen Peroxide in the body and a great deal of scientific material supports almost every one. Hydrogen Peroxide is produced in the body in different amounts for different purposes. It is part of a system which helps you use the OXYGEN you breathe. It is part of a system which helps your body regulate all living cell membranes. It is a hormonal regulator, necessary for your body to produce several hormonal substances such as estrogen, progesterone and thyroid. It is important in the regulation of blood sugar and the production of energy in all cells. It helps regulate certain chemicals necessary to operate the brain and nervous system. It is used in the defense system of the body against infections and has been found to be important in regulating the immune system. Scientists are discovering the function of Hydrogen Peroxide in the body is far more complex and important than previously realized.

### **WHAT HAS IT BEEN USED TO TREAT?**

Oxidative therapy, using Hydrogen Peroxide, has been reported in the scientific literature and by physicians in the treatment of the following conditions or diseases with varying degrees of success.

(References available to professionals on request from IBOM)

#### **Heart and Blood Vessel Diseases**

1. Peripheral Vascular Disease (poor circulation) 2. Cerebral Vascular Disease (stroke and memory) 3. Cardiovascular Disease (heart disease) 4. Coronary Spasm (Angina) 5. Cardioconversion (heart stopped) 6. Heart Arrhythmias (irregular heart beat) 7. Gangrene of Fingers and Toes 8. Reynards Syndrome 9. Temporal Arteritis 10. Vascular and Cluster Headaches

#### **Pulmonary Diseases**

11. Chronic Obstructive Pulmonary Disease (lung) 12. Emphysema (lung disease) 13. Asthma (allergy, lung) 14. Bronchiectasis 15. PCP (Pneumonia in AIDS) 16. Chronic Bronchitis 17. Infectious Diseases 18. Influenza 19. Herpes Zoster (shingles) 20. Herpes Simplex (fever blister) 21. Systemic Chronic Candidiasis (Candida) 22. Chronic Fatigue Syndrome (Ebstein-Barr Virus) 23. HIV (AIDS) Infections 24. Acute and Chronic Viral Infections 25. Chronic Unresponsive Bacterial Infections 26. Parasitic Infections

#### **Immune Disorders**

26. Multiple Sclerosis 27. Rheumatoid Arthritis 28. Diabetes Mellitus Type II 29. Hypersensitive Persons (Environmental and Universal Reactors)

#### **Miscellaneous**

30. Parkinsonism 31. Alzheimer 32. Migraine Headaches 33. Chronic Pain Syndromes (Multiple Etiologies) 34. Pain of Metastatic Carcinoma 35. Blood and Lymph Node Cancers

Physicians from around the world constantly share knowledge and experience and the list of uses for Oxidative Therapy is growing every day. Since Hydrogen Peroxide is a natural substance produced and used in body chemistry, there will be discoveries about its importance in biochemistry for years to come.

### **HOW DO I KNOW IF I WOULD BENEFIT FROM OXIDATIVE THERAPY?**

Only a physician trained in the administration of Oxidative Therapy can answer that question



for you. You may find your condition or illness contained in the list above. If treatment of your condition or illness has been unsatisfactory in the past you may wish to learn more about Oxidative Therapy. The IBOM Foundation can supply you with the names of recognized trained physicians in your area.

### **HOW IS THIS THERAPY GIVEN?**

Very weak, very pure Hydrogen Peroxide (0.0375% or less concentrations) are added to a sugar or salt water solution, the same as used for intravenous feeding in hospitals. This is given in doses from 50 to 500 mL, administered into a large vein usually in the arm. It is given slowly over a period of 1 to 3 hours depending on the total amount given and the condition of the patient. It is painless except for the very small needle stick. Treatments are usually given about once a week in chronic illness but can be given daily in patients with acute illness such as pneumonia or flu. Physicians usually give 5 to 20 treatments, depending on the condition of the patient and the type of illness, The patient is rechecked in 1 and 3 months to evaluate the benefits and determine if additional treatments are indicated. Some patients, especially with chronic illness, may need to take follow up treatments, in series of 5 to 10, or may need maintaining indefinitely on a regular monthly schedule. As many as 50 treatments have been administered to several patients without complications. Your experienced physician must decide how many treatments are necessary in your individual case.

### **WHAT ABOUT THE SAFETY OR SIDE EFFECTS OF THIS THERAPY?**

Over the past 50 years hundreds of patients have received Hydrogen Peroxide without serious side effects. Early use of Hydrogen Peroxide was reported to occasionally cause irritation of the vein being infused. This troublesome side effect was eliminated after the concentration and rate of infusion were adjusted downward. The IBOM Foundation publishes and distributes a Protocol (How To Do It Booklet!) on the proper administration of Hydrogen Peroxide (see page 20 of this document). It is available to any IBOM trained physician. A Protocol is the best way for physicians to properly learn about any new therapy.

### **IS THIS THERAPY EXPENSIVE?**

Expense is a relative term. Persons with chronic diseases pay thousands of dollars annually to physicians, pharmacies and hospitals for drugs and therapies which do little more than maintain them at their current level of sickness. If Oxidative Therapy could save you 1/2 to 3/4 of your current expenses would you consider it expensive? The expense of any therapy varies more with the type of illness than type of therapy. Persons with serious complicated illnesses require more costly test to diagnose and monitor than less ill patients. Much of todays medical cost is in the testing rather than treatment. Don't be afraid to ask your physician, in advance, about cost.

