Ozonated Liquids in Dental Practice – A Review.
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Part 3: The Chemistry of Ozone in Water.

Abstract: In Part 3 of Ozonated Liquids in Dental Practice, the uses of ozone are examined in the sterilisation process of potable water supplies. There are many advantages to the use of ozone in water purification, in terms of cost, low chemical requirements and predictability of outcome. The historical perspective of ozone water treatment is discussed, as well as research that shows the potential uses of ozonated water.

Introduction.

Ozone has a long history in historical records. The North American Indians noticed that fishing in lakes was more productive after a thunderstorm with lightning. Similarly, the ancient Greeks also noticed this odour, which they termed 'ozein'. These fishing groups preferentially fished after electric storms, a custom which is still practiced in modern times, since the upper layer of lake water is enriched with dioxygen and oxidised debris. Ozone found in water is not a product arising from chemical reactions from the water body bed, or from the deep layers.

Ozone dissolved in water is from surface diffusion in the superficial layers close to the water surface, and partially obeys Henry's law of partial pressures of gas. In the 1700's a number of people investigated gas behaviour in the laboratory. Robert Boyle investigated the relationship between the volume of a dry ideal gas and its pressure. Since there are four variables that can be altered in a gas sample, in order to investigate how one variable will affect another, all other variables must be held constant or fixed. Boyle fixed the amount of gas and its temperature during his investigation. He found that when he manipulated the pressure that the volume responded in the opposite direction. For example, when Boyle increased the pressure on a gas sample the volume would decrease. Mathematically, 'PV = C', where 'C' is a constant value if the gas is behaving as an Ideal Gas. A practical math expression of Boyle's findings is as follows: $P_1V_1 = P_2V_2$ where the variables with the subscript 1mean initial values before the manipulation and the variables with the subscript 2 mean final values after the manipulation.

One of the most common uses of ozone is for the commercial treatment of potable water. With pre-treated water, bacteria are devitalised within 2 seconds by ozone by rapid rupture of their cell membranes. In comparison, chlorine when used as a water disinfectant diffuses into the cell and requires up to 30 minutes to achieve bactericidal effects.

The rate of bacterial lysis is dependent upon the ozone concentration: the greater the degree of contamination, the greater the ozone concentration has to be. To maintain clean water, lower maintenance concentrations of chlorine are used. Scientists and doctors studied the ozonation system at the Oudshoorn plant in Holland and later constructed a 19,000 M^3/day (5 mgd) plant using ozonation for disinfection at Nice, France in the early 20th Century. Nice is often referred to as the birthplace of ozonation for drinking water treatment. Over 6000 cites and towns around the world use ozone as their every-day disinfection and sterilisation technique for this basic requirement for life.

All living organisms, including man, are continually exposed to zone during their daily lives. There have been many who have commented on the deleterious health effects of this reactive oxygen species (ROS), but in view of the positive benefits of the ROS, this is now being questioned. This will be discussed further later. There are many areas of employment where man is exposed to sources of ozone. These are laser printers and some office photocopying equipment, x-ray generators and other high voltage electrical equipment used in medical, dental and veterinary procedures and industrial manufacturing, water purification processes, when ozone is used as an oxidant for bleaching purposes, and electric arc welding and mercury lamps (*Dickermann et al 1954, Burleson et al 1975*).

The Chemistry of Ozone in Water.

Modern science has unlocked more of nature’s secrets, and it is now understood that different chemical molecular structures have unique properties in terms of solubility, and polarity. Pressure is the most important factor when dissolving gases in liquids. If the solute is a gas and the solvent is a liquid then changes in pressure will affect solubility and this aspect was investigated by Henry, resulting in Henry's Law. In addition, temperature and solvent polarity also play an important role.

