A Review of the Use of Ozone in Healthcare.

An Introduction to Ozone; Ozone, Tri-Oxygen chemical formulae $O_3$, is a naturally occurring gas, and was first described in 1785 by a Dutch chemist, Martinus Van Marum. It was formally named in 1840 by Christian Schönbein, a German-Swiss chemist. This gas is a molecule consisting of three atoms of oxygen. It is a very unstable gas, quickly breaking down into oxygen and releasing a single oxygen atom that is very reactive. Ozone must be created at the point of usage, as it cannot be stored for any extended length of time. There are a considerable number of published papers in the scientific literature that illustrate the wide range of therapeutic effects ozone can have and it has uses in medical, dental, veterinary and industrial applications. Ozone gas in high concentrations has been shown to have dangerous effects on lung and skin tissue, and should only be applied by suitably trained healthcare workers. Ozone therapy has been utilised and studied since the mid 1800’s. Its effects are proven, consistent, safe and ozone therapy has minimal unwanted side effects. Medical ozone is used to disinfect living tissues and instruments, to treat disease and to produce sterile water. It’s mechanism of action is by the rapid inactivation of bacteria, viruses, fungi, yeast and protozoa, stimulation of oxygen metabolism, and activation of the immune system in animals and humans. There are a number of different application techniques, such as treating external wounds by transcutaneous bagging, washing with ozonated water or the use of a soap made with ozone-treated plant extracts. Another example would be the use of ozonated water and plant oils, the use of which is particularly useful in dental and medical applications, applied as a spray, wash or by direct placement on a wound or treatment area. Diseases that can be effectively managed and treated include infected wounds, dental decay, gum disease, hard and soft tissue healing, circulatory disorders, geriatric conditions, macular degeneration, viral diseases, rheumatism, arthritis, cancer, SARS and AIDS.
Trioxygen – A Brief History; Trioxygen, commonly known as Ozone, the tri-atomic state of di-oxygen (O), symbol $\text{O}_3$, was first noticed in 1785. Van Marum noticed that air near his electrostatic machine acquired a characteristic odour when electric sparks were passed. In 1801, Cruickshank observed the same odour at the anode during electrolysis of water. Finally, in 1840 Schönbein named the substance which gave off this odour, 'ozone', from the Greek word "ozein" - to smell, although some historical authors have suggested another German scientist, Christian Fernandez, should be credited with the discovery of ozone. In 1857 Werner Von Siemens designed an ozone generator that has since evolved into the present day cylindrical dielectric type that makes up most of the commercially available ozone generators in use, and which has sometimes been called the "Siemens Type" ozone generator.

The formula for ozone, $\text{O}_3$, was not determined until 1865 by Jacques-Louis Soret and confirmed by Schönbein in 1867. It is a molecule consisting of three atoms of oxygen in an unstable structure. The gas is pale blue in colour, has a distinct odour and can be explosive in liquid or solid form. It has a half-life of about 20 minutes at room temperature and pressure. It is found and forms at high altitude where it has a protective role for all life forms and is known as the ozone layer. The ozone layer filters out harmful effects of UV radiation by a cascade photochemical reaction. The ozone layer was discovered in 1913 by the French physicists Charles Fabry and Henri Buisson, and the photochemical mechanisms of the ozone layer were discovered by the British physicist Sidney Chapman in 1930.

Ozone has had a chequered history in healthcare usage. 1870 saw the first report on ozone being used therapeutically to purify blood by Dr C Lender in Germany. There is evidence of the use of ozone as a disinfectant from 1881 as mentioned by Dr Kellogg in his book on diphtheria. In October of 1893, the world's first water treatment plant using ozone was installed in Ousbaden, Holland, and today there are over 7000 municipalities around the world that use ozone to clean their water and sewage. In 1885, the Florida Medical Association published "Ozone" by Dr Charles J Kenworth MD, detailing the use
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of ozone for therapeutic purposes and in 1886 the ability of ozone to disinfect polluted water was recognized in Europe. Test results from Germany showed that ozone was effective against bacteria and in 1893 ozone was reported in algae control. In September 1896 the electrical genius Nikola Tesla patented his first ozone generator, and in 1900 he formed the Tesla Ozone Company. Tesla sold ozone machines to doctors for medical use, and modern ozone production units are still based on one of his designs from the 1920s. Tesla also produced ozonated olive oil and sold it to naturopaths. In 1898, the Institute for Oxygen Therapy was started in Berlin by Drs Thauerkauf and Luth. These doctors injected ozone into animals and bonded ozone to magnesium, producing 'Homozon'.

