OZONE - A new horizon in dentistry

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Dedicated to

My parents ***Mrs. Leelaben Raiyani and Mr. Madhubhai Raiyani,*** *for their encouragement and guidance throughout my life, because of them I achieve this goal.*

My sister ***Priyanka,*** *for always being there.*

My guide ***Dr. Ruchi Arora and Dr. Deepak P. Bhayya, for*** *support and encouragement in successful completion of this work.*

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Contents

INTRODUCTION

The word "Ozone" was introduced by Schonbein in 1840. He subjected oxygen to electrical discharges and noted "the odour of electrical matter". It was then concluded that odour was due to a gas which he named Ozone, from the Greek "Ozein" (odorant) and described several of its properties. Numerous researchers since that time have worked to elucidate the nature and actions of ozone. Mariniak and Delarive showed that it is an allotropic form of oxygen, and Mulliken and Dewar clarified its molecular architecture. [1]

Ozone is a natural gaseous molecule made up of three oxygen atoms. Ozone therapy can be defined as a versatile bio-oxidative therapy in which oxygen/ozone is administered via gas or dissolved in water or oil base to obtain therapeutic benefits (Bayson A *et al.,* 2004). The word ozone originates from the Greek word ozein, which means odor and was first used by German chemist Christian Friedrich Schonbein, father of ozone therapy (1799-1868) in 1840.[2]

Ozone (also known as triatomic oxygen and trioxygen O_3, molecular weight 47.98g/mol) is a naturally occurring compound consisting of three oxygen atoms. It is found in nature, in the form of a gas in the stratosphere in a concentration of 1-10 ppm, being continually created from and destroyed into molecular O_2. Ozone in stratosphere has a critical role in both the thermal structure of the stratosphere as well as the ecological framework for life on the Earth's surface. It is one of the most important gases in the stratosphere due to its ability to filter UV rays.[3]

Ozone gas is immunostimulating, potent analgesic, detoxicating, antimicrobial, bioenergetics and has biosynthetic properties as it causes activation of the metabolism of carbohydrates, proteins and lipids. In dentistry it has three basic forms of application - ozonated water, ozonated olive oil and oxygen/ozone gas. Ozonated water and olive oil forms an ideal delivery system as they have the capacity to entrap

and then release oxygen/ozone. These forms of application are used alone or in combination for the treatment of dental disease.[4]

M.Arita *et al*. (2005) showed that the microbial plaques have the tendency to accumulate on the denture surfaces which consists mainly of *C. albicans* thus causing denture stomatitis. The bacterial count can be effectively reduced by rinsing the dentures with flowing ozonated water (2 or 4 mg/l) for one minute. Application of Ozonized water and Ozonated oil daily accelerate the healing rate thus effective in the treatment of alveolitis. It also reduces the post-extraction healing time by forming a pseudo-membrane over the socket, so protecting it from any physical and mechanical insults. The use of Ozone solution in the form of gargles and local application showed favorable results in healing of fracture of the mandible. Additionally there was established immunomodulating action of ozone on the local immunity factors in oral cavity, demonstrated by the rise of the secretory immunoglobulin A (IgA) level.[4]

Ramzy M. *et al*. (2005) showed that the use of oral hygiene instructions, scaling and root planning together with subgingival irrigation with ozonized water is useful in the management of aggressive periodontitis. Ozonated water (4mg/l) strongly inhibits the formation of dental plaque and reduces the number of sub gingival pathogens. Ozonated water has strong bactericidal activity against bacteria in plaque biofilm so it shows considerable improvement when applied in cases of chronic gingival and periodontal diseases. Both gaseous and aqueous ozone can be used as additional treatment modality along with mechanical debridement.[4]

Macedo *et al.* (2002) described the application of ozonated oil on mandibular osteomyelitis and demonstrated faster healing times than conventional protocols. The results of other studies also prove that the use of ozone tend to accelerate the healing of soft tissue conditions, i.e. aphthous ulcers, herpes labialis, ANUG and other oral infections. Oxygen/ozone therapy has an inhibiting effect in the development of pit and fissure caries, root caries, and interproximal carious lesions. Ozone has been

shown to attack extrinsic discoloration, but has not much useful in intrinsic stains. The use of ozonated water followed by peroxide treatment significantly increases the efficacy and reduces the time necessary to generate the desired effect. Smear layer present over the exposed root surface prevents the penetration of ionic Calcium and Fluorine deep into the dentinal tubules. Ozone removes this smear layer, opens up the dentinal tubules, broadens their diameter and then Calcium and Fluoride ions flow into the tubules easily, deeply and effectively to plug the dentinal tubules, preventing the fluid exchange through these tubules. For this purpose, ozone is sprayed onto the exposed dentine for 60 seconds followed by mineral wash repetitively.[4]

L.A.Sechi. *et al.* (2008) noted a valuable antimicrobial activity against all tested micro- organisms especially against Mycobacterium by ozonized sunflower oil (Oleozon). Ozonized oils can be used to sterile the root canals and to clear the canals of necrotic debris by its effervescent properties. Irrigation is more quick and efficient than the conventional irrigation by the sodium hypochlorite and sodium peroxide combination.[4]

Ozone has been used in dental therapy for over 3 ½ years by 4,000 dentists with no reports of side effects (E. Lynch, personal communication. May 2005). Also, in clinical studies in over 2,000 patients, no adverse effects have been reported. Ozone as a therapeutic agent is similar to many medicaments that are only effective if applied in the correct dose and for valid procedures.[5]

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

- As a powerful disinfectant.
- Ability to control bleeding.
- In its ability to clean wounds in bones and soft tissues.

- Ozone can improve healing.

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

- As mouth rinse (especially in gingivitis, thrush, and stomatitis).
- As a spray to clean the affected area, and to disinfect oral mucosa, cavities and in general dental surgery.
- As an ozone/water jet to clean cavities of teeth being capped, receiving root canal therapy, and in treating painful gingivitis and stomatitis.[6]

Ozone is one of the most powerful antimicrobial agents available for use in medicine and dentistry. In the 1920s Dr. Edwin Parr, a Swiss dentist, started to use O_3 as part of his disinfection system. Ozone therapy is a well-established alternative and complementary therapy in most of the European countries. A systematic review was performed on studies investigating the effects of ozone on oral tissues and microorganisms and unveils the uses of ozone in dentistry in all aspects.[7]

The first application of ozone in medical field seems to have been for treating gaseous, post-traumatic gangrene in German soldiers during the 1st world war (Bocci V 2004) However a big step forward was the invention of a reliable ozoniser for medical use by the physicist Joachim Hansler (1908- 1981). The idea to use ozone in medicine developed slowly during the last century and it was stimulated by the lack of antibiotics and the disinfectant properties of ozone.[2]

Ozone, which is used for medical purposes, is a gas mixture comprised of 95 to 99.95% oxygen and 0.05 to 5% pure ozone. Due to proven therapeutic advantages of ozone, many fields in dentistry could benefit from ozone therapy.[2]

The first dentist who used ozone was Edward Fisch in 1950 for treating Austrian surgeon Ernst Payr for a gangrenous pulpite and thereby inspired him to begin a line of investigations dedicated to ozone use in health care.[2]

The medical profession has used ozone for more than 100 years its times for dentistry to replace ‘amputation’ with this radically different approach that patients definitely prefer.[8]

HISTORY

1885- Florida Medical Association published "Ozone" by Charles J. Kenworthy, M. D. M.R.S.V. from Jacksonville Florida. 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, its subsequent revisions and the FDA as well Therefore, ozone's medical usage is grand fathered in the United States and held as perfectly legal for any M.D. to use without censure.

1896- Sept 22, Inventor genius Nikola Tesla patented the first ozone generator in the U.S.

1898- Institute for Oxygen Therapy-Healing started in Berlin by Thauerkauf and Luth. First injection of ozone into animals, First bonding of ozone to solid form products (Haemozon, now Homozon).

1898- Dr. Benedict Lust from Germany practicing in NY. He was the originator and founder of Naturopathy and wrote many books and articles on ozone.

1900- Medical ozone was used in the U.S. by Nikola Tesla who formed the "Tesla Ozone Company"9 which was the first company to use high voltage, high frequency, low amperage AC systems and was granted many ozone patents. Medical ozone and ozone products were used widely in the beginning of the century and their use actually predates the FDA's inception in 1906.

1902- J.H. Clarke's, "A dictionary of Practical Materia Medica," London, describes the successful medical use of "Oxygenium" in treating Anemia, Cough, Cancer, Diabetes, Influenza, Morphine poisoning, Canker Sores, Strychnine poisoning, Whooping-cough.

1904- Ozone charged olive oil has been sold in pharmacies for years all over the U.S. and used by thousands of physicians under the trade name "Glycozone." As reported in nineteenth edition of "The Medical Uses of Hydrozone and Glycozone" by Chas. Marchand.

1910- (+/-) Dr. Eberhart was used ozone in Tuberculosis, Anemia and Chlorosis, Chronic middle ear deafness and Tinnitus, Whooping Cough, Asthma, Bronchitis and Hay Fever, Insomnia, Pneumonia, Nervous Disability, Diabetes, Gout.

Dr. George Stoker, London, reported nine cases of tuberculosis treated within a year at the Stoker Oxygen.

1913- Eastern American Association for Oxygen Therapy was formed by Dr. Blass and German associates.

1914- Nov 20th, Dr. Charles O. Linder was advertising the availability "At a great expense" on his part, of his new medical ozone machine in the vol, No. 1 "Not yet named Magazine" at the Apple Show near Spokane, WA. He was passing the ozone through Eucalyptus, Pine, and Cedar oils as scrubbers before inhalation of the gas.

1920- Dr. Charles S. Neiswanger, M.D. published "Electro Therapeutical Practice" Ritchie and Company, Chicago. "A ready reference guide for physicians in the use of electricity and the X-Rays."

"Ozone as a therapeutic agent." Dr. Neiswanger was the President and Professor General Electro- Therapy Illinois School of Electro Therapeutics; Chicago Hospital College of Medicine. "Ozone acts as a powerful antiseptic in contact with diseased mucous surfaces, consequently its beneficial action is quickly apparent in the treatment of bronchial and laryngeal affections, catarrh, hay fever and all diseases of the respiratory organs."

1929- "Ozone and Its Therapeutic Action." Book nameed 114 diseases and applications of ozone and prints the research from the centers and doctors centers using ozone.

1930- May 3rd, Journal of The American Medical Association article: "The Therapeutic Use of Oxygen in Coronary Thrombosis" by Robert L. Levy, M.D. and Alvan L. Barach, M.D. Oxygen tents help oxygen starved heart attack victims.

1930- German dental physician E.A. Fisch was regularly using ozone in his dental practice in Zurich, Switzerland and wrote large number of ozone papers in Italian, French and German. Patented the "Cytozon," the first dental use ozone apparatus.

1931- Dr. Otto Warburg wins first Nobel Prize for work proving cancer is caused by a lack of oxygen in the cells. He stated in "The Prime Cause and Prevention of Cancer" that the cause of cancer is no longer a mystery, we know it occurs whenever any cell is denied 60% of its oxygen requirements. This occurs through a buildup of pollution or toxicity within and around the cell which blocks and then damages the cellular oxygen respiration mechanism.

1932-Renowned Austrian surgeon Dr. Erwin Payr received ozone therapy and thereby learned of medical ozone by treatment from E. A. Fisch and went on to use ozone in his medical practice, increasing its acceptability in surgery.