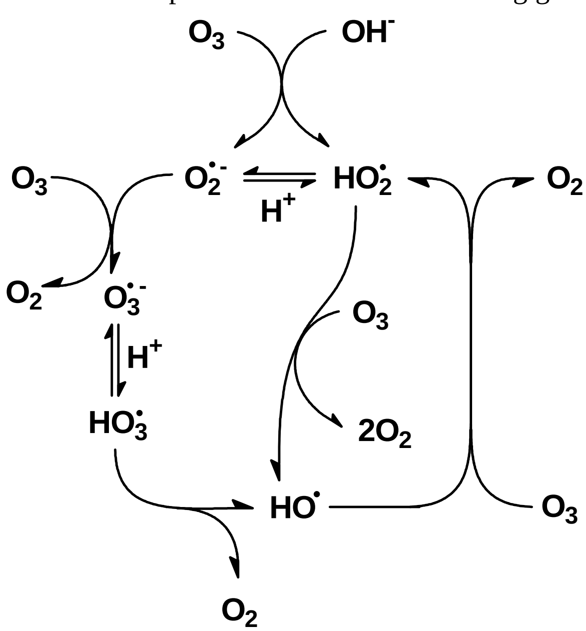

Fig 3.1. The main reactions of ozone with water

If the solute in question is a gas, increasing the pressure increases the amount of gas in the solvent (in this case water) and therefore the concentration of gas. This is Henry's Law: C = k P where C is the concentration, P is the pressure and k is the Henry's law constant for the particular gas/solvent combination - effectively an equilibrium constant.

However, Henry assumed that there was no reaction between the solute and solvent. As ozone, the solvent, reacts with the solute, the water, the gas only partially obeys this gas law, and it can only be used as a guide to the potential concentration achievable.

As a guide, if pure water is used, decreasing the water temperature to just above zero, and pressurising the container to 2 or 3 atmospheres, about 5% volume of gas will dissolve.

For most practical applications, it can be assumed that ozone has a life span of about 10 hours if the water is kept cold. This time can be extended if the container is pressurised. Dissolved ozone will gradually break down to give oxygen and hydroxyl, chemical formulae OH^-, radicals which will undergo further reactions in the water. However, as soon as the water is allowed to return to room pressure and temperature, ozone will boil off and start to break down to oxygen.

Ozone has played a significant role in the treatment process of industrial wastes and effluents in the past and will continue to do so in the future. The utilisation of ozone in industrial situations has a long and impressive history, one that pre-dates current environmental concerns. It is used to clean and sterilise water in the production of micro-chips, and to sterilise water used in the manufacture of soft drinks (for example Cadbury Schweppes use ozone to sterilise their water prior to the manufacture of their range of soft drinks).

When ozone is used to treat drinking water, it is effective in eliminating colour, taste, and odor. Its competition, chlorine, which is used in many facilities as a disinfectant, has recently been found in scientific studies to have a tendency to create carcinogens as it breaks down. For this reason, there is increased pressure to reduce or eliminate chlorine as a primary disinfectant to water. Ozone is 150 times more powerful than chlorine and 3500 times faster acting. It eliminates harmful metals as well, by causing these metals to clump together which allow them to be large enough to filter out. Because of ozone's short life, it quickly converts to pure oxygen and thus adds much needed oxygen to the water. Since ozone water purification systems require very few chemicals, they are healthier and very cost-effective in long-term applications.

The OH^- radical is an extremely reactive species that can contribute to tissue injury, and ozone is known to promote free radical generation both *in vivo* and *ex-vivo* (*Goldstein and Balchum 1967, Goldstein et al 1969, Menzel 1970, Roehm et al 1971, Freeman et al 1979, Dillard et al 1978*). Since the reduction potential of the $O_3/O_3^{\cdot -}$ couple is about +1.6 volts, (*Pryor et al 1976*) electron transfer reactions of ozone with thiols and catechol-like compounds, as well as many other biological electron donors, are thermodynamic possibilities. In addition, the effects of free radicals on the pathogenesis of periodontal tissue destruction were extensively assessed (*Embery and Waddington 1994, Moseley et al 1997, Waddington et al 2000*).