Beginning in 1898, Dr Benedict Lust, a German doctor practicing in New York, who was the originator and founder Naturopathy, wrote many articles and books on ozone. In 1902, J H Clarke's "A Dictionary of Practical Materia Medica," London describes the successful use of ozonated water in treating anaemia, cancer, diabetes, influenza, morphine poisoning, canker sores, strychnine poisoning and whooping cough. In 1903 at Niagara Falls, NY a water purification plant went on-line, and by 1915 at least 49 major ozone installations for water purification are on line throughout Europe. In the early 1900’s, the London Underground was ventilated with ozone to keep the air in the tunnels fresh and bacteria free.

In 1911, "A Working Manual of High Frequency Currents" was published by Dr Noble Eberhart MD. Dr Eberhart was head of the Department of Physiologic Therapeutics at Loyola University. He used ozone to treat tuberculosis, anaemia, chlorosis, tinnitus, whooping cough, asthma, bronchitis, hay fever, insomnia, pneumonia, diabetes, gout and syphilis. In 1913, the Eastern Association for Oxygen Therapy was formed by Dr Blass and his German associates.

During World War 1 ozone was used to treat wounds, trench foot, gangrene and the effects of poison gas. Dr Albert Wolff of Berlin also used ozone for colon cancer, cervical cancer and decubitis ulcers in 1915. Around World War I poisonous gas
research lead to the development of inexpensive chlorine gas, and due to the costs of large scale ozone manufacture, interest in ozone for water purification began to decline.

In 1920, Dr Charles Neiswanger MD, the President of the Chicago Hospital College of Medicine, published "Electro Therapeutical Practice." Chapter 32 was entitled "Ozone as a Therapeutic Agent." In 1926, Dr Otto Warburg of the Kaiser Institute in Berlin announced that the cause of cancer is lack of oxygen at the cellular level. Dr Otto Warburg received the Nobel Prize for Medicine in 1931 and again in 1944, the only person to ever receive two Nobel Prizes for Medicine. He was also nominated for a third.

In 1929, a book called "Ozone and Its Therapeutic Action" was published in the US listing 114 diseases and how to treat them with ozone. Its authors were the heads of all the leading American hospitals. A Swiss dentist, Dr Edwin A Fisch was using ozone in dentistry before 1932, and introduced it to the German surgeon Dr Erwin Payr who used it from that time forward. Drs Aubourg and Lacoste were French physicians using ozone insufflation from 1934-1938.

The use of ozone in the United States can be traced back to the 1940's and in 1948; Dr William Turska of Oregon began using ozone, employing a machine of his own design. In 1951, Dr Turska wrote the article "Oxidation". Dr Turska pioneered injection of ozone into the portal vein, thereby reaching the liver.

From 1953 onward, the German doctor Hans Wolff used ozone in his practice, writing the book "Medical Ozone," and training many doctors in ozone therapy. In 1957, Dr J Hansler patented an ozone generator which has formed the basis of the German expansion of ozone therapy over the last 35 years. Today over 7000 German doctors use ozone therapy daily.

In 1961, Dr Hans Wolff introduced the techniques of major and minor autohemotherapy. By 1965 Scotland (UK) was using ozone for colour control in surface water, and this is the first report of ozone being used to control colour of substances. At the same time,
Swiss research lead to the use of ozone to oxidize micro pollutants such as phenolic compounds and several pesticides.

In 1977, Dr Renate Viebahn provided a technical overview of ozone action in the body, and in 1979, Dr George Freibott began treating his first AIDS patient with ozone. A paper published in 1980 by Dr Horst Kief also reported success treating AIDS with ozone. In 1987, Drs Rilling and Viebahn published "The Use of Ozone in Medicine," which is regarded by many as the standard text on the subject. In 1990, the Cuban ozone institute reported on their success in treating glaucoma, conjunctivitis and retinitis pigmentosa with ozone.