1935-Nov, Societe Francais d'Electrotherapie et de Radiologie published M. Sourdeau (Le Mans) paper on "Ozone in Therapy" Four machines to produce ozone had been installed in the Electro- Radiology service in Beaujon-Clichy.

1938- Parisian Medical Bulletin 8000 applications of ozone, there were no accidents or harmful side effects.

1938- Paul Aubourg "Results of 119 cases of coliform infection treated by ozone in Beaujon Clichy." Presse Med 1938; 46:1987- 1900.

1940's- German Doctor Hans Wolfe wrote the book "Medical Ozone."

1940's- FDA started seizing ozone machines, and this policy continues to this day.

1940's- "Polyzone," "Aetheozone," and other ozone machines were marketed in the U.S.

1942- ″Gordon Detoxification and Hydro Surgery - Theory and Practice" book published covering medical uses of ozone as colon cleanser.

1943- During the Second World war, Dr. Robert Mayer treated the FBI prisoners of war in the Ellis Island, NY POW camp. Dr. Mayer subsequently learned of medical ozone from one of the German prisoners and had since been applying

ozone to patients in the United States for over 45 years. Dr. Mayer was a pediatrician, and had safely and effectively given ozone therapy to over 12 thousand people, most of them children. He pioneered the technique of ozone being injected directly into the spinal fluid to end meningitis. Dr. Mayer had authored many medical papers including:

"Using Ozone As a Chemotherapeutic Agent For the Treatment Of Diseases" Out of compassion, he recently came out of retirement (he's in his seventies) and began treating hundreds of AIDS patients with medical ozone.

1944- Dr. Otto Warburg won the second Nobel Prize for his work linking cancer to damaged cell respiration due to a lack of oxygen at the cellular level.

1951- June, Dr. William Turska, Chairman of the Committee on Scientific Research of the American Naturopathic Association published in the Journal of the American Naturopathic Association "Oxidation." Dr. Turska pioneered the breathing of Aethozol (ozone passed through selected oils). He also pioneered and maintained one of the best methods of putting ozone into the body was to put up to 250 cc's directly into the portal circulation via the rectal veins with no pain, discomfort, or side effects. With repeated application, this completely cleaned the liver.

1953- Dr. Hans Wolff, general practitioner in Frankfurt, Germany started his own ozone clinic after coming into contact with and learning about ozone from Dr. Hanseler.

1954- "Oxygen: Master Of Cancer" book was published by Frank Totney.

1956-Feb 24, Two time Nobel Prize winner Dr. Otto Warburg (who won this prestigious award for discovering and proving that cellular respiration, once damaged by a lack of oxygen, caused cells to mutate uncontrollably and turn into cancer cells) published in SCIENCE 24 February 1956, Volume 123, Number 3191 "On the Origin Of Cancer Cells."

1961-Encyclopedia of Chemical Technology, Volume 16, Third Edition, by John Wiley and Sons. The symptoms of breathing high concentrations of ozone are

acute, there appear to be no chronic affects among normally healthy people because the body has the ability to repair such damages. "No free radical reactions which directly involve ozone have been observed. During the 80 year history of the large scale usage of ozone, there has never been a human death attributed to it."

1971-Dr. Hans Wolf (President) and Prof. Dr. Siegfried Rilling (Vice President) founded The German Medical Society for Ozone Therapy.

1972-The International Association For Oxygen Therapy, Dr. George Freibott, President, emerged. Association formed out of International Oxidation Institute, which came from the Eastern American Association for Oxygen Therapy.

1975-U.S. G.A.O. Government General Accounting Office studied the FDA and revealed that 150 FDA officials owned stock in the companies they were supposed to regulate.

1976- The FDA publishes in the Federal Register 21 CFR 801.415 Dated 2/13/76, amended 7/24/85, and 9/27/89: "Ozone is a toxic gas with no known medical uses." Ed McCabe comments in "The Family News:"

"Printing this statement in a publication paid for with our taxes is either a blatant attempt at suppression of truth from the highest levels, or one of the poorest research jobs ever done. It obviously favors competitive therapies, and ignores well over 50 years of safe and effective medical use on hundreds of thousands of humans - backed up with thousands of medical references and clinical studies in Switzerland, Italy, France, Germany, Australia, New Zealand, Mexico, and the U.S."

1978-FDA reports 1.5 million people were hospitalized in the USA due to side effects from medication. On the other hand, medical ozone has been legally used in clinics worldwide on a daily basis since the forties. In Germany, Ozone side effects were typically minor irritations that are caused by incorrect application and quickly disappear. This side effect rate is incredibly far, far, lower than

U.S. drug therapy side effect rates wherein each year approximately 140,000 people die from prescription drug usage. That's two and a half times more Americans than were killed in Vietnam.

1979- First case of AIDS treated by medical ozone therapy. Dr. George Freibott, ND from the International Association of Oxygen Therapy saw his first AIDS case. A Haitian living in Avon Park, Florida came to him with Kaposi's Sarcoma mouth lesions and was treated with medical ozone in rectal insufflations, ozone colonics, and direct ozone IV injection off and on for 1 1\2 years, only once a week. All external lesions were healed.

1979- Dr. Hans Wolff published his book on ozone.

1980- Aug 22nd, Sweet F, Kao M S, Lee S-CD (Dept. of obstetrics and Gynecology, Washington University School of Medicine, St Louis, Mo) and W. Hagar (St Louis Air Pollution Control) publish in "Science" Vol. 209:931-933, a U.S. peer reviewed scientific journal, their study: "Ozone Selectively Inhibits Human Cancer Cell Growth." They announce "Evidently the mechanisms for defense against ozone damage are impaired in human cancer cells." "All of the cancer cells (lung, breast, uterine and endometrial) showed marked dose dependent growth inhibition in ozone at 0.3 and 0.5 ppm" while the normal cells were not affected. "Evidently cancer cells are less able to compensate for the oxidative burden of ozone than normal cells." They also stated that ozone inhibits cancer 40 to 60%, and up to 90% in a dose dependant manner, yet there was no response from mainstream medicine.

1980- Jan, 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.

1980- May, By now, The German Medical Society had 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.

1982- German medical textbook published: "Medical Ozone" 2nd Ed. by Dr. Ewald Fischer Medical Publications in Heidelberg.

1983- ″Ozone as Therapy in Herpes Simplex and Herpes Zoster Diseases;" Mattassi R. MD, D'Angelo F. MD, Franchina A. MD, Bassi, P. MD. Santa Corona Hospital, Division of Vascular Surgery and Neurology, Milano, Italy 58 cases of Herpes Simplex showed complete recovery in two to five days following ozone therapy. "Results, Herpes Zoster: in all patients healing of skin lesions were observed after a minimum of 5 and a maximum of 12 ozone injections. Herpes Simplex: all patients healed after 1-5 injections.(Daily endovenous injections of 20cc of an oxygen-ozone mixture).

1983- June, The chairman of neurosurgery at Jefferson Medical College in Philadelphia, Dr. Jewell Osterholm, announced that stroke damage can be reversed with spinal injections of an oxygen-rich mixture. Experiments on lab cats showed the procedure does reverse stroke damage.

1985- International Ozone Association published Robert A. Mayer's, Experience of a pediatrician using ozone as a chemotherapeutic agent for the treatment of diseases of children.

1985- Jan, "The Biochemical Process Underlying Ozone Therapy" published in Germany by Renate Viebahn.

1985- Professor Viebahn is in constant contact with most of Europe's ozone using clinics. Her paper demonstrated ozone's ability to disinfect and sterilize,employ bactericidal and virucidal mechanisms, is a circulatory enhancer, penetrates viruses.

1986- Dr. Alexander Preuss in Stuttgart, FRG, "Positive Treatment Results in AIDS Therapy; OzoNachrichten 5 (1986) Heft 1/2, published case histories of AIDS patients treated with ozone who are now completely healthy and back at work. Details printed in "Oxygen Therapies" by Ed McCabe, Energy Publications, 1988.

1986- Dec 30, Patent # 4,632,980 was granted and now held by Medizone, Inc. NYC, NY. "OZONE DECONTAMINATION OF BLOOD and BLOOD PRODUCTS" Medizone stated all stored blood can be decontaminated with ozone, and all HIV can be eliminated. Medizone applied for human test approval. Despite 50 years of medical ozone's use on humans by over 7,000 physicians, and flawless animal studies, the FDA won't allow human testing in the U.S.

1987- Dr. Horst Kief, Heidelberg, FRG, announced successful treatment of 3 AIDS patients brought from Stage 8 back to Stage 1 at his German clinic using autohemotherapy ozone/1 gram vitamin C therapies. Dr. Kief states "You can kill the AIDS virus with ozone therapy... No side effects." 15 ARC patients exhibited "full remission." Gained weight, T cells went from 300 back up to 1500 (normal), gone back to work. "One patient was so weak he couldn't turn on the radio. After only 3 treatments, he walks to the bathroom unaided." Typical treatment twice a week (method now outdated), continues for 7 to 11 months.

1987- Dr. Hans Neiper, an ozone using doctor in Hanover, FRG, worked with NASA, past president of a German Oncology in an interview by videographer Jeff Harsh, talked about his colon cancer work. Although he could not divulge the name of his patients, "President Reagan is a very nice man." That's the fact."

1987-Cuban(FDA equivalent) National Inst. For Scientific Research conducted ozone animal studies proving ozone is non- toxic, non-mutagenic, non-carcinogenic. (Ozone won't cause toxicity, mutations or cancer)

1987-Clinical human examinations: "An adult human tolerates 800 ml of an ozone/oxygen gas mixture applied rectally over a period of one minute without any complaints." "Gas absorption is slow, on average within one hour." Both the oxygen and the oxygen/ozone mixture is absorbed through the wall of the large intestine, enters the blood stream and results in a PaO2 increase within the entire organism." "No adverse effects occur when ozone is applied."

(Ozone is) Recommended for colitis and proctitis and is "superior to all previously known methods of therapy. In proctology, we view the indication of rectal insufflation to be valid for colitis." "16 patients with hepatitis B were given ozone and compared to a control group. Those who got the ozone had an increase in wellbeing and 75% of those treated could be placed in the "healed" category within a period of 14 days.

1988-"International Bio-Oxidative Medical Foundation" Charles H. Farr, M.D. President, is formed by several hundred U.S. M.D.'s trying to advance oxygen therapies in the U.S. by publishing their successful clinical results. Yearly meetings attended by physicians from all over the world.

1988-Dr. Gerard Sunnen published: "Ozone in Medicine: Overview and Future Directions" in The Journal of Advancement in Medicine. Dr. Sunnen, at the Bellevue Medical Center in New York City, lists medical ozone as commonly being used worldwide on: "Herpes, AIDS, and Flu. Wounds, burns, staph infections, fungal and radiation injuries, and gangrene. Colitis, fistulae, hemorrhoids and anal infections. It promotes healing. Blood ozone treatments have been used to treat virus infections including: AIDS, hepatitis, flu, some cancers, diabetes and arteriosclerosis. Used in dental surgery, periodontal disease, mixed in water and swallowed for use on gastric cancer, and applied as a wash in intestinal or bladder inflammation. Mixed with olive oil it is used on

fungal growths and skin ulcers. Ozone baths are used to irrigate the skin, to disinfect and treat eczema and skin ulcers. "All of the world's blood supplies may be made bacteria and virus free (AIDS, etc.) by passing 40-50 mcg/ml of ozone through them."