### **DOES INSURANCE PAY FOR OXIDATIVE THERAPY?**

This usually depends on your insurance company and type of policy. Generally, however, insurance companies will not pay for medical service or care which may be classified as 'not usual and customary'. Usual and customary simply means all physicians are providing the same service or treatment for the same disease. Obviously, the average physician is not using Oxidative Therapy and most are not even familiar with the therapy. A qualified physician can more easily answer this question on an individual basis.

**CAN MY PHYSICIAN ADMINISTER THIS THERAPY?**

Any licensed physician may administer this therapy. Only trained and experienced physicians however are recognized by the IBOM Foundation. Interested physicians can qualify for recognition by contacting the IBOM Foundation for information regarding training seminars.

**HOW DO I LOCATE A PHYSICIAN TRAINED IN OXIDATIVE THERAPY?**

For more information contact the IBOM Foundation.

International Bio-oxidative Medicine Foundation P.O.Box 61767 Dallas/Fort Worth Texas,  
75261 USA 817-481-9772

# **Growing Demand for Oxygen Therapies**

by  
Zoltan P. Rona, MD, Msc.

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Oxygen therapies are extremely controversial. Many physicians and clinics offering them in Canada and the United States have been forced out of practice by various government agencies. Yet, in the past decade these therapies - including ozone, hydrogen peroxide, coenzyme Q10, liquid stabilized oxygen and other oral supplements - have gained more prominence and credibility. Escalating demand for oxygen therapies is linked to increasing rates of allergies, chronic fatigue syndrome, AIDS and cancer.

For the most part, both ozone and hydrogen peroxide therapies are only available in Mexico, some Caribbean countries like the Bahamas, Cuba and the Dominican Republic as well as in Europe, especially Germany and eastern Europe. The reasons for this are all political, not medical or scientific. If you want ozone or hydrogen peroxide therapies, don't call your doctor. Call your travel agent.

## **HOW DO OXYGEN THERAPIES WORK?**

Hydrogen peroxide and ozone are naturally occurring gases that are capable of providing more oxygen to cells, tissues and organs. Both therapies have been used around the world for nearly a century by conventional and alternative medical doctors alike in oral, rectal, vaginal, intramuscular and intravenous forms.

Both ozone and hydrogen peroxide break down in the body to extra oxygen. They destroy viruses, bacteria, fungi, parasites, pyrogens and, according to some, cancer cells. There is no bacteria, virus, fungus or spore that can survive in the presence of ozone or peroxide. This explains the benefit in chronic viral conditions and candidiasis.

Cancer cells can be killed by ozone or peroxide, yet healthy cells are unaffected. The theory is that cancer is a plant cell which can be killed by its waste product, oxygen, while non-cancerous cells are resistant to this type of destruction. An increasing volume of scientific research supports the fact that ozone or peroxide therapy can help in the successful treatment of a long list of infectious and degenerative diseases.

## **CAN THEY BE TOXIC?**

There is a great deal of confusion and misunderstanding about oxygen therapies and potential toxicity. If ozone is inhaled in large quantities, it can be toxic. Overdoses (beyond the usual therapeutic doses) of either hydrogen peroxide or ozone can cause inflammation, nausea, indigestion, diarrhea, coughing, chest pain, asthma, dizziness and headaches. Combined with environmental pollutants like petrochemical hydrocarbons, ozone can irreversibly damage lung and other body tissues.

The same is true, however, of hydrogen peroxide, oxygen, water and any other nutrient. To categorically say, that "ozone is toxic" or "hydrogen peroxide is toxic" is almost as ridiculous as saying that "water is toxic." Toxicity is a matter of degree. It is a biochemical fact that the body manufactures its own hydrogen peroxide under certain conditions. For ozone, hydrogen

peroxide, oxygen and water to become toxic, amounts far greater than the recommended levels used in therapy would have to be consumed.

Safety of oxygen therapies is further ensured when they are used as part of a comprehensive health-promoting program that includes an optimal diet and antioxidant supplements like beta carotene, vitamin C, vitamin E and selenium. By and large, the medical use of oxidative therapies is safe and effective for a broad range of conditions. Beware of ozone and hydrogen peroxide promoters who claim that oxygen therapies are all you need to treat cancer or AIDS. Using these therapies in isolation from all others could lead to problems.

### **NATURAL SOURCES OF HYDROGEN PEROXIDE**

Hydrogen peroxide is normally found in the waters of many famous healing spas around the world, but also in several areas of the human body including mother's milk. Our natural friendly bacterial flora, lactobacillus acidophilus, manufactures hydrogen peroxide as a defence against candida albicans and other potential pathogens. **A high vitamin C intake stimulates the production of hydrogen peroxide to combat invasive organisms.** Hydrogen peroxide transports sugar throughout the body. It also has the ability to reverse plaque formation in arteriosclerotic disease, thereby preventing a host of heart conditions.

Medical ozone is more bactericidal, fungicidal and viricidal than any other natural substance, including hydrogen peroxide. In fact, studies prove that ozone infused into donated blood samples can kill viruses 100 per cent of the time. Ozone does not damage healthy cells. Blood banking centres worldwide are seriously considering using medical ozone in all donated samples, rather than just testing blood samples for the presence of viruses. Herpes, Epstein-Barr, influenza, mumps, measles, HIV, cytomegalovirus, hepatitis and other viruses have been documented to be destroyed by ozone exposure. Atherosclerotic plaques have also been reduced by intravenous ozone therapy.

Ozone is used to purify water in many European countries. Unlike chlorine, it does not produce any carcinogenic by-products. Chlorine and other chemicals from gasoline and diesel-powered vehicles are linked to countless chronic diseases, including cancer. The city of Los Angeles has replaced chlorination for drinking water by the largest ozone water purification system in the world. Other major North American cities will soon follow suit.