For therapeutic use, ozone is generated by passing oxygen through two high tension electrodes. During generation of ozone some 60 multiple molecular combinations can be found. These last only for nanoseconds breaking down rapidly during collision of the molecules. The quality of the ozone is determined by the purity of the oxygen source. Bottled oxygen provides the purest raw material, followed by oxygen produced from oxygen-concentrators.

Several vital factors are important for successful ozone treatment in addition to the quality and concentration of ozone used for the treatment. The contact time between the ozone and tissues is important. The longer the ozone is in contact with the tissues to be treated, the more effective the treatment is. As mentioned before, ozone is relatively unstable with a half life of 5 – 30 minutes. Contact time is the time when the diatomic molecule which is ozone is in contact with organic or chemical matter in the atmosphere, water or body fluids. When contact happens one oxygen atom breaks away. This is called the singlet O. Singlet O is a very aggressive oxidiser: it oxidises the chemicals or metals into oxides. It will also oxidise all bacteria, moulds and fungi, viruses and parasites. Unhealthy cells such as cancer cells are also oxidised. Ozone thus is a non-chemical disinfectant. It is the second most powerful oxidiser in nature, second to Fluorine. In comparison to ozone, fluorine is a very toxic gas and has no part to play in medical therapeutics.

The contact time can be defined as the length of time the tissues are exposed to ozone before ozone disintegrates. The longer the contact time, the better the micro-biological kill rate. Baysan showed that by increasing the contact time from 10 seconds to 20 seconds, the bacterial kill rate changed from ozone being a disinfectant to acquiring sterilising effect (*Baysan 2002*). The stability of ozone also depends on the alkalinity or acidity of the tissue and body fluid. In an alkaline milieu ozone is more stable and the contact time is increased with better results. Since ozone when disintegrated reverts back to oxygen, it is environmentally friendly.

Life process depends on the balanced functioning of the Redox system. The Redox system is the acronym for the process of **Red**uction and **ox**idation going on to sustain the life process. In lay language oxidation means frying or burning, and reduction means putting out the fire. For oxidation to occur, oxygen needs to be supplied. Oxidation is necessary for energy production. Oxidation cannot continuously occur without control. It is like a fire used to cook food. When the cooking is finished, the fire is put out. In the body oxidation is stopped by reduction i.e. the oxygen is removed.

Ozone is a polymer of oxygen and is a very aggressive oxidant. It is also ten times more soluble in water and body fluids than oxygen. As a result of the reaction of this singlet O on substances, a hydroxyl radical and super oxide is formed. The singlet O also reacts with the hydrogen peroxide in the body. Hydrogen peroxide (H_2O_2) is produced in the body during normal cellular metabolism. This singlet O reacts with H_2O_2 forming hydroxyperoxyl radical. This is known popularly as peroxide. Peroxides are destructive free radicals.

Ozone also acts on contact with unsaturated fatty acids producing H_2O_2. This is further acted upon by ozone resulting in molecular oxygen, hydroxyl radical and hydrogen radical.

A few amino acids react to ozone. The majority of proteins are not susceptible to ozone. Ozone can also inhibit certain enzymatic activity in the body. Ozone also reacts with nucleic acids causing a break in the nuclear strands.

All the above reactions mentioned are due to the singlet O that separates from the O_3 molecules, when ozone comes in contact with the body fluids and organic matter. This single O is a free radical. A free radical is formed when an atom has no electron to share with another atom. The electrons orbit the nucleus of the atoms in pairs. When one of the pair separates or is lost the single electron, since it cannot survive alone, desperately seeks a partner. In the process of search for another electron to pair with, the single electron or the free radical can cause much damage to the tissues. Many chemical reactions occur through free radicals. Free radicals cause polymerisation and precipitation of soluble proteins and cross linking of DNA molecules. All this prevents normal functioning of the cell. When cells cannot function efficiently, ill health results.