1988- June, Dr. Scott Ricke and inventor Basil Wainwright conducted an HIV in vivo scientific study involving five patients in Nogales, Mexico. In just ten days of treatment, Ozone and a new AIDS monoclonal measurement process developed by Epitope, Inc. demonstrated a reduction of 28% and higher of viral activity.

1988- By Dr. Horst Kief "Ozone is highly effective against viruses. The present study provided statistical proof of its extraordinary efficacy in cases of chronic aggressive hepatitis. In the case of AIDS and ARC patients, hyperbaric ozone therapy can lead to astonishing improvement in the clinical status."

1988- Boguslaw Lipinski, Ph.D., Boston Cardiovascular Health Center and Tufts University School of Medicine, Wellesley, MA published "Rationale For Treatment Of Cancer With Ozone." Citing 35 medical references, Dr. Lipinski concludes "Preliminary clinical studies indicate that oxidative therapy might produce desirable results in cancer treatment."

1989- William Campbell Douglass, M.D. published "AIDS, The End Of Civilization" In it he says, "At present we have the ambulance- at-the-bottom-of-the-cliff mentality in which the only solution entertained is to pick up the bodies rather than go to the top of the cliff and solve the problem." Dr. Douglass visited scores of empty villages in Africa where whole tribes had died of AIDS. He reported seeing mound after mound of burial sites along roadsides in which natives were buried when and where they fell dead. Dr. Douglass is now actively promoting blood ozonation\UV (photophoresis) treatments in the U.S.

1989- April-May, Raum and Zeit Vol 1, No. 1, "The Treatment of Virus Infections with Ozone-Oxygen Mixtures;" Alexander Preuss M.D. (Preuss's work was featured in Ed McCabe's book "Oxygen Therapies" in 1988). He cited 8 of his

AIDS case studies wherein ozone therapy had dramatically improved their health. "Therefore I may conclude that AIDS in the state of an opportunistic infection is treatable for at least 17 months - nobody has to die from it any longer."

1989- First modern u.s. hospital test of ozone on humans stopped George Perez, M.D., Dir. of Virology at Saint Michaels Med Center, Newark, NJ and Chief Investigator of the hospital's Institutional Review Board was commissioned to undertake a 75 days institutional review board supervised ozone/AIDS protocol. 5 terminally ill AIDS patients underwent only 15 days of ozone treatments at Saint Michaels Hospital in Newark, New Jersey. The T4 counts of the patients were from a low of 5 to a high of 86. At the start, one was so badly covered with herpes lesions he couldn't wear clothes. All had T-cell counts of below 200. By the end of the 15 days each treatments, the herpes patient's skin had healed, and all had been released from the hospital. No adverse side effects or toxicity could be found. T/4 counts remained stable or increased. Viral protein core (p24) counts decreased - indicating mass virus destruction. Four M.D.'s state ozone therapy is nontoxic and should be adopted.

1990- Experimental Chemotherapy 1990;36:147-154, "In vitro Synergistic Activity of 5-Fluorouracil with Low-Dose Ozone against a Chemo resistant Tumor Cell Line and Fresh Human Tumor Cells" "Our results indicate that ozone in combination with 5- fluorouracil (5-FU) makes a 5-FU resistant cell line susceptible for the combined treatment modality. Furthermore, ozone acts synergistically or at least additive to chemotherapy in different tumor cell suspensions, derived from the breast and the colon."

1991-Susan M. Lark, M.D. Los Altos, CA sends Ed McCabe a draft copy of her article entitled "Ozone and Its Uses In Medical Therapy". She reviewed the reseach studies on ozone therapy and concluded "the studies find bennefit in the clinical use of ozone for a varitey of conditions with a minumum of side effects."

1991-March, Proceedings of the 10th World Ozone Conference in Monaco " The efficacy of O2/O3 Low Pressure Application In Badly Healing Wounds" Horst Werkmeister - Former head of the Radiography Department, Lutheran Hospital, Oberhausen Germany. "There is little inconvenience to the patient, ozone is not capable of engendering further damage, and produces a significant stimulation of wound healing in a large number of cases due to its disinfectant and pronouncedly hyperemizing effect."

1991-March, Proceedings of the 10th World Ozone Conference in Monaco "Resolution of Intractable Diarrhea of Unknown Etiology in Patients With AIDS Treated by Medical Ozone - A pilot study." Ozone rectal insufflation stops AIDS patients' diarrhea.

1991- Dr. Robert Mayer (using ozone over 50 years, since the forties) had late stage AIDS patients in his research center clinical study some whom only had a count of 5 T cells. Normal is 600-1500+. Although they had a count of only 5 T cells, they were completely healthy. In a hope indicating development, local FDA office told Dr. Mayer to go ahead and use ozone, as long as he only makes it himself in his own office with his own self-manufactured machine.

1991- A brave humanitarian U.S. M.D. (Dr. J.B., ret.) in a southern state came forward with his secret clinical ozone/hyperbaric therapy results. All his testing were performed at a major hospital and within independent labs. Out of 248 HIV POSITIVE patients, he reported bringing 113 to HIV NEGATIVE, each within 60 Days, using ozone autohemo therapy immediately followed by hyperbaric therapy.

1991-Nov 5th, Lymphokine and Cytokine Research Vol. 10, Number 5, 1991 published "Studies on the Biological Effects of Ozone: 2. Induction of Tumor Necrosis Factor on Human Leucocytes, Luana Paulesu, Enrico Luzzi, and Velio Bocci. "Because ozonation of blood is a procedure followed in several European countries for the treatment of viral diseases and tumors, the release of factors with antiviral and Immune modulatory activities by leukocytes may

explain the mechanism of action of ozone and of Autohemotherapy." The "ozone concentration is critical in terms of TNF production and of cell mitogenesis. Owing to the presence of erythrocytes, higher concentrations are required to be effective in blood than in PBMC."

1991- Dec, Dr. Robert Mayer joined the doctors reporting patients sero-converted to HIV NEGATIVE through use of ozone autohemotherapy.

1992- June, Ed McCabe and Dr. John Pittman met with Dr. Killian, Deputy Director of the NIH's N.I.A.I.D. (AIDS institute). He and his assistant were very enthusiastic about ozone once they saw the proof they were brought that ozone was successful in treating AIDS patients. Later, upon follow up, they were very closed mouthed, without enthusiasm, and acted like they never heard a word they were told.

1992-Bolton, A. "Report on Scientific Studies to Elucidate "Ozone-O-Med" Treatment of Peripheral Vascular Disease" Intermune Life Sciences, Etobicoke, Ontario, 1992

1992- Sep, Medical Hypothesis. 1992 Sep; 39(1): 30-4 "Ozonation of blood for the therapy of viral diseases and immune deficiencies. A hypothesis." By V. Bocci. In the last three decades major ozone autohemotherapy has been used in Europe in uncontrolled trials carried out in patients with many illnesses, particularly chronic viral diseases and neoplasms. It appeared that the treatment may activate the host's immune system by inducing the production of immune active cytokines, and it may now be possible to rationalize the procedure, improve the regimen and assess the outcome.Once this is done, owing to the large range of medical applications and the simplicity of the procedure, autohemotherapy could become very valuable particularly in undeveloped countries.

1992-Oct, Pol-Tyg-Lek 1992 Oct 19-26; 47(42-43): 964-6 (Non English Polish Medical Journal) "Clinical assessment of treatment results for Atherosclerotic ischemia of the lower extremities with intra arterial ozone injections" Seven

Polish researchers gave 10 injections of O3 into the femoral arteries of 50 patients with atherosclerotic ischemia of the lower extremities and to 49 diabetic patients. "The treatment showed a significant improvement in both groups. The treatment with O3 is both valuable and safe."

1993- May American Surgery Journal 59(5): 297-303 "Irrigation of the abdominal cavity in the treatment of experimentally induced microbial peritonitis: efficacy of ozonated saline." Nine researchers implanted gel capsules of fecal slurry into the peritoneal cavities of rats. "Ozonated saline statistically proved the most effective irrigating solution for reducing abscess formation in survivors."

1993-Aug-Sept, International Ozone Association holds Eleventh Ozone World Congress and Exhibition August 29 to September 3rd, 1993 in San Francisco. Reports on ozone trials at IOA were:

- Occlusive lower limb arterial disease - O. Rokitansky, J.
- Washuttl and L. Groger – Austria
- Occlusive lower limb arterial disease - R. Mattassi – Italy
- Immune monitoring - H Baltin – Germany
- Artherosclerosis - N.Zhulina, C. Kontorschikova and N. Morozova – Russia
- Cardiopathology - F. Hernandez et al – Cuba
- Hypoxic states - S. Peretyagin – Russia
- Hypoxic impairments - C. Kontorschikova – Russia
- Myocardium fractals - A. Gavrilushkin, S. Peretyagin and O. Birjukova – Russia
- Chelation - M. Foster - U.S.A.
- Diverse Pathology - G. Glady – France
- Dermatology - S. L. Krivatkin – Russia
- Staph - T. Shimoyama et. al. Japan
- Sickle Cell Anemia - M. Gomez et. al. – Cuba

- Ozone produced auto vaccine - J. Greenberg – Germany
- Rheumatic diseases - Z. Fahmy – Germany
- Catostrophic injured children - S. N. Gorbunov et. al. – Russia
- Rectal Insufflation of Rats study - S. Mendez et. al. – Cuba
- Genetics - E. Prieto et al - Cuba
- Anaesthetized horses - P. Scrollavezza et. al. - Italy
- Optic Nerve disfunction - R. Santiesteban et. al. - Cuba
- Cerebro vascular accident - E. Devesa - Cuba
- Senile Dementia - M.M. Rodriguez et. al. - Cuba
- Malignant disease - H. Kief - Germany
- Breast cancer - R. Dallaglio et. al. - Italy
- Neuro dermatitis - H. Kief - Germany
- Digestive System - M. Noa - Cuba
- Germ free lab animals - J.M. Mirabal et. al. - Cuba

Quoting Seigfried Rilling, the President Of the German Medical Society for Ozone in his talk on the Germany History of European Ozone, "...Ozone only serves Humanity"

1993- Sept 8th, Medizone Int'l NYC announced co-project with Italian Ministry of Health and the Italian Scientific Society for Oxygen-Ozone Therapy to treat AIDS and Hepatitis-B patients with Medizone's thin film delivery technology. Patients would undergo a one hour treatment on alternate days, during a twelve week trial.

1993- Sept 25, Dr. Gerard V. Sunnen, M.D. writes his "Addendum To 'Ozone In Medicine'; Possible Mechanisms Of Viral Inactivation By Ozone" He details the chemical pathways by which ozone has its effectiveness. 1994 Jan 20th Medical Tribune - Research News - Headline: "Oxygen plus ozone mixture can inactivate HIV in vitro" article by Nathan Horowitz describes upcoming Medizone Phase 1 clinical trials at several research sites in Italy. 300 patients

with HIV infection or hepatitis-B will be randomized to treated or control groups and studied during three months of dosing and nine months of follow up. For 12 weeks 300 cc's of blood will be withdrawn and ozonated and returned to the patient every other day. "Dr Latino's preliminary data are very interesting," said Mark Cohen, Ph.D., a professor of medicine at Louisiana State University School of Medicine in Shreveport. "His studies show that ozone really is capable of killing HIV."