### **LEGAL ALTERNATIVES**

Although the legal status of ozone and hydrogen peroxide therapy in both Canada and most of the U.S. is on shaky grounds, there are safe, effective and legal ways of getting the benefits of oxygen in both liquid and capsule form. A number of Canadian and American companies sell nutritional supplements that liberate oxygen to internal organs and tissues, when swallowed and combined with hydrochloric acid normally present in the stomach. In addition, the natural antioxidant supplement coenzyme Q10 can optimize oxygen in the body. Research indicates that these products are effective but it is unclear exactly how they compare with direct ozone and hydrogen peroxide treatments. Visit your natural health care practitioner for personalized advice on oxygen treatments.

# A Dream Come True

by Robert A. St. Genis

Source: City- April 17- May 15, 1995

In October, 1990 a friend of Michelle Reillo's came to her asking for help. He had zero CD4 cells and was suffering from the severe fatigue associated with HIV. Reillo, aware that fatigue, which often gets confused with depression, is one of the more debilitating symptoms of HIV and causes people to stop working and socializing, was concerned. But, what was the answer? That night she had a dream. In the dream, Reillo sent her friend on "dives" in a hyperbaric chamber to relieve his fatigue. Initially, she wasn't sure as to why it would work, but the dream was inspiring enough to try it. Her friend, absolutely desperate, agreed and Reillo brought him to The University of Maryland Shock Trauma, where she was then a nurse, to begin treatments. Reillo had her friend dive at the equivalent of 33 feet below the water surface three times a week. Within a month, the man's fatigue disappeared.

Reillo then went through the procedures to be granted a study at the University of Maryland. The three-year study involved 25 patients who were treated with 100 percent oxygen at 33 feet three times a week for two months, then twice a week thereafter. The results showed that 13 patients had a statistically significant decrease in tumor necrosis factor (TNF), which is one factor that causes fatigue in HIV-infected individuals. In addition, these patients all had an increase in appetite and thus in weight. If nothing else, Reillo's study made her confident in saying she had improved the quality of life in her patients.

Despite the results of the initial study, the University of Maryland abandoned funding future studies or treatments for HIV-positive individuals in 1993. Reillo says that the National Institutes of Health was contacted while she was at the University of Maryland on a number of occasions. She notes that Dr. Anthony Fauci was faxed by Search Alliance and urged to examine hyperbaric oxygen therapy (HBO) in 1992. Dr. Michael Gottlieb of the UCLA Medical Center was also contacted and spoke with Reillo. The University of Maryland submitted three grant applications to NIH, none of which were approved. The University of Southern Alabama separately applied for a grant to continue their research on hyperbarics and was also denied.

Reillo and some patients who were part of the University of Maryland study believe it's because of the lack of financial incentive. "The politics of AIDS around pharmaceuticals are horrible," Reillo said. "Hyperbarics should not be a threat." Determined to continue her research, Reillo used her own money along with bank loans to open Life Force in Baltimore at 1006 Morton Street. After purchasing and having a chamber installed, completing all other construction, and providing the facility with the necessary office equipment and furnishings, Reillo opened her doors in August, 1993.

Since then, she has continued treating 13 of her original patients, in addition to about 130 others. She maintains about 50 "compliance patients," explaining that many quit the treatments after they feel better. Reillo's persistence has led her to surmise that HBO treatments reduce the viral load in patients by a biochemical reaction whereby oxygen binds to an amino acid and zinc peptides, which are required for RNA replication of HIV.

In addition, Reillo has concluded that HBO therapy, along with medication, helps reduce the recovery time for PCP. A study on the latter discovery was written in the April, 1995 issue of

AIDSPatient Care.

While other research is limited, Reillo is not alone. At the International AIDS Conference in August, 1992 in Florence, Italy, a study was released by Drs. Brazelle, Ryan, and Harley which determined that oxygen under pressure reduces the viral load in patients systems. Laer, at the August 1994 International AIDS Conference in Tokyo, Dr. C.R. Steinhart, Dr. I. Montoya and M.R. Kaiser of Mercy Hospital, Miami, noted that "in three of four patients with mid to late stage disease, HBO subjectively improved quality of life and reduced fatigue." In 1993, The Israeli Naval Hyperbaric Institute conducted a single exposure study in non-HIV infected human subjects and found that HBO causes T-cell subpopulations to shift.

A 1994 study at the Israel Navel Medical Institute conducted on non-HIV infected rats indicated again a shift in T-cells, with there being a decrease in the blood, but increase in the lungs, lymph glands, and spleen. Their hypothesis for this is that they "may represent the activation of protective mechanisms against the toxic effect of oxygen or the early stages of pulmonary oxygen toxicity.

Toxicity is one concern that is often voiced about HBO therapy. At Life Force, Reillo makes sure that her patients receive antioxidant medications as part of their treatment and none of her patients have faced any problems with toxicity. Further, a 10 year study showed that out of 1,505 patients, non suffered pulmonary oxygen toxicity or ocular refractive changes and only .009 percent suffered oxygen convulsions, which ceased after removing the masks from the patients. However, it should be noted that the Under Sea Hyperbaric Medical Society has not yet endorsed hyperbarics for treating HIV.