One of the most common uses of ozone is for the treatment of water. Scientists and doctors studied the ozonation system at Ousbaden, in Holland and later built an industrial plant at Nice, France. Nice, rather than Ousbaden, for some reason is referred to as "the birthplace of ozonation for drinking water treatment".

From a scientific view point, the gas’s correct name is ‘trioxygen’ as it is a gas made up of three oxygen molecules. Ozone is found in low concentrations at ground level and is more noticeable after thunder storms, by the sea-side, and has been found to be released in certain geological events.[1]

Ozone Generation; Ozone used in industry is measured in μmol/mol, ppm (parts per million), nmol/mol, μg/m3, mg/hr (milligrams per hour) or weight percent. Applied concentrations vary from 1 to 5% for ozone generated from ambient air feeds, to 6 to 14% in oxygen for older generation methods. Electrolytic methods where a PEM cell is used can achieve up 20 to 30% dissolved ozone concentrations in the output water.

Where ozone is generated from ambient air, temperature, air pressure and water vapour or humidity influence how much ozone will be produced using traditional generation methods such as corona discharge or ultraviolet light. Where humid ambient air is used as a feed gas, the older ozone generation systems will produce less than 50% the system’s theoretical capacity than when operated with dry air. New generators
using electrolytic methods can achieve higher purity and dissolution through using water molecules as the source of ozone production.

**Corona discharge**; Corona discharge is the most common type of ozone generator for most industrial and personal uses. While variations of the "hot spark" coronal discharge method of ozone production exist, including medical grade and industrial grade ozone generators, these units usually work by means of a corona discharge tube. They are typically cost-effective and do not require an oxygen source other than the ambient air to produce ozone concentrations of 3–6%. Fluctuations in ambient air, due to weather or other environmental conditions, cause variability in ozone production. However, they also produce nitrogen oxides as a by-product. Use of an air dryer can reduce or eliminate nitric acid formation by removing water vapour and increase ozone production. Use of an oxygen concentrator can further increase the ozone production and further reduce the risk of nitric acid formation by removing not only the water vapour, but also the bulk of the nitrogen.

**Ultraviolet light**; Ultra-Violet (UV) ozone generators, or vacuum-ultraviolet (VUV) ozone generators, employ a light source that generates a narrow-band ultraviolet light, a subset of that produced by the Sun. While standard UV ozone generators tend to be less expensive, they usually produce ozone in concentrations of 0.5% or lower. Air has to be exposed to UV light for a longer time period, making this method impractical for use in situations that deal with rapidly moving air or water streams (in-duct air sterilization, for example). Production of ozone is one of the potential side-effects of ultraviolet germicidal irradiation. VUV ozone generators are used in swimming pool and spa applications ranging to millions of gallons of water. VUV ozone generators, unlike corona discharge generators, do not produce harmful nitrogen by-products and also unlike corona discharge systems, VUV ozone generators work extremely well in humid air environments.

**Cold plasma**; In the cold plasma method, pure oxygen gas is exposed to a plasma created by dielectric barrier discharge. The diatomic oxygen is split into single atoms, which then recombine in triplets to form ozone. Cold plasma units are driven by pure oxygen gas as the input gas source and produce a maximum concentration of
about 5% ozone. They produce far greater quantities of ozone in a given space of time compared to ultraviolet production.

Some cold plasma units also have the capability of producing short-lived allotropes of oxygen which include O₄, O₅, O₆, O₇, etc. These species are even more reactive than ordinary O₃.

*Electrolytic*; Electrolytic ozone generation splits water molecules into H₂, O₂, and O₃. In most electrolytic methods, the hydrogen gas is removed to leave oxygen and ozone as the only reaction products. Electrolytic generation of ozone through a permeable Electronic Membrane (PEM) cell can achieve higher dissolution in water without other competing gases found in the corona discharge method, such as nitrogen gases present in ambient air. Electrolytic ozone generation can achieve concentrations of 20–30% and is independent of air quality because water is used as the starting substrate.