1994- March 25, Dallas, Texas was the site of the IBOM International Bio-Oxidative Medicine Foundation's 5th annual meeting. Phone 405/691-1452. MD's from all over the world highlighted their own work successfully using ozone and/or hydrogen peroxide and other oxidative compounds in medicine, and attending special educational workshops. Among the papers presented were:

"Sponteneity of Oxidation in Nature" Majid Ali, MD.

"Ozone in Medicine" Frank Shallenberger MD.

"Hydrogen Peroxide and Free Radicals" Charles H. Farr MD Ph.D.

"Complex Oxidative Compounds" George Freibott ND.

"Experiences in the further Treatment of AIDS, Cancer and Chemical Toxicity/Hypersensitivity Using Bio-Oxidative and Nutritional Therapies" Robert Allen MBBS (Australia)

"The Cause of All Disease from a Wholistic Perspective" Ed McCabe.

"Oxidative Therapy and the Answer to AIDS" Robert Willner MD, Ph.D.

"AIDS, Immunology and Ozone" Frank Shallenberger, MD.

"Experiences With Medical Ozone" Stanley W. Beyrle, N.M.D.

"Ozone May Inactivate HIV by Reducing p120-CD4 Binding Affinity, Lysing the HIV Lipid Envelope, and Oxidizing the HIV core" Oscar K. M. Hsu (Harvard)

1994-April Before the above conversations with the CDC, their AIDS reference computerized National AIDS Information and Education Program - CDC National AIDS Clearinghouse databank had a synopsis of the story where Ed

McCabe had testified before the NIH in 1992 about the effectiveness of ozone therapy. The story had subsequently been printed in the "Washington Post" Health section, 06/23/94, page 8. by David Brown. One week after the above conversations, all references of Mr. McCabe's testimony and the resulting Washington Post newspaper story had completely disappeared from the CDC computer. Around 4/7/94. The database is privately owned by Information Inc., Behesda, MD.[9]

MECHANISM OF ACTION

Mechanism of action of ozone in blood

Owing to the potent antioxidant capacity of blood due to its hydrophilic, lipophilic antioxidants and cellular enzymes, some of the ozone dose dissolved in the water of plasma is instantly quenched by free antioxidants (mainly uric acid, ascorbic acid, reduced glutathione-GSH, cysteine and albumin). While the remaining ozone reacts with polyunsaturated fatty acid (PUFA) mostly present in the three hydrophobic tasks of albumin.[10]

$$-R\text{-}CH{=}CH\text{-}R + H_2O{+}O_3 \_ 2RCHO + H_2O_2$$

Thus, the potential energy of ozone is finally transferred into two fundamental messengers such as H_2O_2 as a reactive oxygen species (ROS) and aldehydic molecules of which 4 hydroxynonenal (4-HNE) and trans-4- hydroxy lhexenal (4-HHE) are the relevant lipid oxidation products (LOP). [10]

$$\text{Plasmatic water} + O_3 \_ H_2O_2 + \text{4-HNE} + \text{HHE}$$

Due to the high ozone reactivity, these biochemical reactions occur in few seconds and in fact, within the canonical five minutes of mixing an average 200 ml of human blood ex-vivo in a sterile glass bottle with the 200 ml corresponding volume of the gas mixture ($O_2 + O_3$). Ozone is totally exhausted while about 95% oxygen, dissolved in the plasma water, fully saturates hemoglobin. Blood oxygenation goes up to about 400 mm Hg in the bottle is useful, but it has only a little practical relevance because oxygenated-ozonated blood is normally re infused via venous route into the donor during the next 20 minutes and is abundantly diluted with venous blood. Therefore ozone represents the medical drug while pure oxygen is only necessary for generating ozone. [10]

During the initial fast and multiple reactions of ozone with the plasmatic components, a variable amount of the ozone dose is neutralized by the wealth of the hydrophilic antioxidants. It is not worthy that, with the exception of uric acid oxidized to Allantoin, Dehydroascorbate and GSH disulfide are reduced back to their normal value in less than twenty minutes due to the exceptional efficiency of the recycling system based on a multitude of reducing molecules such as Alpha- lipoate, Vitamin E, Thioredoxin, and last but not least NADPH acting in a well-coordinated sequence of electron donations. [10]

Most importantly, H_2O_2 being unionized, rapidly enters into all blood cells and the chemical gradient between plasma-cells has been measured to be about 10% of the extracellular concentration. In other words, when the highest ozone concentration is mixed with blood, depending upon the inter individual variability of antioxidant potency (1.28-1.83 m mol/L plasma), the highest H_2O_2 concentration measured in plasma is about 40 μM and therefore inside the cells is at most 4 μM. This sudden inflow of small amount of H_2O_2 inside blood cells is the indispensable stimulus to activate a series of biochemical reactions as follows:

i) In the Erythrocytes:

Activation of glycolysis with increase of ATP and 2,3-diphosphoglycerate take place. Functionally, the oxyhemoglobin sigmoid curve shifts to the right and increases the release of oxygen at the tissue level. The erythrocytes mop up most of the H_2O_2 and promptly reduce it to water by GSH. The sudden formation of GSSG (oxidized glutathione) alters the GSH/ GSSG ratio but the cell quickly correct it by either extruding some glutathione-disulphide or by reducing it via GSH reductase at the expense of either ascorbic acid or thioredoxin, which has two-SH groups. Moreover, the activation of glucose-6-phosphate dehydrogenase (G6PDH) provides reducing power and activate glycolysis.[10] Ozone reduces or eliminates clumping of red blood cells and its flexibility is restored, along with oxygen carrying ability.

There is a stimulation of the production of glutathione peroxidase, catalase and superoxide dismutase which act as free radical scavengers.[7]

ii) In the Leukocytes:

Neutrophil phagocytic activity is enhanced. Inside monocytes and lymphocytes, H_2O_2 activates a tyrosine-kinase with consequent phosphorylation of IkB, one of the trimeric components at rest of the NF-kB. The phosphorylated IkB detaches from the trimer and it is broken down in the proteasome. The remaining eterodimer p50-p65 is transferred into the nucleus where it can activate about 100 genes. Of great significance it is the final release of some cytokines (IFNg and IL-8) and of some acute-phase proteins.[10] Ozone behaves as a weak cytokine such as tumor necrosis factor-α (TNF- α), interleukin-2, interleukin-6,interleukin-8, transforming growth factor-β (TGF-β) inducer. Ozone reacts with the unsaturated fatty acids of the lipid layer in cellular membranes, forming hydrogen peroxides, one of the most significant cytokine inducers.[7]

iii) In the Platelets:

In relation to the ozone concentration, we have measured release of PDGF-AB, TGFb-1 and IL-8. Growth factors have a specific relevance in enhancing ulcer's healing. in peripheral arterial disease (PAD).[10] Hydrogen peroxide generated by blood ozonation activate phospholipase C, phospholipase A_2, cyclo-oxygenases and lipo-oxygenases, and thromboxane synthetase, allowing a step increase ofintracellular Ca_2, release of prostaglandin E_2, prostaglandin F_2a and thromboxane A_2 with irreversible platelet aggregation.[7]

It must be said that the H_2O_2 concentration in the cells (4 μM) is essential for switching on cellular responses and it probably lasts few seconds as GSH-Pxs, peroxiredoxin and catalase promptly reduce it to H_2O. In plasma, the H_2O_2 half-life is less than 1 minute and it is absent during blood reinfusion. [10]

On the other hand, among a variety of LOPs, newly formed lipoperoxide radicals are rapidly reduced to hydroperoxide while among a variety of alkenals, the bulk originated by n-6 polyunsaturated fatty acids (PUFA) is represented by the fairly stable 4-HNE (4-Hydroxy-2-nonenal), while 4-HHE is a product of n-3 PUFA. Both aldehydes are amphipathic molecules reacting with free GSH, carnosine and mainly albumin. They eventually act as useful messengers and their toxicity is quenched by three processes schematically indicated as: a) Detoxification, b) Dilution, and c) Excretion. Specifically:

a) Small aliquots are broken down at once by enzymes such as GSH-S-transferases and aldehyde dehydrogenase or by other detoxifying enzymes described by Awasthi et al.

b) The bulk is bound to the -SH group of Cys34 present in domain-I of albumin but also to free GSH. Eleven nucleophilic residues (Lys199 and His146) can also bind up as many as eleven aldehydic molecules. Moreover, GSH can be oxidized to a sulfonic acid while the -SH group of albumin may be oxidized to sulfenic acid.

Thus, owing to the high albumin amount (about 280 g in man), the bound alkenals undergo a great dilution in the body fluids implying a most important loss of toxicity. Alkenals does not have a membrane receptor but the albumin adduct can transport it everywhere in the body.

c) Aldehydes are also excreted into bile and urine after hepatic detoxification and renal excretion as mercapturic acid conjugates. [10]

An interesting aspect is that albumin can transport alkenal adducts in all body tissues, from liver to endocrine glands and the central nervous system. Thus 4-HNE-Cys adducts can be released at many sites and inform a variety of cells of a transient, acute oxidative stress. At submicromolar or picomolar levels, 4-HNE can act as a well-known signaling molecule able to activate the synthesis of g-glutamate cysteine

ligase, g-glutamyl transferase, g-glutamyl transpeptidase, HSP- 70, heme-oxygenase-I (HO-1) and antioxidant enzymes such as superoxide dismutase (SOD), GSH-peroxidase, catalase and last but not least important, G6PDH, a critical enzyme electron-donor during erythropoiesis in the bone marrow. [10]

There is a wide consensus on the relevance of the induction of protective molecules during repeated oxidative stress and it is of interest that these small stresses are of crucial importance for preventing and treating hypertension, stroke and heart infarction. Indeed, in clinical trial in peripheral arterial disease (PAD) ozone therapy has proved to be better than the orthodox infusion of iloprost. [10]

Ozone therapy is based upon a real hormetic concept where the optimal ozone dose must never overwhelm the potent antioxidant capacity of blood. At the time of ozonated blood infusion, 4-HNE-Cys adduct can also act on the vast expanse of endothelial cells and, by stimulating the endothelial nitric oxide synthase (eNOS) enhances the biosynthesis of NO via the 5-electron oxidation of L-arginine. NO, S-nitrosothiols and a trace of CO released with bilirubin via the up regulation of HO-1 activity allows vasodilation, thus improving tissue oxygenation in ischemic tissues. Moreover, an increased production of NO counteracts the excessive endothelial release of O_2 - caused by the chronic inflammation typical of atherosclerosis. [10]

Thus, both NO and CO released in trace amounts, accomplish the task of important physiological mediators. Finally, the majority of patients, undergoing several treatments, report a feeling of euphoria and a sense of wellness probably due to an improved hormonal secretion and/or better utilization of neurotransmitters. Most importantly, by using the above reported therapeutic range of ozone concentrations strictly related to the blood volume, it must be noted that neither acute nor chronic toxicity has been ever observed during or after ozone therapy. [10]

In conclusion, it can be stated that the M-O_3-AHT owing to the precise volume of blood, the precise volume of ozone of which the exact concentration is

photometrically determined. Hence, the real dose, makes it the unsurpassed method because ozone instantly reacts with several blood substrates in a quantitative and predictable fashion. [10]

SYSTEM OF GENERATION OF OZONE

There are four different systems for generating ozone gas:

(1)Ultraviolet system:

Produces low concentrations of ozone. It is used in esthetics, saunas, and for air purification.[3] Ozone is created naturally when ultraviolet radiation from the sun contacts the oxygen in the earth's atmosphere. In industry an ultraviolet bulb is used, which produces low concentrations compared with other method.[11]

(2)Corona Discharge system:

Produces high concentrations of ozone. It is the most common system used in the medical / dental field. It is easy to handle and it has a controlled ozone production rate.[3] Electrical sparks are passed through an oxygen rich environment, e.g. lightning or any electrical device, which produces sparks. This method is often misleadingly called, cold spark, as the sparks are far from cold. Many room air purifiers frequently use this method.[11]

(3)Cold plasma system:

Used in air and water purification.[3] An ionic flow is induced in a glass cathode tube filled with a noble gas, which is highly electrified. This unit is enveloped in a second tube, usually 316 L grade steel, through which pure oxygen is passed. This is the second electrode, which acts only as a ground and dose not receive any direct current, hence avoiding atcing and metal ion pollution. The flow of plasma within the tube induces the oxygen to reform as O_3.[11]

(4)Electromagnetic:

This method used quartz glass tubes through which oxygen flows, with copper wire wound around the inner and outer tubes. A high frequency voltage is passed through the coils, producing a strong electromagnetic field. A fan or heat sink is needed to dissipate the heat, as heat destroys ozone. Quartz glass is required due to the possible contamination caused by heating regular glass to high temperatures.[11]

MEDICAL USES OF OZONE

Ozone therapy has found its way into medical practice in Germany, where it is successfully used. Germany was the first country to start manufacturing medical ozonators and to use ozone-oxygen mixtures in vascular surgery, stomatology and geriatrics. Italian ozone-therapists have focused their activity on medical cosmetology. Specialized ozone therapeutic clinics operate in Switzerland and other countries of West Europe. Cuba is well- known for its Ozone Research Center. Interesting and promising results with the help of medical ozone have been received in some clinics of the USA, Mexico, Brazil and Japan. Ozone therapy was found to be efficient, easy to use, ensuring good tolerance and no side- effects. According to the chosen therapeutic concentration ozone can produce its immune-modulating, anti-inflammatory, bactericidal, virucidal, fungicidal, analgesic and other effects.

Medical ozone proves to be of great therapeutic potential for in numerous cases it exceeds the resources of medication-based methods. The procedures of its application are simple, economically preferable and beneficial. However, medical communities and practical health service still prefer not to notice the available convincing facts and evidences that might bring it into wide practice. By now, enough experimental and clinical findings have been made ozone therapy application for effective and safe management of patients with various pathologies.

Ozone Therapy in Different Pathologies

Ozone therapy in surgery

Contaminated surgery was one of the first to recognize ozone therapy and it is contaminated surgery where it has been widely used.

1) General Peritonitis
2) Diffuse Peritonitis

1) General Peritonitis

In the treatment of general peritonitis, including the cases complicated by "intestinal insufficiency" ozone has been used for its powerful bactericidal properties concerning aerobic and anaerobic microorganisms. It was found to be effective in reduction of lipid peroxidation (LP) processes and of antioxidant defense system (AOS), in reparation and immune system stimulation, in intoxication control.

Medical ozone displays its best therapeutic capacities when used in combination with conventional treatment and included into a complex management of a patient.

Routes:

- Ozone therapy during the operation
- Intra-operational sanitation of abdominal cavity with ozonated physiological saline. Ozone therapy in postoperative period.
- peritoneal lavage with ozonated physiological saline or programmed laparostomy.
- Intravenous infusions of ozonated physiological saline.
- Major auto hemo therapy.

Management:

a. Ozone therapy during the operation

Intra-operational sanitation of abdominal cavity with ozonated physiological saline (volume not less than 5-7 liters, ozone concentration 4-5mg/l) is to be done for 20 minutes on having eliminated the source of peritonitis and small intestine decompression. Laparotomy is to be completed with drainage of the abdominal cavity and adjustment of silicone tubes for lavage to follow.

b. Ozone therapy in postoperative period

In postoperative period, lavage procedures of the abdominal cavity are recommended. The first procedure is done 4-6 hours after the operation for 25-30 minutes with the use of ozonated saline via the tubes adjusted in the upper part of the abdominal cavity. The saline being continuously ozonated is introduced via intravenous infusion drip. The procedure is repeated twice – 4-6 and 8-12 hours later. On the average postoperative lavage is done within the period of 72 hours following the operation.

Programmed laparotomy proved to be an effective method in the treatment of peritonitis. On having the surgical intervention performed, the source of peritonitis eliminated. The sanitation of the abdominal cavity done and small intestine being decompressed (naso-intestinal tube), the abdominal cavity is not to be closed completely with the edges brought together over the cellophane drape covering the intestines. During the first 24 hours after the operation peritoneal lavage is done every 8 hours with ozonated saline, ozone concentration being 5-6mg/l, the volume - not less than 5 liters. The lavage is done till the flushing waters become clean. Prior to bracing of the abdominal wall, the abdominal cavity is filled with 0,5l of ozonated saline. Drainage is done via small pelvis. On the second postoperative day the procedure is done every 12 hours. On the third day the procedure is done only once followed by laparorhaphy.

Intravenous infusions are done with 200ml of ozonated saline once a day during the first two postoperative days, and then every second day. Major auto-hemotherapy is done within the first 12 hours after the operation and then every second day. The course consists of 2-3 procedures. Such a course of complex schemes of treatment resulted in earlier control of endotoxicosis events, normalization of biochemical and immunological parameters and less cases of early postoperative complications (from 33% to 14%) with 15% decrease in lethal outcome (Векслер Н.Ю. с соавт. 2000,Семенов С.В. с соавт.,2000, Снигоренко с соавт. 2000)

2) Localized peritonitis

Routes:

- Intra-operational sanitation of the abscess cavity with ozonated physiological saline
- Intravenous infusions of ozonated saline
- Minor auto-hemotherapy
- Major auto-hemotherapy

Management:

Intra-operation sanitation of the abdominal cavity is done with 0,5-0,8liter of ozonated saline. The lavage is done only in the area of inflammatory process, followed by carefull suction of flushing waters. Biluminal drainage tube is brought to the peritonitis focus and taken out through a special micro-incision. Laparorrhaphy is done up to aponeurosis with retention sutures upon the skin. During the first post-operative day the lavage procedure is done 3 times with 30-50ml of ozonated saline, ozone concentration - 5-6mg/l. After a period of 15-20 minutes the remnants of the saline are either sucked out with a syringe or removed by the natural way.

Intravenous infusions of 200ml of ozonated saline are done one procedure for the first two days and then every second day. The course consists of 4-5 procedures. Two procedures of minor auto-hemotherapy are done every second day and major auto-hemotherapy – 1-2 procedures a week. In cases when peritonitis is progressing relaparotomy is performed, followed by sanitation and one of the recommended techniques of intra-operation and post-operation abdominal sanitation.

Contaminated wounds of Soft Tissues

Optimal results can be achieved in a complex treatment of contaminated wounds when, alongside with major auto-hemotherapy or intravenous infusions of

ozonated saline and minor auto-hemotherapy, the wound is ozonized with wet tampon and then the limb is put into a plastic bag (Родоман Г.В. с соавт., 2000).

Routes:

- Major auto-hemotherapy
- Intravenous infusions with ozonated saline (or rectal insufflations with Ozone / oxygen gaseous mixtures)
- Minor auto-hemotherapy
- Wound aeration with ozone/oxygen mixture in a plastic bag under high or low pressure
- Wound treatment with a stream of ozone/oxygen mixture under the sphere
- Stimulation of biological active points in wounds of low extremities
- Sterile dressings with ozonated oil

Management:

In the course of treatment the phase of wound process should be taken into consideration. The treatment should be a complex one and include all forms of ozone therapy.

a. Wound aeration with ozone/oxygen mixture- The procedure starts with mechanical (sparing) wound cleansing from detritus, then a drape soaked in ozonated saline or distilled water is put into the wound. Aeration is performed either in a plastic bag or under a sphere for 20-30 minutes, ozone concentration 5-6 mg/l.

   Wound aeration is to be done 2-3 times a day until the wound is cleansed from pyonecrotic discharge. On development of granulation tissue and epithelization the procedures are done every second day with ozone concentration of 2-2,5mg/l. When marginal epithelization appears, the concentration is diminished to 0,8-1,2mg/l.

b. Major Auto-hemotherapy - The course consists of 5-6 procedures. The first 3 procedures are done every second day, the rest – every third day.
c. Intravenous infusions or rectal insufflations with ozonated saline - The procedures can be done as an alternative to major auto-hemotherapy. The course consists of 8-10 procedures, the first three are to be done daily, the rest – every second day.
d. Minor Auto-hemotherapy - The course consists of 3-5 procedures done every second day in combination with intravenous infusions or rectal insufflations with ozonated saline.
e. Dressings with Ozonated oil - The dressings are to be applied as soon as wound epithelialization appears. Stimulation of Biological Active Points

The procedures are recommended when wounds are on lower limbs by making subcutaneous injections of ozone/oxygen mixtures, volume-0,5-1,0ml., ozone concentration –10mg/l. The shin points are – BL-40, BL-57; foot points are- Liv-1, St-45, GB-44.

Osteomyelitis of long tubular bones

Ozone therapy proved to be effective in the treatment of osteomyelitis and purulent arthritis (Зайцев А.Б. 1998, 2000)

Routes:

- Ozonated saline to soak the dressings (Ozonated dressings)
- Aeration with ozone/oxygen mixture in a plastic bag
- Intravenous infusions with ozonated saline
- Minor Auto-hemotherapy
- Major Auto-hemotherapy
- Intra-osseous infusions with ozonated saline

Management:

The treatment includes all the routes of ozone therapy enlisted above.

Regarding the stage of the purulent process, ozonated dressings are to be changed once or twice every day. Plastic bags are to be put on for 20-30 minutes, ozone concentration-5-6mg/l. The procedures are done until the fistulas are closed and pyorrhea disappears.

Intravenous infusions with ozonated saline are to be done daily within the first three days and then - every second day (up to 10-12 procedures) Minor Auto-hemotherapy is to be done every second day (up to 4-5 procedures).

Intra-osseous injections of ozonated saline are to be done daily within the first three days and then - every second day (up to 10-15 procedures). Intravenous infusions with ozonated saline and minor auto-hemotherapy can be substituted by 6-8 procedures of major auto-hemotherapy done every second day.

Arthroempyesis

Routes:

- Abarthrosis puncture washing with ozonated saline.
- Abarthrosis flushing drainage with ozonated saline.
- Intravenous infusions with ozonated saline
- Minor auto-hemotherapy
- Intra- and peri-articular injections of ozone/oxygen mixtures
- Major auto-hemotherapy

Management:

Arthrocentesis is done with the evacuation of purulent materials and abarthrosis washing with ozonated saline is done till the washing waters become clean.

In cases when puncture washing appears to be ineffective, it is necessary to prepare the flushing drainage system to wash articular cavity. To do it micro-incisions are to be done along the lateral articular surface and micro-drainages are put into the articular cavity and anchored to the skin. One of the drainages is used for the continuous instillation of ozonated saline. The saline ozonation is done by a non-stop barbotage, with ozone concentration in the saline being 4-5mg/l.

Puncture washing and flushing drainage are to be done at least for two days, till the beginning of the inflammatory regress. Then the drainage system is removed, followed by intra- and peri-articular injections of ozone/oxygen mixtures (up to 4-5 procedures).