The costs of hyperbaric oxygen therapy is another consideration. Life Force charges \$125.00 per session for visits. This fee is considered low compared to other hyperbaric clinics, but a "maintenance patient" will face over \$1,200 a month in charges for the therapy. Many insurance companies will cover hyperbaric if prescribed by the patient's physician. Reillo says she will not turn anyone away because of their inability to pay. "If people don't have any insurance, we will work something out." Dr. Mark Smith of Tucson, Arizona, feels that "cost is all kind of relative in this disease. Depending on what the (HIV) patient is facing, they can expect \$10,000 to \$15,000 a month at times (for treatment and care)." He continues, "For what [HBO] does in comparison to AZT, it's relatively low."

Smith, infected with HIV and with zero CD4 cells, has purchased his own hyperbaric oxygen chamber and has been administering HBO treatments since May, 1994. Smith has had tuberculosis and PCP and only weighed 110 pounds when he started. Today, he weighs 160 pounds, is able to work out three times a wee, and claims "if it weren't for hyperbarics, I probably wouldn't be here today." Smith doesn't want to speculate why more people aren't investigating hyperbarics, though he explains that "the theoretical negatives are far more unproven than the positives we have proven to date."

Reillo's patents are equally enthusiastic. Tim Good, 47, HIV positive for eight years, claims, "The has stopped the progression by about 83 percent since I started. This is a great deterrent. This is one of the great unknown treatments." Tom, 38, HIV positive for 10 years and a patient of Reillo's for the past four also believes that HBO treatments have stopped the progression of the disease, stating, "I have tried a dozen types of experimental therapies and this is the only one that has worked. The proof is I'm doing nothing else right now, no drugs or anything and my counts remain stable."

Doug Garriott, 52, HIV positive since 1982 and one of Reillo's first patients doesn't understand why more people aren't coming for treatment, stating, "I certainly think [HBO therapy] kept me alive for the last four years and I know it can do that for other people."

Hyperbarics are not new to the world of medical science. For more than 30 years, the U.S. Navy has used hyperbarics for treating deep sea divers suffering from the bends, a potentially fatal condition that is caused by surfacing too quickly. Dr. John M. Alexander at Northridge Hospital Medical Center in Los Angeles, once a Naval medical officer, now uses hyperbarics to treat such patients as diabetics with foot ulcers that don't heal, cancer sufferers with radiation-induced tissue damage, and victims of carbon monoxide poisoning. Hyperbaric treatments for non-diving diseases date back to the 1950s when surgeons used the treatments to carry out cardiovascular procedures that required stopping blood circulation. They were abandoned for this purpose with the introduction of heart-lung bypass machines and widely disregarded in general in the mid 1970s. Yet, while there were only 37 facilities operating in the United States in 1977, there are nearly 260 today. Still, despite evidence showing positive effects of hyperbarics in areas outside of HIV, hyperbarics "remains an ill-defined field, and HBO data often consists of small (test) series without standardized patient populations or treatment schedules," according to a 1990 article in the Journal of The American Medical Association.

Most organizations involved with HIV also remain uninformed and in certain cases simply disinterested. The AIDS Information Clearinghouse, operated by the Centers for Disease Control, had no information available regarding HBO therapy, stating that they only tend to hold information regarding pharmaceutical-based options. The National Association of People With AIDS was not able to locate any information on hyperbarics. Project Inform and The Gay Men's Health Crisis did not respond to inquiries regarding the form of treatment.

Contrarily, the National Institute of Allergies and Infectious Diseases, who did have access to some material including Reillo's studies, stated, "At the current time, we are not supporting research in hyperbaric oxygen therapy nor have we seen a formal submission of data. We do, however, always welcome interesting data and would look forward to the results of additional research." The AIDS Treatment Data Network was able to reply with the above mentioned Steinhart and Bitterman studies, in addition to Reillo's and has voiced an interest in more information.

For hyperbarics to gain any real recognition, whether it be in treating foot ulcers or symptoms associated with HIV, it is evident that controlled studies need to be conducted. The health care profession is, at best, skeptical about treatments that have not been sufficiently researched and most patients are comforted knowing that doctors do not prescribe treatments that may not benefit their patients.

# **Pure Oxygen May Aid Heart Attack Victims Medicine: Preliminary research finds that pressurized chamber used to treat 'the bends' in divers can lessen chest pain and help keep cardiac muscle tissue alive.**

by SHERYL STOLBERG, TIMES MEDICAL WRITER

Los Angeles Times Monday November 16, 1992  
Home Edition Part A, Page 3

Dr. George Hart is a retired Navy physician who makes his living operating on people's hearts and lungs. Twelve years ago, as he lay in the emergency room at Long Beach Memorial Medical Center after suffering a heart attack while driving to work, the cardiovascular surgeon took his treatment into his own hands.

He ordered his nurse to put him in a hyperbaric oxygen chamber--the kind used to treat deep sea divers who suffer from decompression illness, known as "the bends." Within 30 minutes, Hart said, the intense pain in his chest was gone.

That experience in September, 1980, led Hart on a quest to determine if emergency treatment in pressurized hyperbaric chambers is beneficial to heart attack patients. Today, at an annual scientific conference hosted by the American Heart Assn. in New Orleans, he and his colleagues are scheduled to report that their preliminary studies show that the treatment works. In a study of 49 patients who had just suffered heart attacks, physicians at Long Beach Memorial found that use of hyperbaric chambers, when combined with clot-dissolving drugs, relieved chest

pain and significantly reduced damage to the heart muscle contrasted with administering the drugs alone.

In some heart attacks, blood clots close off the coronary artery, cutting off oxygen to the heart and causing the muscle to scar. Decades ago, doctors theorized that hyperbaric oxygen chambers--in which patients are provided with pure oxygen--might help prevent this scarring.