The singlet oxygen is in a very high energy state and initiates oxidation. Oxidation in turn causes the production of free radicals. When ozone creates all these damaging reactions it seems illogical that it could be a healer. All the healthy cells in the tissues and organs in the body have free radical scavengers and nutrients to prevent oxidation. They are all protected from possible damage by the singlet oxygen and resulting free radicals. Only unhealthy cells which have lost this protective mechanism and organisms which are devoid of antioxidants and scavengers are destroyed. These antioxidants are Vitamins C & E, Beta Carotene, Selenium, Methionine, and Glutathione. Zinc helps activation of antioxidants. Other antioxidants are found in raw tomatoes,

grape seed extract, pine bark and red wine. Including these substances in daily diet and taking them as supplements will enhance the antioxidant activity of the tissue.
The cells contain free radicals scavengers such as superoxidase dermatase, catalase, and hydralase. They scavenge the free radicals produced and neutralise them. They inhibit the uncontrolled activity of free radicals and their destruction of tissues by the singlet oxygen. Thus all healthy cells and tissues containing antioxidant and free radicals scavengers are protected from damage. Degenerate cells such as cancer cells, viruses, bacteria and fungi which do not have the protection of the antioxidants and free radical scavengers, will be oxidised by free radicals produced by singlet oxygen. Hence ozone is able to destroy them and sterilise the tissue fluids. Moreover ozone acts as a catalyst for the cells to increase the concentration of these protective substances.

As a bonus, when the singlet oxygen is released the remaining part of the molecule, ozone reverts back to health giving life sustaining oxygen, which circulates in the body nourishing the oxygen starved tissues.

Various other beneficial reactions result with ozone therapy. The electrons in the atoms of the ozone molecules jump from inner orbit, the L level, to K level, the outer orbit, and back. In this quantum jumping of the electrons much electrical and magnetic activity is created and is released. These electromagnetic reactions and electro voltaic reactions result in profuse photon and energy transfer stimulating many beneficial reactions leading to cellular health.

The ability of ozone to sterilise and deodorise by powerful oxidation is used in water purification, in many large cities all over the world. The human body is made up of 57 % of its weight in water. This water is distributed all over the body as blood, lymph, extra cellular and intra cellular fluid. It makes sense that ozone can also sterilise the body fluids helping to get rid of noxious and toxic chemicals and organisms.

By its electro magnetic reaction ozone also stimulates and modulates the immune system, particularly the lymphocytes. Stimulating the lymphocytes and other cells, special substance called interleukins are produced.

Oxygen has to be metabolised by bio chemical processes such as glycolysis, citric acid, cycle, and mitrochronical respiration. All these reactions are enhanced, when ozone is introduced into the blood.

Ozone is more efficient than chlorine for water purification: an ozone level of 0.04ppm in just 4 minutes has been shown to eliminate bacteria, mold and fungus. Giardia and Cryptosporidium cysts are susceptible to ozone but are unaffected by normal levels of chlorine in water. Ozone is 25 times more effective than hypochlorous acid, 2,500 times more effective than hypochlorite, and 5,000 times more than chloramine. (Results measured by the time needed to kill 99.99% of all micro-organisms). Any unreacted ozone simply breaks down into oxygen. Compare ozone to chlorine. Chlorine *reacts* with organic materials to form chloroform, carbon tetrachloride etc generally known as trihalomethanes. Trihalomethanes have been implicated as the carcinogens found in the development of kidney, bladder and colon cancer. In the USA, the FDA and EPA certify ozone as able to destroy 99.9992% of all pathogenic germs in the purification of water whilst destroying 99.9992% of pollutants in the water simultaneously.

The research into ozonated fluids have examined the effects of drinking ozonated water on gut infections (*vanden Bossche et al 1994*), and Khadre and Yousef (*Khadre and Yousef 2001*) examined the sporicidal action of ozone and hydrogen peroxide. This study built on the earlier work of Vestergard (*Vestergard 1994*) who was looking at establishing and maintaining pathogen free conditions in aqueous solutions using ozone. Vestergard's paper examined the use of ozone in space applications for the elimination of pathogens using ozone. Vestergard's area of research was creating pathogen free conditions in aqueous solutions containing organic matter. This research, although concerned with hydroponic agricultural systems, can be carried into general potable water studies. The use of a portable water steriliser using ozone in rural areas, as well as by campers in remote rural locations to create sterile and potable water, is supported by this paper.