Alongside with the topical treatment, intravenous infusions with ozonated saline are done daily till the regress of the inflammation and then – every second day. The course of treatment consists of 10-12 procedures of intravenous infusions and 4-5procedure of minor auto-hemotherapy. Intravenous infusions with ozonated saline and minor auto-hemotherapy can be substituted by 6-8 procedures of major auto-hemotherapy done every second day.

Note. Artificial ankylosis is obligatory until the pyo-inflammatory process subsides.

Trophic ulcers / Decubitus ulcers

Applications with ozonated oil are successfully used in the treatment of trophic ulcers of different etiology (Кузнецов Н.А. с соавт. 2000, Газин И.К. 2000, Горбунов С.Н. 2000).

Routes:

- Intravenous infusions with ozonated saline or rectal insufflations with ozone/o_2 mixture
- Minor Auto-hemotherapy
- Major Auto-hemotherapy

- Aeration with ozone/oxygen mixture in a plastic bag under high or low gas pressure
- Ulcer treatment with the stream of ozone/oxygen gas mixture under the sphere
- Stimulation of biologically active points, when wound is located in the lower extremity
- Microinjections with ozone/oxygen mixture along the ulcer ends

Management:

The course of treatment should include all kinds of enlisted route procedures. The obligatory condition is to clean the ulcer surface completely from the incrustation. Ulcer Aeration with Ozone/Oxygen Mixture The procedure is to be done daily in a plastic bag or under the sphere for 20 minutes with ozone concentration of 6-7mg/l until the ulcer gets cleared off the purulent coat. With the development of granulation tissue and epithelization the procedures are done every second day with ozone concentration of 2-2,5mg/l, with development of marginal epithelization the concentration is diminished to 0, 8-1,2mg/l.

The skin of the treated surface is to be damp. That is why it is to be either covered with wet napkin or wiped with a damp cloth. The ulcer surface is to be filled with gauze dressing soaked with ozonated saline.

a. Dressings with Ozonated Oil_- The dressings are to be applied with the beginning of ulcer epithelization. Intravenous infusions with ozonated saline, minor auto-hemotherapy, major Auto-hemotherapy.

   Along with topical treatment intravenous infusions are done daily till the abatement of the inflammatory process and then every second day up to 12-15 procedures. Minor auto-hemotherapy are done up to 6-8 procedures. Intravenous infusions and minor auto-hemotherapy procedures can be substituted by 10-12 procedures of major auto-hemotherapy, the first four procedures are to be done every second day, the rest - two times a week.

b. Microinjections with ozone/oxygen mixture - Microinjections are done daily until the ulcer detersion.

c. Stimulation of biological active points - The procedures are done when ulcers are localized on lower limbs by subcutaneous injections of ozone/oxygen mixtures with volume of 0,5-1,0ml, and ozone concentration –10mg/l. The shin points are – BL-40, BL-57; foot points are- Liv-1, St-45, GB-44.

Osteoarthrosis

Intra-articular injections of ozone/oxygen mixtures proved to be very efficient in the treatment of osteoarthrosis.

Routes:

- Intra-articular(intrasynovial) injections of ozone/oxygen mixtures
- Peri-articular injections of ozone/oxygen mixtures
- Intravenous infusions with ozonated saline or rectal insufflations with ozone/oxygen mixture
- Minor auto-hemotherapy

Management:

The course of treatment should combine all the above listed routes Intra-articular injections of ozone/oxygen mixtures are to be done every second day and alternated with intravenous infusions with ozonated saline (or rectal insufflations with ozone/oxygen mixture) and peri-articular injections. Minor auto-hemotherapy is to be done once a week. The early stages of osteoartrosis require a 2-3 week treatment course, while the late ones – 4 or 5 weeks.

Atherosclerosis obliterans of peripheral vessels

In instituting the course of ozone therapy we regarded the stages of chronic arterial insufficiency (CAI), which are used for differential treatment and regular medical check-up (В.Ф. Болгов с соавт.,2000):

CAI-1 stage – 1 and 2a stages of ischemia;

CAI-2 stage – 2b and 3a stages of ischemia;

CAI-3 stage - 3b and 4 stages of ischemia.

Routes:

- Intravenous infusions with ozonated saline
- Rectal insufflations with ozone/oxygen mixture
- Major Auto-hemotherapy
- Minor Auto-hemotherapy
- Stimulation of biological active points in the lower extremities with ozone/oxygen injections
- Aeration with ozone/oxygen mixture in a plastic bag under excessive gas pressure

Management:

The management depends on the stage of chronic arterial insufficiency. Patients with the CAI-1 stage undergo through 10 procedures of Intravenous infusions with ozonated saline or rectal insufflations with ozone/oxygen mixture done every second day and 2-3 minor auto-hemotherapy procedures done every third day. This scheme can be substituted by 6-8 major auto-hemotherapy procedures. These patients are also administered 2 procedures of stimulation of biological active points.

Patients with the CAI-2 stage undergo through 10 procedures of Intravenous infusions with ozonated saline or rectal insufflations with ozone/oxygen mixture done every second day and 3-4 minor auto-hemotherapy procedures done every second day. This scheme can be substituted by 6-8 major auto-hemotherapy procedures. The patients receive 4-5 procedures for stimulation of biological active points done every second day. The treatment is complemented with aeration with ozone/oxygen mixture in a plastic bag under excessive gas pressure. Each procedure (10 for the course) lasts for 20 minutes, ozone concentration being 5-6mg/l, and is done every second day.

Patients with the CAI-3 stage undergo through 10-12 procedures of intravenous infusions with ozonated saline or rectal insufflations with ozone/oxygen mixture done every second day, 4 - 5 minor auto-hemotherapy procedures done every third day. This scheme can be substituted by 8 -10 major auto-hemotherapy procedures. The stimulation of biological active points includes 4 –5 procedures. Aeration with ozone/oxygen mixture in a plastic bag under excessive gas pressure is obligatory. The procedures are administered every second day to patients without any trophic skin changes in the foot and the shin. Daily procedures are administered in cases with trophic changes. The number of the procedures – from 10 to 20, ozone concentration being 5-6mg/l; duration – 20-30 minutes

The results received in 147 patients that underwent the course of treatment in are presented in the following table (Болгов В.Ф. с соавт.,2000)

Results of Ozone Therapy done in Patients with Obliterating Atherosclerosis in Lower Extremeties

The stage of Chronic Artherial Insufficiency	Number of patients	Results		
		Positive	Satisfactory	Unacceptable
CAI-1 stage	6	6	-	-
CAI-2 stage	109	106	2	1
CAI-3 stage	32	30	2	-
Results of Treatment (%)		96%	3%	1%

Ozone Therapy In Internal Diseases

Atherosclerosis and ischemic heart disease (ihd)

Ozone has been found to produce hypolipidemic effect. According to different authors (Камышева Е.П. с соавт., 1998, Густов А.В. с соавт., 1999, Быков с соавт., 2000), after the course of ozone therapy patients with atherosclerosis had

evident decrease in the levels of total cholesterin (6,4-18,4%), of lipoproteins of low density(7 - 28,7%), of triglycerides (10,5 - 17,2%) and increase of lipoproteins of high density(3,7 – 6,8%) levels.

The development of atherosclerosis is known to be caused not only by hyper cholesterolaemia but also by disorders in regulation of free radical processes. Lipoproteins of low density undergo the process of oxidative modification in the liver and become more atherogenic. On being secreted into the blood, they start intensively accumulate, due to macrophages, in the endothelial cells in the damaged area and then get transformed into foam cells, which make the basis for atherosclerotic plaque.

Ozone therapy when using small doses of ozone increases LP processes and, what is more important, it activates antioxidant defense system, thus eliminating lipoprotein toxicity, decreasing their capacity to penetrate the vessel wall, making it more resistant. Hence, ozone therapy can be regarded as an antisclerotic method of treatment.

Ozone therapy proved to be effective in all IHD patients (stenocardia, cardiosclerosis, arrhythmias) at various stages of the disease from mild forms to severe ones). Its efficiency was found to be more pronounced in severe forms for it helps to control hypoxia in tissues which develops with the advance of heart insufficiency. In tissues with insufficient blood circulation the oxygen uptake by cells is done in much greater volume under ozone influence, This effect cannot be achieved with the help of medication orders. This statement seems to be extremely important for it explains the positive effect of the method.

Routes:

- Intravenous infusions with 200ml of ozonated saline with ozone concentration of 20μg/kg of patient's weight (ozone concentration at the output from the generator)
- Rectal insufflations with ozone/oxygen mixture, ozone dose being 75μg/kg of

patient's weight

- Major Auto-hemotherapy, ozone dose being 1-3 mg.

Management:

In the course of treatment we use one of these routes The management is done according to the patient's condition, which is evaluated on the basis of the accepted functional classes (FC):

- 6-8 procedures for FC-I patients;
- 8-10 procedures for FC-II patients;
- 8-10 procedures for FC- III and FC- IV patients.

The first 2 procedures of intravenous infusions or rectal insufflations are to be done every day, the rest – every second day. The procedures (6-8) of major auto-hemotherapy are to be done twice a week.

Note. In cases when patients are on conventional treatment and start ozone therapy, coronaroactive preparations are not discontinued immediately. The dose is gradually diminished with the improvement of patient's condition.

The following table presents the results we received on having used ozone therapy for 142 patients with different FC of IHD.

The Results of Ozone Therapy in 142 Patients with IHD

Severity of the Disease	Number of Patients	Results of Treatment		
		Positive	satisfactory	unacceptable
I	3	3	-	-
II	82	74	6	2
III	50	45	4	1
IV	7	7	-	-
Results of Treatment (%)		91 %	7 %	2%

The improvement in the condition of patients with stenocardia was defined by the less episodes of heart strokes and nitroglycerinum intake. Angina attacks were

completely regulated in 50% of patients; in 41% of patients the number of attacks was double decreased.

Hypertensive disease

Ozone therapy is a pathogenic method for hypertension treatment. It corrects the decreased energy of cells, the main component of pathogenesis. No other available hypotensive preparations are known to have such properties. In the management of hypertensive disease ozone therapy can be used as a monotherapy and in combination with other medications. As a monotherapy it is efficient in patients at the initial stage of the disease, in mild, labile hypertension. Positive results were received in 70% of patients.

Patients with steady hypertension are to combine ozone therapy with hypotensive preparations. According to our findings, conventional hypotensive preparations can be administered in lower doses when combined with ozone therapy. In combined treatment clinical manifestations of hypertensive disease, such as headaches, dizziness, heart pains – either disappeared within a shorter time period or abated.

Routes:

- Intravenous infusions with 200ml of ozonated saline with ozone concentration of 20μg/kg of patient's weight (ozone concentration at the output from the generator)
- Rectal insufflations with ozone/oxygen mixture, ozone dose being 75μg/kg of patient's weight
- Major Auto-hemotherapy, ozone dose being 1-3 mg.

Management:

In the course of treatment, we use one of these routes. The treatment with intravenous infusions or rectal insufflations starts with 2-3 daily procedures, the rest

3-4 procedures are done every second day. With the decrease of arterial pressure the number of procedures is diminished to two procedures a week, and then one procedure a week. The total number of procedures is 8-10. Major auto-hemotherapy is done twice week with a total number of procedures up to 6-8.