Studies in this area were abandoned with the introduction of clot-dissolving drugs in the 1970s. Yet, according to Dr. Myrvin Ellestad, who directed the Long Beach Memorial research, the drugs can take two hours to dissolve the clots, during which time the heart usually sustains damage because of continued oxygen deficiency.

In the hyperbaric chamber, Ellestad said, patients receive oxygen at twice the normal atmospheric pressure, which increases the blood's oxygen level by about 15 times. "This very high oxygen

level penetrates everything in the body, and we think it stops the damage in the heart during the time the medicine is dissolving."

The clinical trials followed an animal study about 10 years ago in which a Cleveland researcher, spurred by Hart's 1980 experience, induced heart attacks in dogs and treated some with hyperbaric oxygen.

The researcher later dissected the animals' hearts and found that dogs that received oxygen treatment and clot-dissolving drugs sustained damage to just 5% of their heart muscle. By contrast, dogs that were treated with clot-dissolving drugs or oxygen alone sustained damage to 50% of the heart muscle.

In the randomized human trials at Long Beach Memorial, doctors treated 24 patients with clot-dissolving agents only and 25 with the drugs and oxygen chamber. They found that electrocardiogram tests of patients who received the oxygen treatment showed that the heart



resumed normal electrical activity twice as fast as in patients who were not placed in the chambers.

Moreover, patients who received the oxygen had significantly lower levels of the enzyme creatine phosphokinase, which is released during a heart attack and indicates the extent of heart muscle damage. And the doctors found that the heart's "ejection fraction"--its ability to pump blood-- was increased by about 5% with the oxygen treatment contrasted with the drugs-only therapy.

The treatment may have some drawbacks. Most hospitals are not equipped with hyperbaric chambers, which cost about \$80,000 and are used to treat stroke victims and speed healing of wounds. In addition, medical personnel would have to be trained in their use.

And one heart expert, Dr. Joseph Ornato of the Medical College of Virginia, said putting patients in the chambers may be risky because doctors and nurses might not be able to monitor the patients adequately in the event of an emergency, such as a second heart attack.

Ornato called the study an "interesting, yet relatively preliminary observation."

Ellestad agreed, saying he would like to study at least 1,000 patients. "We're enthusiastic about the treatment, although we are the first to admit that you need a lot more patients before it is totally proven."

But the 62-year-old Hart, who said his family has a history of heart trouble, is convinced. Hart said he has had several heart surgeries--including a quadruple bypass--since his 1980 heart attack, and that his heart has suffered little damage except for an incident during a trip overseas where the hospital that treated him did not have a hyperbaric chamber.

"Now," he said, "I don't plan to visit too many places unless they have immediate availability of a hyperbaric chamber."

Copyright, The Times Mirror Company; Los Angeles Times, 1992.

STOLBERG, SHERYL, Pure Oxygen May Aid Heart Attack Victims; Medicine: Preliminary research finds that pressurized chamber used to treat 'the bends' in divers can lessen chest pain and help keep cardiac muscle tissue al., Los Angeles Times, 11-16-1992, pp A-3.

# Hyperbaric oxygen for treatment of closed head injury.

by Richard A. Neubauer, MD & Sheldon F. Gottlieb PhD

Unfortunately the figures had to be omitted

## ABSTRACT

Traumatic and vascular brain injuries consist of acute episodes followed by development of chronic components of varying magnitude and duration whose potentials for recovery differ. We discuss a case of closed head injury in which interventional hyperbaric oxygen (HBO) with single photon emission computed tomography were used as aids in determining the presence of recoverable neurons, to follow therapeutic progress, and to determine the end point of therapy. This case also shows the successful use of intensive HBO as a therapeutic modality.

BRAIN INJURIES, regardless of their cause, share common pathophysiologic pathways[1] that result in the destruction of neurons, and, to a varying extent, formation of idling neurons.[2- 5] Diagnosis, prognosis, and treatment of central nervous system dysfunction requires the ability to differentiate between viable idling neurons and dead ones. To provide effective therapy for brain injury, the clinician must consider the locations and extent of irreparably damaged cells as well as ischemic penumbral zones.[2,3-6] This case study suggests that single photon emission computed tomography (SPECT) imaging, used in conjunction with interventional hyperbaric oxygen (HBO) therapy, is useful, not only in identifying potentially recoverable brain tissue, eg, idling neurons, in cases of stroke[2] and hypoxic encephalopathy,[3] but also in treating cases of closed head injury. It may be used to monitor the effectiveness of therapy and to determine the end point of therapy.

## METHODS

Initial and delayed SPECT brain imaging was done using N- isopropyl- [[sup 123]I]-p-iodoamphetamine (iofetamine hydrochloride I 123, IMP [SPECTamine, Medi-Physics Inc, Paramus, NJ]) and the techniques outlined by Neubauer et al.[2,3] IMP imaging was done using an ADAC ARC 3300 computer interfaced to a Phillips rotating gamma camera. Unlike scans in previous studies,[2,3] the final scan in this case was done using technetium Tc 99m dl-hexamethylpropyleneamine oxime (exametazime, dl HM-PAO [Cerotec, Amersham Corp, Amersham, England]) complex and a Picker SX 300 SPECT camera. Tracer change was unavoidable because the supplier stopped manufacturing IMP (last commercially available IMP source, April 4, 1991). Technetium scans were done using a split dose protocol; half the dose was given for the initial scans, and half was given after an hour of exposure to HBO (4 to 6 hours after the first injection).