The use of aqueous ozone in food cleansing is approved by the FDA in the USA. In 1999, Kim *et al* (*Kim et al 1999*) reviewed the use of ozone in the food industry. Young *et al* demonstrated that mycotoxins could be removed by washing food produce with ozonated water (*Young et al 2006*). Crowe *et al* (*Crowe et al 2006*) evaluated the use of ozone to remove fertilizers on soft fruit and later examined the use of ozone as an alternative to chlorine to disinfect and wash blueberries (*Crowe et al 2007*). In 2007, further studies by Bialka and Demirci (*Bialka and Demirci 2007, Bialka and Demirci 2007*) examined the use of ozone to eliminate Escherichia coli from harvested soft fruit. In the meat industry, ozone has been used to eradicate Clostridium perfringens (*Novak and Yuan 2004*), Escherichia coli and Salmonella (*Castillo et al 2003*).

The referenced research for the use of ozonated fluids in dentistry date back to the 1950's. Wuhrmann and Meyrath examined the bactericidal effect of aqueous ozone solutions (*Wuhrmann and Meyrath 1955*), effectively repeating the observations of Dr Edwin Fisch in 1932. In the 1960's, Onouchi (*Onouchi 1965*) examined the bactericidal action of aqueous solution of O_3 in dentistry.

There are many benefits to drinking ozonated water, to control oral hygiene and as a source of sterile water. However, patients should also be informed that there is an interaction of aqueous ozone with anti-microbials. This research has been published, illustrating the importance of potential interactions of dissolved ozone and prescribed anti-microbials. Patients who are taking a course of antibiotics may need to be informed that the use of ozonated water inactivates antibacterial agents (*Dodd et al 2006*) and in particular amoxicillin (*Andreozzi et al 2005*), progesterone (*Barron et al 2006*) and tetracycline (*Dalmázio et al 2007*). For concern to dentists is that ozone may inactivate the anti-microbial effects of triclosan (*Suarez et al 2007*).

A current topic of debate in dental material science and long term potential effects, are endocrine disruptors found in resin-based dental restorative materials. Deborde *et al* (*Deborde et al 2005*) showed endocrine disruptors were destroyed by ozonated water and Ledakowicz *et al* showed resin acids were removed from water by the action of ozone (*Ledakowicz et al 2006*). These papers potentially point towards a pathway to remove these chemicals from the body system after placement of 'modern' tooth-coloured or 'white' fillings.

Papers examining the sterilisation of municipal water supplies have shown the accelerated chemical reactions of ozone with organic impurities, when compared to chlorine. For example, the chemical kinetics of ozone is extensively discussed by Onstad et al 2007 (*Onstad et al 2007*). This and other studies agree that the mode of sterilisation is via the ^{-}OH radical (*von Gunten 2003*) and organic micropollutants are oxidized with ozone selectively. In a later paper, von Gunten (*von Gunten 2003*) discussed the '*excellent disinfectant*' effects of ozone and this effect '*can even be used to inactivate microorganisms such as protozoa which are very resistant to conventional disinfectants*'. von Gunten continues to discuss inactivation rates for six bacterial species, E. coli, Bacillus subtilis spores, Rotavirus, Giardia lamblia cysts, Giardia muris cysts, Cryptosporidium parvum oocysts. He states that the apparent activation energy for the

inactivation of bacteria is in the same order as most chemical reactions (35-50 kJ mol(-1)), whereas it is much higher for the inactivation of protozoa (80 kJ mol(-1)). This requires significantly higher ozone exposures at low temperatures to get a similar inactivation for protozoa.
In a second later paper, von Gunten (*von Gunten 2007*) further elaborates on the treatment of drinking water. His paper shows the oxidation of organic and inorganic compounds during ozonation can occur via ozone or OH radicals or a combination thereof, as Ozone is an electrophile with a high selectivity. The reactions of ozone with inorganic compounds are typically fast and occur by an oxygen atom transfer reaction. The by-product of main concern is bromate, which is formed in bromide-containing waters. A low drinking water standard of 10 microgL(-1) has been set for bromate. In certain cases (bromide > approximately 50 microgL(-1)), it may be necessary to use control measures to lower bromate formation by lowering the pH, adding ammonia or by a chlorination-ammonia process.