Diabetes mellitus

Ozone therapy appears to be an effective method for DM treatment. The reason is in ozone mechanisms when it can perform a number of processes, which provide its positive effect.

First, ozone improves the penetration of cellular membranes for glucose. It is achieved by stimulating pentose-phosphate pathway and aerobic glycolisis that in case of DM are inhibited. It promotes hyperglycemia decrease due to better transport of glucose into tissues.

It was observed a group of 70 patients with insulin-dependent and non-insulin-dependent diabetes. After the course of ozone therapy the average level of hyperglycemia had a 26% decrease.

Ozone activates glucose metabolism that results in increasing content of 2,3 diphosphoglycerate in erythrocytes which provides better oxygen supply into the tissues. Patients with diabetes mellitus have the so called glycosylated hemoglobin forming very strong bonds with oxygen, thus, inducing hypoxia and determining the severity of the disease. That is why hypoxia control with the help of ozone therapy is of the key importance in the course of treatment.

After the course of ozone therapy, the patients had significant decrease in the levels of urine, cholesterol and fibrinogen.

Routes:

- Intravenous infusions with ozonated saline
- Rectal insufflations with ozone/oxygen mixture

- Major Auto-hemotherapy
- Minor Auto-hemotherapy
- Subcutaneous microinjections with ozone/oxygen mixture
- Stimulation of biological active points with ozone/oxygen injections

Management:

The basic treatment includes intravenous infusions of ozonated saline or rectal insufflations with ozone/oxygen mixtures which are done every second day (8-10 procedures). These procedures can be substituted with major auto-hemotherapy, which is done twice a day up to 6-8 procedures for the course of treatment. Other procedures are administered according to the type of diabetes mellitus and the presence of complications.

In DM, Type-2 the treatment course also includes stimulation of biological active points with ozone/oxygen injections using the conventional schemes.

In signs of secondary immune deficiency (pustular inflammatory diseases) in addition to the basic course of treatment subcutaneous microinjections with ozone/oxygen mixture are done in the area of purulent foci. Minor auto-hemotherapy is done every second day up to 6-8 procedures for the course.

Chronic bronchitis. Bronchial asthma

Ozone immune modulating properties are of primary importance in the treatment of chronic bronchitis. Ozone therapy provides anti-infection immune response to viral-bacterial infection invading the human body. It is revealed in intensifying local and general immunity which is suppressed in chronic bronchitis.

The principles in the treatment of bronchial asthma are known to be the following: activation of immune system and elimination of the following factors - viral and bacterial infection, bronchoconstriction, allergic reactions, hypoxia.

Ozone therapy efficiency is explained by its ability to influence various aspects of pathological process. First of all, it is its capacity to cope with bronchospasm as a result of dilatation effect on the smooth muscle of NO-radical which is formed in the endothelial cells due to ozone.

Ozone capacity to cope with tissue hypoxia is also of great significance. Patients with bronchial asthma are known to suffer from hypoxia resulting from pulmonary insufficiency caused by bronchospasmus. Ozone provides blood saturation with oxygen by-passing the lungs and delivering it to tissues via erythrocytes, thus improving blood rheology and eliminating hypoxia.

Immune modulating ozone effect can be revealed in activation of cytokines (interferon, tumor necrosis factor, interleukins) production by lymphocytes and monocytes.

Stimulation of immune system helps to suppress the inflammatory process, decreasing the activity of effector cells and diminishing their release of biological active substances responsible for bronchospastic reactions.

Routes:

- Intravenous infusions with ozonated saline
- Rectal insufflations with ozone/oxygen mixture
- Major Auto-hemotherapy
- Stimulation of biological active points with ozone/oxygen injections
- Inhalations with ozonated distilled water

Management**:**

The treatment is a complex one, including all the above enumerated routes. The course starts with 2 intravenous infusions of ozonated saline or rectal insufflations done daily. On improving the condition the next 5-7 procedures are done every

second day and then once or twice a week (up to 7-10 procedures for the whole course).

Acupuncture with ozone/oxygen mixture is done according to conventional accepted methods.

Inhalations with ozonated distilled water are done once or twice a day daily for a period of 10-15 days.

Major auto-hemotherapy is administered in cases when positive effect is not received after 7-10 days of treatment and it is done instead of intravenous infusions or rectal insufflations. Procedures are done every second day up to 4-8 for the course of treatment.

The results of ozone therapy in chronic bronchitis in our practice are the following: the condition improved in 79% of patients, 29% having significant improvement(complete elimination of such symptoms as cough, breathlessness, weakness, rales) and 21% having satisfactory improvement.

Ozone therapy in 42 patients with bronchial asthma followed in our clinic gave the following results. The majority of patients (83%) had a moderate course of the disease. All the patients were on broncholytic preparations, some of them taking steroid hormones. After the course of ozone therapy the valid improvement in the condition was noted in 86% of patients who had half fewer episodes of suffocation and could reduce he dose of conventional preparations. In 7% of patients we achieved a complete control of asthmatic attacks and discontinue the intake of medications. In the rest 7% of cases we could not achieve improvement in their condition.

Chronic pyelonephritis

Routes:

- Intravenous infusions with ozonated saline
- Rectal insufflations with ozone/oxygen mixture

- Major Auto-hemotherapy
- Minor Auto-hemotherapy

Management:

The treatment combines minor auto-hemotherapy (6-8 injections) with intravenous infusions of ozonated saline or with rectal insufflations with ozone/oxygen mixture (8 - 10 procedures). During the first three days the procedures are to be done daily and then every second day. Major auto-hemotherapy (6-8 procedures) is to be done twice a week and can be used as an alternate method, substituting the first three.

Chronic gastritis. Type "B"

Ozone therapy proved to be an effective remedy in the treatment of chronic gastritis. Ozone due to its properties produces therapeutic effect on all the main pathogenic mechanisms responsible for the development of the disease. It produces bactericidal effect on Helicobacter Pylori (up to 93,7%).

Its anti-inflammatory effect is achieved due to oxidation of arachidonic acid, known as a precursor for prostaglandin E that starts the inflammatory process. To add to that, ozone produces its immune-modulating, anti-aggregation and analgetic effect (Андосов С.В. с соавт., 2000).

Ozonated oil and ozonated water produce bactericidal effect and deliver active oxygen to tissue, shortening the healing processes.

Ozone has been found to produce changes in the local immunity, increasing the release of secretory IgA by lymphocytes and plasmatic cells, responsible for the immune defense of the surface cells of the stomach.

Routes:

- Ozonated water.
- Ozonated oil

- Minor Auto-hemotherapy
- Stimulation of biological active points with ozone/oxygen injections

Management:

The treatment consists of daily intake of ozonated water (100-150ml) 30-40 minutes before meals 1-3 times a day. Ozonated oil is to be taken 3 times a day 15 minutes following the intake of ozonated water, starting with 1 teaspoonful, gradually increasing the dose to tablespoonful, if patients tolerate it well. The water and oil are to be taken for 2 – 3 weeks.

Minor auto-hemotherapy is to be done according to the following scheme. The first 3 procedures are to be done daily, the next 3 – every second day, and the remaining procedures – twice a week. The course consists of 8-10 procedures.

Acupunctures with ozone/oxygen mixture are done according to the conventional methods.

Ozone therapy was instituted to 101 patients. The received results were assessed as "significant improvement" in 57%, "improvement" – in 40% and satisfactory in 3% of cases. Clinical results were confirmed by endoscopic findings that revealed significant decrease or disappearance of inflammation, signs of hyperaemia and mucous edema.

Ulcer

Multifunctional ozone effect in the treatment of peptic ulcer is revealed first of all in its anti-inflammatory and anti-helicobacterial action. It results in accelerating the epithelization processes, infiltrate elimination in mucous membrane within a shorter period, compared with the traditional therapy. V.Maximov (1998) considering different schemes of ulcer treatment comes to the conclusion, that ozone therapy can substitute antibiotics and metronidasol preparations, providing better results regarding the ulcer healing and the degree of HP eradication.

Ozone therapy was found to produce positive effect on general and local immunity.

Ulcer of the stomach

Routes:

- Ozonated water.
- Ozonated oil
- Rectal insufflations with ozone/oxygen mixture
- Minor Auto-hemotherapy
- Intravenous infusions with ozonated saline
- Major Auto-hemotherapy
- Stimulation of biological active points with ozone/oxygen injections

Management:

Ozonated water and ozonated oil are to be taken following the scheme of the chronic gastritis.

The treatment begins with rectal insufflations with ozone/oxygen mixture done every second day up to 5-6 procedures. Starting from the second week the treatment is complemented with Minor auto-hemotherapy alternately with rectal insufflations. During the 3-d and the 4-th weeks the same procedures are done every second or third day. In cases when rectal insufflations are unacceptable, they are substituted by intravenous infusions with ozonated saline up to 12-15 procedures done every second day or by major auto-hemotherapy done twice a week with 6-8 procedures for the course.

Microinjections into paravertebral points with ozone/oxygen mixture are to be done every second day on the Th 6 - Th 9 level (up to 5-8 procedures for the course).

Ozone acupuncture is done according to the conventional methods.

Ulcer Of The Duodenum

Routes:

- Ozonated water.
- Ozonated oil
- Minor Auto-hemotherapy
- Major Auto-hemotherapy
- Intravenous infusions with ozonated saline
- Rectal insufflations with ozone/oxygen mixture
- Stimulation of biological active points with ozone/oxygen injections

Management:

Ozonated water and ozonated oil are to be taken following the scheme of the chronic gastritis.

The course begins with minor auto-hemotherapy procedures. The first 3 procedures are to be done daily, then 2 or 3 procedures are to be done every second day, the remaining ones are to be done twice a week. The course includes 8-10 procedures.

Starting with the second week the treatment is complemented with intravenous infusions with ozonated saline or rectal insufflations with ozone/oxygen mixture up to 3-4 procedures that are alternated with minor Auto-hemotherapy.

Intravenous infusions of ozonated saline and minor auto-hemotherapy can be substituted by major auto-hemotherapy (8-10 procedures), the first two procedures are to be done every second day and afterwards – twice a week.

Ozone acupuncture is done according to the conventional methods. The treatment course lasts 3-4 weeks. After cicatrization, ozonated oil is kept on to be taken 1 spoonful before going to bed at night for a period of 1-1,5 month. In our practice we used ozone therapy as a mono therapy in 69 patients at the stage of

exacerbation, 10 suffering from ulcer of the stomach, 59 from duodenal ulcer. The results of treatment were regarded as "significant improvement" in 8 patients with complete healing of the ulcerative defect and disappearance of all the symptoms. In 2 cases the results were assessed as "improvement of the condition", for the healing was not complete, though the symptoms disappeared completely.

The condition of patients treated for duodenal ulcer was regarded as "significant improvement" in 56% of cases, "improvement of the condition" – in 39%. "Partial improvement" was assessed in 5% of patients that had incomplete healing of the ulcer defect and some of the remaining symptoms.

Chronic nonulcerative colitis

Ozone therapy in the management of patients with chronic non-ulcerative colitis takes a special place regarding the following reasons.

First, the use of rectal insufflations with ozone /oxygen mixture produces both topical anti-inflammatory effect and general multi-faceted including anti-hypoxic, immune-modulating, etc due to ozone capacity to be quickly absorbed by blood.

Second, chronic colitis is often concomitant with dysbacteriosis. Ozone advantages become evident, for if does not produce any harmful effect on flora of the intestine, compared with antibacterial preparations such as antibiotics and sulfanilamides.