## CASE REPORT

In December 1989 a 40-year-old white man was involved in a single- car accident. He was unconscious at the scene and was improperly intubated. He was subsequently transferred to a hospital, where he was reintubated. Computed tomography (CT) revealed fracture of the zygomatic bone; it also showed air in the intercranial region. After 2 weeks in the intensive care unit, the patient was transferred to a coma management program. At that time, he did not respond to commands or open his eyes spontaneously. The arms moved randomly, and there was marked spasticity of all extremities. He remained comatose for 28 days, eventually advancing from level 2 to level 7 on the Los Ranchos Amigos Coma Scale. When discharged in

June 1990, he required total life support and care despite the fact that he had received intensive physical and cognitive rehabilitation with neuropsychologic and nutritional support. His wife was told that because of severe motor, memory, speech, language, and cognitive impairments, no further improvement could be expected and was advised to place him in a nursing home.

In June 1990, he was brought to us for further rehabilitative efforts using HBO. Detailed independent neuropsychologic and physical examinations confirmed the disabilities while providing objective baseline data.

SPECT-IMP scans (Fig 1) revealed a marked defect of the right posterior temporoparietal cortex and a diffusely diminished cerebral cortex. After a single 1-hour exposure to 1.5 atmospheres absolute (ATA) oxygen, repeat injection of tracer agent, and repeat scan, there was filling of the right defect and increased tracer uptake in the left parieto-occipital cortex (Fig 2).

Based on these data, an intensive course of HBO therapy in a Vickers monoplace chamber was instituted as follows: 1.5 ATA for 1 hour twice a day for the first 28 treatments, 1.75 ATA for the next 106 treatments, and 1.5 ATA for the final 54 treatments, for a total of 188 treatments. After the 93rd treatment, the patient showed good motor, cognitive, linguistic, and speech improvement as documented by video taping, brain jogging computer' using the Parrot software program and neuropsychologic examinations. Images depicting SPECT/IMP scans 24 hours after the 160th treatment (Fig 3) indicated frontal and left parietal deficits but no longer showed the large right posterior parietal defect. Images made after the 161st treatment (Fig 3) showed further improvement in tracer uptake, suggesting the continued presence of potentially recoverable tissue and thereby providing scientific justification for further HBO therapy.

The conclusion of all therapeutic departments was that HBO therapy and rehabilitative intervention resulted in significant improvement in all areas of previously identified deficits. The clinical psychologist summarized his conclusions as follows: "During this time [the patient] has had markedly dramatic improvement in many of his cognitive functions. He has become ambulatory, acquired good communication skills with others again, has become independent once more in his self-help skills, and regained much of his short-term and long-term memory. He seems to have responded to the hyperbaric treatment programs."

The final SPECT scan revealed normalized images with intact cortical uptake (Fig 4). The patient was fully ambulatory (although he occasionally used a cane), was self-sufficient, and required only minimal care; he returned to his home city. It was recommended that he obtain some additional cognitive-linguistic rehabilitation as well as vocational rehabilitation. He planned to return to work.

## **DISCUSSION**

Currently, opinions vary in regard to assessment, prognostication, and treatment of acute or chronic neurologic deficits resulting from traumatic or vascular brain injury or from toxic and anoxic episodes. Brain injury imposes a tremendous expense and personal burden on involved parties and society. This case report shows that SPECT imaging before and after HBO therapy is useful in identifying potentially recoverable brain tissue, in monitoring the effectiveness of therapy, and in helping to identify the end point of therapy. CT scans and magnetic resonance imaging (MRI) provide anatomic information concerning brain injury. Sequential SPECT imaging with HBO intervention (SPECT/HBO) provides functional information,[7] especially early in the evolution of defects, thereby allowing earlier intervention than other imaging techniques. SPECT/HBO imaging, in delineating a defect volume greater than that revealed by either CT or MRI, may be indicating tissue with recoverable idling neurons. The motor and

cognitive improvements could be correlated with recovery of specific previously hypometabolic brain areas. Also, our data support the hypothesis that traumatic, vascular, and anoxic brain injuries and long-standing ischemic hypoxia have a common pathophysiology and may include a penumbra of recoverable tissue. We propose that HBO therapy be used routinely as an early diagnostic tool and as an adjunct to physical rehabilitation for patients with brain injuries. We also believe that research in this area would be promising.

PHOTO: FIGURE 1. Initial SPECT/IMP scan, axial view (one atmosphere pressure). Note perfusion/metabolism defect.

PHOTO: FIGURE 2. SPECT/IMP scan, axial view, taken after 1 hour's exposure to 1.5 atmospheres absolute oxygen. Scan was done within 4 hours of first scan (Fig 1). Note improvement in perfusion/metabolism in previously deficient areas.

PHOTO: FIGURE 3. (Upper images) SPECT/IMP scans, axial view, taken 24 hours after 160th hyperbaric treatment and immediately before 161st treatment showing frontal and left parietal perfusion/metabolism deficits; large right posterior parietal deficit is no longer seen. (Lower images) Scans taken after 161st hyper-baric treatment showing oxygen-induced improvement in tracer uptake and, therefore, potential for further healing with continued therapy.

PHOTO: FIGURE 4. SPECT/dl HM-PAO scan, transaxial view, after 188 hyperbaric treatments. Note normal perfusion/metabolism.

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# My experiences with O<sub>2</sub>/O<sub>3</sub>

by Randall Prue

March 15, 1996

I want to relate to you my experiences with oxygen and ozone products.