**Ozone as the Janus in Medicine**; Although O₃ can attack lung tissue, researchers have shown in numerous published articles and scientific papers that it has many positive therapeutic effects.[2-4] Indeed, some researchers have described ozone as the ultimate 'Janus'. Janus is the Roman god of gates and doors, beginnings and endings, and is represented with a double-faced head, each looking in opposite directions. In the context of ozone, on one face ozone can cause severe problems with lung tissue, yet on the other face ozone can act in synergy with pharmaceuticals or alone to set up accelerated healing and health.[3] The recent manufacture of calibrated medical ozone generators has allowed the mechanisms, action and possible toxicity of O₃ to be evaluated in clinical trials.[3] Ozone has a capacity to oxidize organic compounds,[5] and has well-known toxic effects on human and animal respiratory tract tissue when present in smog.[6-8] For medical uses ozone gas is produced from medical grade pure oxygen, and is administered in precise therapeutic doses, never via direct inhalation, and the literature shows that it has excellent general health benefits, with uses in the treatment of dental caries, decreased blood cholesterol and stimulation of antioxidative responses, increased oxygenation in resting muscle and is used in complementary treatment of hypoxic and ischemic syndromes.[9-11] However a large
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number of unsubstantiated claims are made on the world wide web and in general advertising that have dubious scientific validity at best. For example, there is no scientific evidence to show ozone treatment leads to weight-loss. Hence a number of ozone associations have been setup to counter these ‘false’ claims, inform the public and train individuals to offer and deliver safe and effective treatment.

History of Ozone Treatment; Ozone therapy has been utilised and extensively studied for many decades. Its reported effects are proven, consistent and with minimal side effects. Medical ozone, used to disinfect tissues and treat disease, has been used for over 150 years. Its use to treat infections, wounds and multiple diseases, and ozone’s effectiveness has been well-documented in the scientific literature. It has been used to disinfect drinking water since the late 1800’s and now ozone disinfection of drinking water can be found in virtually every country in the world. In the early 1900’s ozone was used to treat over 100 diseases, and published papers exist as far back as 1902 with a more general discussion in the 1895 Florida Medical Journal.[12]

During the first world war ozone was used to treat infected wounds and it was found that \( \text{O}_3 \) not only effectively dealt with infections, but also had hemodynamic and anti-inflammatory properties.[13] In the late 1980s as HIV and AIDS was first reported, ozone autohemotherapy (O3-AHT) treatment for AIDS patients was reported.[14] Ozone showed promise in laboratory tests to treat AIDS. Unfortunately O3-AHT proved to be less effective when patients were treated with the protocol used at that time.[14] However more recent work has shown promising results.

The unique bio-compatible properties of ozone suggest a possible role in the treatment of severe acute respiratory syndrome (SARS). SARS is a viral respiratory disease in humans caused by the SARS coronavirus. Ozone could be used either as a stand-alone therapy or as an adjunct to standard treatment regimens, and owing to the reactivity of ozone, it is possible ozone will be effective across the entire SARS virus group.[15] The same would apply to avian-flu virus that has seen a recent recurrence.

Ozone can also be used to treat cancers successfully.[16-19] Published papers show successful treatment of a wide variety of cancers, and up until the 1950’s, ozone was the treatment of choice in the USA. There are a growing number of clinicians in the USA
who use a combination of diet supplementation, life-style changes and ozone in a combined treatment for cancer with successful outcomes.