Studies to look at increasing the solubility of ozone in fluids have identified that the use of ultrasonics (*Zhang et al 2007*) increases ozone solubility, and allows the use of less powerful ozone generators . This is of importance to developing countries and rural areas where these units could be run from solar power.

Dental researchers have started to examine the effects of ozonated fluids in periodontal disease. Huth *et al* in two papers in 2006 and 2007 (*Huth et al 2006, Huth et al 2007*) examined the effect of ozone on periodontal tissues. The 2007 paper compared traditional periodontal anti-microbial products with the use of ozonated water. Both papers concluded that ozonated water has an excellent anti-microbial effect.
Huth *et al* (*Huth et al 2007*) in their later paper examined the effect of ozone on the influence on the host immune response. These researchers chose the NF-kappaB system, a paradigm for inflammation-associated signaling/transcription. Their results showed that that NF-kappaB activity in oral cells in periodontal ligament tissue from root surfaces of periodontally damaged teeth, was inhibited following incubation with ozonized medium. The Huth 2007 study establishes a condition under which aqueous ozone exerts inhibitory effects on the NF-kappaB system, suggesting that it has an anti-inflammatory capacity (*Huth et al 2007*).

Low *et al* (*Low et al 2006*) evaluated the effects of ozone-treated surface-modified porous silicon, with a view to achieve mammalian cell adhesion onto the modified surface. The success of these researchers opens alternatives to titanium implant materials. Silicone products are white-coloured, and may offer cosmetic advantages when placed in the aesthetic anterior region.

Water pollutant studies have shown how ozone can be used to treat multiple water sources to manufacture potable water (*Frinak et al 2006, Ku et al 2007, Al Momani et al 2008*), and treat waste effluent (*Ledakowicz et al 2006, Ku et al 2007, Sung et al 2007, Pi et al 2007, Dietrich et al 2007*).

The anti-microbial effect of ozone has also been looked at in terms of treating infectious endophthalmitis, which is usually fatal. Takahashi *et al* (*Takahashi et al 2004*). In this study, ozonated water was used to flush the anterior chamber as prophylaxis against infectious endophthalmitis with excellent anti-microbial effects.

Ozone has been used for years as a disinfectant in water. TSO_3 has developed an ozone sterilizer for heat sensitive medical instruments. The inactivation kinetics of *Geobacillus stearothermophilus* spores alone, or mixed with hard water or serum has been studied. *G. stearothermophilus* spores were the most resistant micro-organism in the TSO_3 ozone sterilizer.

Survivor curve and negative fraction analysis were performed to estimate the D-value of the spores as a function of the critical process parameter. In the TSO_3-125L sterilizer, microorganisms inactivation follows the Chicks and Watson's law for chemical disinfectant, a first order rate kinetic was found. In contrast to steam and Ethylene oxide sterilization process, the ozone process is dose dependent.

Véliz E, *et al* (*Véliz E, et al, 2004*) showed that small domestic ozonators were very efficient at reducing and eliminating micro-organisms in drinking water. The best operating conditions were: a water pressure at the equipment inlet of 1 kg/cm^2, a water flow of 1 L/minute, an ozone concentration higher than 0.3 mg/L, and a continuous time operation of 10 minutes. This allowed the production of 10 litres of ozonated water. If an air-supply is used instead of an oxygen source, and assuming at worst 10% efficiency, then 20 minutes of ozone bubbled through a sparging stone would seem to suffice.

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