In 1990, I was administering 35% H<sub>2</sub>O<sub>2</sub> orally to bovines (a dairy herd), 30 ppm, added to their drinking water. All the water on the farm was treated, so it was also in all cleanup water, etc. That's a low dose. Somebody must know how to convert it to % or whatever they want. I know how, but I'm not big on technical points. The cows became extremely healthy. Bacteria counts dropped and butterfat went up. Those 2 criteria convert immediately to \$\$ for the farmer. He is paid more for his milk the very next pickup. So, I started taking it myself. Circumstances moved me away from that work and from my source of H<sub>2</sub>O<sub>2</sub>, so I just stopped taking it, always thinking in the back of my mind, I'd have to find a way to get a smaller quantity than the 15 gallons drums the farmers use.

Summer 1995, I found the 16 oz. 35% food grade that are becoming more and more common and started taking it again.

In October 1995, I was asked to research oxygen as related to cancer. I was given information from a researcher who used herself as subject. She has been battling Lyme disease for many years and is acutely aware of any progress. In her research for noticeable effects of the oxygen products on her cancer, she noticed that her Lyme disease had disappeared after 3 weeks of H<sub>2</sub>O<sub>2</sub> ingestion and bathing according to the popular doses found in O<sub>2</sub>xygen Therapies by Ed McCabe. Once she started chemotherapy in December, she noticed that the Lyme disease returned. My hypothesis is that the chemo has such a debilitating effect on the immune system that the Lyme disease was able to get in again.

As a side effect to providing her with the information she wanted, I decided to re-initiate my own use of H<sub>2</sub>O<sub>2</sub>. I had been without any since I was no longer on the farm where we had barrels of it for the bovines. I found smaller quantities and purchased a 15- gallon drum for bathing and cleaning. I also obtained a magnesium oxide powder, bound to ozone, with Vitamin C and bioflavinoids, stabilized at a high pH. This is 'a la' magozone/homozone. I also obtained Donsbach's OxyGen (magnesium peroxide, aloe and colloidal minerals).

Initially, I took 10-15 drops per day of 35% food grade H<sub>2</sub>O<sub>2</sub>. I noticed an energy increase. I'm a person who is chronically well, so it's often hard to use myself for this type of research. After a few weeks, I began the MgO powder. I experienced a profound awareness of my light body / spirit body (semantics at discretion of reader). It was an experience I have had before as a result of other experiments. An awareness of the sub-atomic space which is the major composition of all matter. The symptoms of this experience are the same as the ones induced by other means (let's say radio-electro-magnetically induced). I was acutely aware of my real state as a human being: a spirit involved with the atoms that form the matter of my body. In this state, I was aware of how clean air is (should be); aware that oxygen and ozone are nature's universal cleansers and how clean and pristen this planet was when we first arrived. I sensed the beginnings of life on this planet, and in contrast, looked at the mess we've made of it.

I began wanting my body to be clean, as well as my environment. One day, I stood in the tub

after a peroxide bath and scrubbed the walls for a half an hour. They were due for a cleaning. I have not turned into a clean freak. I'm not all that fussy about dust and whatnot around the house (with 2 dogs and a bunch of plants), but the oxygen therapies I have tried have made me very aware of how clean and beautiful this planet was, could be and should be.

After a few days on the MgO, my sinuses began to drain, involuntarily and uncontrollably. What I mean is there is no warning to get kleenex or blow your nose. The stuff just runs out -- very liquid and it's obviously stuff that shouldn't be there (yellow/green stuff). After a month or so without the MgO, I got more (February), took it again, and the same thing happened again. It lasts a day or two. The typical colon cleanse also happened both times. That's soft stools caused by a liquefying of accumulated toxic waste in the intestines. It's converted to water and oxygen/ozone. The water comes out and the gases are absorbed into your blood.

One day, after a month or so, I had a surprise washing my face. By now, I had switched to the OxyGen from the 35% (much more palatable, but more expensive). On the wash cloth, I found dry flakes of skin that kept coming off. I wondered if it was drying my skin out, until I realized that I was removing dead skin. Under it was soft baby skin. I mean really just like a baby's skin. As a gardener, I am used to having rough hands. My skin is so new and soft now, that I have to be careful not to drop things. I'm getting used to it.

In the peroxide baths (6 oz. 35% per tub, or more), I invariably leave behind a layer of dead skin. To me this means that cell division has been accelerated, which is the key to longevity, health, anti-aging... call it what you want.

I'm sure I will remember more of what has happened to me and will forward that to you as it comes to mind, but something truly astonishing happened on Thursday, February 22, 1996. I was asked to witness an experiment which a man in his 30's decided to perform on himself. Roughly a week previous, he had a finger bitten by frost. He was told that a blood sucker (leech) would draw the blood out and apparently lots of people know about this.

Unfortunately, the medical system knows this but does not keep leeches. Leeches and frost tend to happen in diametrically-opposed seasons. It would cost him \$250. to have a dozen leeches shipped up from U.S. The medical system graciously offered to remove his finger -- free! Or rather paid for my all of us via medicare.

He decided to try an alternate approach to preseving his digit. He soaked it in 5% H<sub>2</sub>O<sub>2</sub> (35% food grade 1:6 in water) for about 5 minutes. When he removed his finger from the water, I could not tell which one had been frost-bitten. It was the same colour as all the others. It had been a dark purple, approaching black. He felt a tugging, rubbing sensation while soaking. He has continued soaking several times a day since then and reports that the colour has returned to a normal red/purple (normal under the circumstances). When soaked, the blood circulation appears to increase dramatically. The congestion blocks up between soaks, but with each session, there is a gradual improvement. I must mention that at the same time, he is taking the MgO and H<sub>2</sub>O<sub>2</sub> orally, as part of his experiment.