**How Ozone works; Inactivation of bacteria, viruses, fungi, yeast and protozoa:** Ozone therapy disrupts the bacterial cell wall through oxidation. When ozone contacts fungi, O\(_3\) inhibits cell growth at certain growth and reproductive stages. With viruses, O\(_3\) damages the viral outer protective shell called the ‘capsid’ and halts the reproductive cycle by a process called peroxidation. The weak enzyme coatings on cells which make them vulnerable to invasion by viruses make them susceptible to oxidation and elimination from the body, which then replaces them with healthy cells.[18]

**Stimulation of oxygen metabolism:** Ozone therapy causes an increase in the red blood cell glycolysis rate. This leads to the stimulation of 2,3-diphosphoglycerate which leads to an increase in the amount of oxygen released to the tissues. Ozone activates the Krebs cycle to boost the production of cell energy. There is a stimulation of production of enzymes which act as free radical scavengers and cell-wall protectors and prostacycline, a vasodilator, is also induced by O\(_3\).[19]

**Activation of the immune system:** Ozone administered at a concentration of between 30 and 55 μg/cc causes the greatest increase in the production of interferon and the greatest output of tumour necrosis factor (an important part to ozone treatment of cancers) and interleukin-2. The production of interleukin-2 launches an entire cascade of immunological reactions.[19]

**Mechanism of action of O\(_3\) on the human lung:** Ozone exposure at high concentrations induces an asthmatic-type of response with sudden inflammation of the airway tissues. Patients can experience a cough, decreased lung function, shortness of breath, and breathing difficulty with mild to severe presentation.[19]

**Clinical Trials with Ozone;** When ozone is used as part of a treatment protocol for chronic pulmonary obstructive disease (COPD), and cystic fibrosis, the results showed better results when ozone was administered just before drug administration, and Ozone was shown to enhance the drug effects. [20]
Ozone injected into joints has been used for pain control in osteoarthritis of the knee, shoulder and arm joints, and for lumbar-herniated disc. [21&22]

**Advantages of Ozone Treatment:** Ozone has a number of advantages over conventional pharmaceutical products. Ozone should be regarded as a therapeutic agent and considered to be a drug. Most pharmaceutical drugs are not targeted, so the whole body becomes exposed to a serum-level concentration of the drug, which may cause a number of unwanted side effects. Ozone can be administered as a targeted drug, for example as an injection into a joint, body cavity or surface application, or via the blood stream for a whole-body treatment.

Diabetic complications have been attributed to the oxidative stress in the body. Ozone has been found to activate the antioxidant system affecting the level of glycaemia or sugars in the blood. Ozone prevented oxidative stress by normalising the organic peroxide levels by activating superoxide dismutase.[23&24] Ozone was found to completely inactivate the HIV virus in laboratory experiments, without causing damage the host cells.[14&25] Ozone was also found to increase the host immunity by increasing the production of cytokine.[26] In one laboratory study O$_3$ was seen to be very effective in reducing the concentrations of *Acinetobacter baumannii*, *Clostridium difficile* and methicillin-resistant *Staphylococcus aureus* in dry and wet samples; this and other studies support the use of ozone’s as a disinfectant.[27&28] In another study, when a low ozone concentration was used in air conditioning and in individual rooms, the incidence of flu and cold infections fell.[29]

Ozone is now used for sterilisation in purpose-built units in some Canadian hospitals. When ozone is introduced into a steam chamber, the action of heat and moisture can lead to a deep tissue clean and detoxification. One significant advantage of ozone treatment is that unwanted side-effects usually found with standard pharmaceutical drugs are not seen. Routine drugs have a high rate of hospitalisation and death due to both side effects, interactions with other medication, and poor patient compliance. This makes ozone probably the safest treatment that can be offered.

**Disadvantages of ozone treatment:** If ozone is inhaled, fats known as lipids in the lung tissue react with ozone, to cause sudden inflammation. This effect can be mild.
resulting in a cough, or more severe leading to breathlessness and an asthmatic-like attack.[6,27&28] Enzyme inactivation by ozone can result in cell injury or eventual cell death. Combinations of ozone and nitrous oxide that occur in air pollution and smog can create hazardous conditions for people in cities and industrial areas.[30&31] Whilst this is nature’s way to cleanse polluted air, this is often cited as a reason to ban ozone units in some countries. It is stressed that medical ozone is very different from the ozone found in smog & air pollution. Lung tissue and cell damage can be prevented and reversed by dietary antioxidants or free radical scavengers, like vitamin E and C. [32&33]

**Recent Developments in Ozone Research;** Recent research has shown that ozone is produced as part of the body’s defence mechanism in humans. This has been confirmed by subsequent research.[34&35] The role of ozone as a human cell disinfectant and as part of the bodies defence against bacteria, fungi and viruses is confirmed. Ozone is used as an antibacterial agent to treat oral infections caused by *Actinomyces naeslundii, Lactobacilli casei* and *Streptococcus mutans*. Exposure of about 60 seconds showed a 99.9% killing efficiency. It has been used to stop the process of dental decay which can lead to remineralisation and relief of dental pain.[9]

When ozone is dissolved in plant oils, it produces a thick gel-like product, and this has found to be an effective and easy to apply anti-microbial agent.[36] This new product contains ‘ozonoids’, and these are used to treat infection, accelerate the healing of bone and soft tissue, and skin regeneration in medical, dental and veterinarian applications.[36-44] Ozone is used to manage agricultural waste water and is used to destroy growth hormones, used to accelerate animal maturity, before these bio-chemicals enter and pollute ground water.[45&46]

In a preliminary report of new HIV research with ozone oils, a reduction in the viral count from 62000 to 3100 in just 6 weeks was observed, with a substantial boost to the CD4 count, indicating that not only was the HIV virus controlled, but the patient’s immune system showed signs of recovery & support.[47] Ozone can be incorporated into various treatment options; for example, ozonated water can be used in colonic irrigation.
treatment, flotation and steam chambers. The use of micro-encapsulation of these oils in skin creams opens a new potential in active tissue healing.

**Conclusion;** Ozone has a long history of use in healthcare. In the 1890s, Willoughby Miller proposed that oral micro-organisms found in dental cavities played a role in pulmonary diseases, gastric problems, and brain abscesses, as well as many other medical conditions.[48] Miller went on to propose that the majority of systemic illnesses seen in man could be related to the oral cavity.

Research from the late 1800's up to recent months shows that ozone treatment is safe, has virtually no unwanted side effects, and can be used to treat a wide range of disease. Recent research is showing a strong link between infections in the mouth and age-related disease such as Alzheimer's and dementia. Viral infections such as Herpes can be effectively controlled, as it is now known that certain cancers have a connection to viruses that can be treated and eliminated with ozone.[49-53] Research has documented the mechanisms of action and interaction of ozone with infective organisms in human cells. There are concerns with high concentrations of ozone and lung tissue damage. However, like every other pill, tablet, capsule or liquid pharmaceutical product, when used and administered by trained healthcare clinicians and therapists, and provided the public follow the recommended treatment protocols, ozone probably provides the safest treatment option for a wide range of disease and promotes general health.

**About the Author;** Dr Julian Holmes lives in Cape Town with his partner Ingrid and their two dogs. Julian qualified first as a dentist over 30 years ago in the UK before his research took him into more general healthcare. He has been involved in ozone clinical care and research for over 20 years. He has some 70 scientific articles and papers published on ozone and its use in healthcare, and lectures world-wide. Some of his papers and articles can be found on [www.the-o-zone.cc](http://www.the-o-zone.cc). Julian is the current President of the International Association for Ozone in Healthcare and Dentistry ([www.iaohd.org](http://www.iaohd.org)), and leads the International Academy where healthcare workers are trained to use ozone safely and offered ozone courses; he is involved in setting up a teaching institute in Aruba with other leading US ozone clinicians. He is an active member of the Ozone
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Association of South African (www.ozoneassociationsa.co.za/) and will be presenting some of his research at OASA’s meeting in Johannesburg, 19-20 September 2013 with other international speakers – contact OASA Chairlady Michelle Nicolopulos michelle.nicolopulos@gmail.com for details and to book your place at this important meeting, which is open for anyone who is involved in the use of ozone. Julian Holmes offers ozone treatment at Ubuntu Medi-Spa, Kloof Street, Cape Town (www.ubuntu-wellness.co.za) and formulates and manufactures a range of ozone products and organic skin creams that are available through GCE www.greycellenterprises.com. Julian’s hobbies are walking, electronics, house renovation, cooking and healthcare. If you want to ask questions on this article or have other health-related questions, you can contact Julian at drjulianholmes@gmail.com.

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