So, it seems that there is an alternative to removing frost-bitten extremities. Of course, it will never catch on. There's more money in ectomies.

Randall Prue

# Chlorine out, ozone in as water purifier

by Emilla Askari

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Of all the deadly technologies developed during World War 1, none was more gruesome, none more cruel than poisonous chlorine gas. One strong whiff and a soldier would start coughing blood. The tortured hacking could go on for days, inevitably, the gas would kill -- hundreds of thousands of young men. In farmhouses and hospitals throughout Europe, people watched. And when the War To End All Wars was done, they gagged at the thought of disinfecting their drinking water with chlorine. Not so across the Atlantic. In America, hundreds of water systems began disinfecting their water with chlorine in the 1920s and '30s. To this day, it is a commonplace chemical that we drink every day, rub from our eyes after staying too long in the pool and use to kill bugs in the water as a matter of course. Soon, however, this will all change. American technology has finally confirmed what the Europeans suspected all along: Adding chlorine to drinking water is not a healthy practice. When chlorine combines with the byproducts of rotting leaves, a family of chemicals called trihalomethanes, or THMs, are formed. THMs are carcinogenic. One study by the President's Council on Environmental Quality found that people drinking chlorinated water had a 13 percent to 93 percent greater chance of developing rectal cancer and a 53 percent greater chance of getting colon cancer than people who drank untreated water. For years, no one knew that people were getting small doses of THMs every time they brushed their teeth or made lemonade. It wasn't until the mid-1970s that the Environmental Protection Agency's water quality lab in Cincinnati first isolated THMs in drinking water. Before that, "We didn't worry about these cancer-causing chemicals because we didn't know they were there," said Pete Rogers, chief of the California Department of Health Services' drinking water branch. "We didn't know how to measure them, and we didn't really know what the long-term effects (of drinking them) were." All that is much clearer now. At the current maximum contaminant level of 100 parts of THM per billion parts of water, the EPA estimates that one additional cancer will strike among 100,000 people who drink two liters of water a day for 70 years. The EPA takes fewer risks with other drinking water contaminants. For example, its recommended level for the industrial solvent trichloroethene, or TCE, is five times stricter when measured by the number of projected cancer deaths. The reason the EPA went easy on THMs: If the standard had been any tougher, water agencies wouldn't have been able to meet it unless they stopped chlorinating. And there was no alternative. Not in this country, not in 1979, when the standard was set. As it was, the water industry balked at having to meet even the lenient 100 parts per billion standard for THMs. The first reaction of the American Waterworks Association, an industry group, was to file a suit attempting to block the standard's implementation. Too hard to meet, the association claimed, especially for agencies that get a lot of their water from rivers and streams, which are heavily laced with THMs' chemical "precursors." Well water, in contrast, doesn't contain THM precursors; it never comes in contact with decaying leaves. Eventually, the suit was settled when the EPA granted variances from the THM standard for some agencies that had a particularly hard time complying. Next year, however, the EPA says it's really going to get tough. It plans to lower the maximum allowable level of THMs to between 50 and 10 parts per

billion. Again, water agencies are balking. This time, however, they also are scrambling to find an other method of disinfecting water. One possibility that has been used for years in Europe: ozone. The gas, which smells like watermelons, disinfects as well as chlorine does. It is more expensive. Europeans pay much more for their water than Americans. But, unlike chlorine, ozone disappears into the air within 24 hours, leaving behind no toxic residuals -- as far as researchers can tell so far. "The fact of the matter is that our analysis of drinking water is incomplete," said William Glaze, a professor at UCLA's School of Public Health who specializes in water treatment. "We're still finding things we didn't know were there." For more than a year, Glaze has been focusing his microscope on water samples from the city of Los Angeles' new filtration plant in Sylmar. The 2-year-old, \$106 million plant is one of the largest in the world that disinfects with ozone. So far, Glaze says he has found nothing alarming in the product of the plant he calls "one of the best in the world." There, where the Los Angeles Aqueduct dumps its relatively pure load of runoff from the Owens Valley, man-made lighting bolts pass through thousands of glass tubes in the plant's huge ozone generators. Inside the tubes, the electricity converts liquid oxygen into ozone. The gas is then piped over to holding tanks the size of small auditoriums. The tanks are filled with water and the ozone is allowed to percolate through it. A thick porthole allows visitors to peek inside the cement tanks and watch the ozone bubble away like champagne. From Egypt, Japan and Monroe, Mich., water managers have come to observe. Some visitors also have come across town, from the mighty Metropolitan Water District of Southern California. MWD, the state's largest water wholesaler, already has converted its treatment plants from chlorine to chloramine, a combination of chlorine and ammonia that's less likely to combine with the THM precursors. But MWD gets all of its water from rivers: the Colorado to the east and the Sacramento to the north. These sources are high in decomposing leaves, and thus in THM precursors. When the new EPA standards come out, MWD is going to have to do even more to reduce THMs. The agency -- which supplies half the water used by coastal Southern California -- is studying the possibility of converting all five of its treatment plants to a combination of ozone and peroxide. The estimate cost: \$150 million. At that price, MWD is fervently hoping that future research doesn't uncover any ozone byproducts as unhealthy as chlorine's. "If there are problems with ozone," said MWD water quality director Michael McGuire, "we're in a hell of a mess."