When rectal insufflations are used ozone gets stuck to mucous membrane and interferes with the infectious process penetrating the microbial cells thus preventing their further reproduction Besides, ozone enforces phagocytosis, improving blood circulation and humoral immunity. It leads to refection of homeostasis, with the normalization of microbial balance and subsiding inflammatory signs.

Contrary to various antiseptics still causing some damaging effect in tissues, ozone does not produce any harmful or ulcerative effect and, more than that, it does not induce any resistance to ozone therapy.

Routes:

- Rectal insufflations with ozone/oxygen mixture
- Minor Auto-hemotherapy
- Stimulation of biological active points in the lower extremities with ozone/oxygen injections

Management:

During the exacerbation period ozone insufflations of gaseous mixture are done every second day with the dose of 100μg per kg of patient's weight for the first two weeks, then 2 times a week with the dose of 75μg/kg. The whole course consists of 10-15 procedures.

Minor auto-hemotherapy is done 1-2 times a week up to 4-6 injections for the course.

Microinjections with ozone/oxygen mixture into the paravertebral points at Th 10 - L5 level are to be done daily or every second day up to 5-7 procedures for the course. Acupuncture procedures with ozone/oxygen mixture are done according to the conventional methods. In colitis of various etiology some authors (В.А.Максимов с совт. -1998) recommend the use of intra-intestinal gaseous ozone up to 200-500ml with the concentration 60 mg/l.

In the Russian Centre of Restorative Medicine and Spa-resort Treatment they recommend rectal insufflations with concentration in the range of 10-40μg/ml and volume of 50-300ml for patients with inflammatory intestinal diseases. In atonic intestine they recommend low concentrations, in spastic conditions - higher concentrations.

Chronic hepatitis

Ozone therapy can be used as a mono-therapy in the management of patients with chronic hepatitis. In the treatment of infectious hepatitis the major effect is achieved due to ozone antiviral property. Inactivation of viruses results from peroxide oxidative activity when virus cell receptors get destroyed and cannot penetrate the host cell. The failure in virus multiplication process is also caused by RNA virus breakdown due to ozone. According to A. Zmyzgova (А.В.Змызговой с соавт.-1998) 2-months ozone therapy courses reveals no viraemia signs in 66% of cases with chronic viral B-hepatitis, and in 60% of cases with chronic C-hepatitis.

Peroxides activate endogenous cellular metabolism in Kupffer's cells, responsible for phagocytosis. Ozone therapy activates both, cellular and humoral immunity. Ozone induces lymphocytes and monocytes to release cytokines and, primarily, interferon which is regarded as one of the most important endogenous defense factors, protecting the body from the viral infection.

Ozone effect in alcoholic hepatitis is explained by the fact that newly-formed peroxides act as a trigger for antioxidant mechanism to detoxicate the glutathione system, which prevents hepatic cell membrane from being damaged due to LP activation processes.

Routes:

- Rectal insufflations with ozone/oxygen mixture
- Minor Auto-hemotherapy
- Intravenous infusions with ozonated saline
- Major Auto-hemotherapy

Management:

Apart from the exacerbation period the most common procedures in chronic hepatitis are rectal insufflations with the dose of ozone of 75μg/kg done alternately

with minor auto-hemotherapy. For the first two weeks rectal insufflations are done every second day and then twice a week up to 20-30 procedures for the course. Minor auto-hemotherapy is done 2 times a week.

The preference for rectal insufflations can be explained by findings published by H.G.Knoch (1987,1988). Ozone/oxygen mixture infused via the rectum is of particular significance in the treatment of different forms of hepatitis. Rapid gas absorption causes immediate rise in the partial oxygen pressure in portal vein, thus providing "the shortcut" for the oxygen to the liver and contributing to the efficiency of the treatment. Rectal insufflations can be substituted with intravenous infusions of ozonated saline or with major auto-hemotherapy.

In cases with the exacerbation of the disease the preference is given to major auto-hemotherapy and intravenous infusions of ozonated saline. During the exacerbation period major mutohemotherapy is done daily with a high dose of 6-8mg up to 5-8 procedures and then 2-3 times a week till the exacerbation subsides. Then the doses is decreased to 1-1,5mg.

Intravenous infusions of ozonated saline (ozone concentration produced by ozone generator is 2mg/l) are done daily during the period of 10-12 days, and then every second day until the exacerbation subsides. After that – 2 times a week. During the exacerbation period rectal insufflations with ozone dose of 100μg/kg of patient's weight are done daily. When exacerbation subsides the procedures are carried according to the conventional protocol.

In the course of treatment the major auto-hemotherapy procedures can be alternated with intravenous infusions of ozonated saline and rectal insufflations with ozone/oxygen mixtures. The course of treatment lasts from 3 to 6 months.

Hepatic cells affected by the virus are less resistant to peroxide action compared with healthy cells. These weakened cells on being exposed to high peroxide concentration get destroyed alongside with viruses and eliminated. This

phenomenon is described by A. Bolcany (1989), who revealed the elevation of transaminase level after the very first procedures of ozone therapy and explained it by the destruction of hepatic cells due to viral invasion.

Ozone Therapy In Gynecology And Obstetrics Gynecology

Inflammatory diseases of the organs in the true pelvis (adnexitis, endometritis, parametritis, pelvioperitonitis)

Routes:

- Intravenous infusions with ozonated saline
- Rectal insufflations with ozone/oxygen mixture
- Major Auto-hemotherapy, ozone dose being 1-3 mg.
- Intrauterine irrigations with ozonated distilled water

Management:

The treatment consists of intravenous infusions with ozonated saline or rectal insufflations with ozone/oxygen mixture. Both can be substituted with major auto-hemotherapy. Daily infusions with 200- 400 ml of ozonated saline, ozone concentration in ozone/oxygen mixture at the output from ozone generator being 1200μg/l are to be done for 5 - 7 days.

Rectal insufflations with ozone/oxygen mixture are done according to the accepted method reckoned on the basis of 75μg/kg of patient's weight. The gas volume is from 300 to 600ml with ozone concentration of 10-40 mg/l.

Major auto-hemotherapy is done twice week with a total number of procedures up to 4-6.

Intrauterine irrigations with ozonated distilled water (400ml) with ozone concentration of 4-5 mg/l are done to provide entire contact with the site of inflammation and to exclude any damage to the mucous membrane in different forms of endometritis. On being ozonated the water via the biluminal catheter is introduced

into the uterine cavity and then evacuated via the same catheter . The procedure can be repeated 3 times during one session, which is done once a day (Гречканев Г.О., Качалина Т.С., Качалина О.В., 2000).

In combination with basic anti-inflammatory therapy the described sanitation of the uterine cavity prevents the generalization of the inflammatory process, shortens the course of treatment and makes it possible to discontinue any other dialysis preparations.

Note. The use of ozone therapy allows to decrease the dose of medications with detoxicating, rheologic, antioxidant, immune-correcting, analgetic and sedative effect.

Profuse bleedings are regarded as the main contra-indication for ozone therapy. Smeared bloody discharge and predisposition to hemorrhage require more careful and accurate control. In cases of surgical intervention ozone therapy can be used in aftercare course.

Inflammatory diseases of genital tracts

Colpitis, bacterial vaginosis

Routes:

- Vaginal irrigations with ozonated saline
- Applications with ozonated oil
- Vaginal insufflations with ozone/oxygen mixture

Management:

Vaginal irrigations with ozonated saline with the volume up to 1liter and ozone concentration of 6-10mg/l are to be done daily(8-10 procedures per course) and are to be complemented with applications with ozonated oil (1-2times a day). These procedures can be substituted by vaginal insufflations with ozone/oxygen mixtures, that are to be done daily within 5-8 days. Using special nozzle to vaginal speculum ozone/oxygen mixture, ozone concentration being 1,5-2,5mg/l, is introduced into the

vagina. Before the insufflation procedure the vagina is to be washed with distilled water for 5-10 minutes at the rate of 0,5-1l/min.

This method resulted in a steady improvement in all 50 patients with nonspecific colpitis, elimination of pathogenic and opportunistic microorganisms in bacteroscopy and restored the immunity balance in vaginal secretion. The use of the method made it possible to discontinue the medicinal therapy. (Качалина Т.С. с соавт.1998, Гречканев с соавт.,2000).

Routes:

- Applications with ozonated oil

Management:

Applications with ozonated oil are to be applied daily on the damaged surface within the period of 8-10 days Note. The oil (100ml) is to be barbotaged with ozone/oxygen mixture for 20 minutes, ozone concentration-10mg/l.

Obstetrics

The use of ozone therapy produces positive effect on the clinical course in such conditions as the risk of miscarriage, gestosis, anaemia of pregnancy, intrauterine growth retardation and risk of complications in obesity. It is linked with the immune-correcting and antioxidant ozone effect. The improvement in oxygen supply, rheology and microcirculation contributes to hormone-producing function (Кулаков В.И. с совт.,2001, Миненков А.А. с соавт.,2001).

Miscarriage. Early toxicosis

Routes:

- Intravenous infusions with ozonated saline or
- Major Auto-hemotherapy, ozone dose being 0,4-0,5 mg.

Management:

Daily instillation infusions of 400 ml of ozonated saline, ozone concentration in ozone/oxygen mixture being 400μg/l, are to be done for 5 days. Ozone therapy proves to be most effective in the end of the first and the beginning of the second trimesters of pregnancy. Major auto-hemotherapy is done twice week with a total number of procedures up to 4-6.

Note. Ozone therapy is contraindicated in genital tract bleedings of different intensity and can be instituted only after its entire termination. The immune-correcting and antioxidant preparations, including vitamins, as well as sex hormones can be discontinued for the time of ozone therapy.

Gestational toxicosis. Anaemia of pregnancy

Routes:

- Intravenous infusions with ozonated saline or
- Major Auto-hemotherapy, ozone dose being 0,4-0,5 mg.

Management:

Daily instillated infusions of 200 ml of ozonated saline, ozone concentration in ozone/oxygen mixture being 400μg/l, are to be done for 5 days. Ozone therapy proves to be most effective in mild and moderate gestosis. Major auto-hemotherapy is done twice week with a total number of procedures up to 4-6.

Note. Ozone therapy is contraindicated in genital tract bleedings of different intensity and can be instituted only after its entire termination. The preparations with anti-oxidant, immune-correcting, sedative, rheologic and detoxicating effect can be discontinued for the time of ozone therapy.

Intrauterine infection

The prevention and treatment of pregnant women that are in the risk group for fetal infection are to be done during the second trimester of pregnancy.

Routes:

- Intravenous infusions of ozonated saline or
- Major Auto-hemotherapy, ozone dose being 0,4-0,5 mg.

Management:

Daily instillation infusions of 200 ml of ozonated saline, ozone concentration in ozone/oxygen mixture being 800μg/l are to be done for 3 – 5 every second day. -6 procedures. .Major auto-hemotherapy is done twice week with a total number of procedures up to 4-6. ***Note.*** Antioxidants and immune-correcting preparations can be cancelled during the course of ozone therapy.

Ozone Therapy In Dermatology

The use of ozone therapy in the management of patients with various inflammatory skin diseases makes it possible to delimit the inflammation and to improve trophical processes. Out of 495 patients that were on ozone therapy a complete disappearance of clinical picture or significant improvement were observed in a patients with dermatosis and herpes(100%); pyodermia(95%); - eczema(75%); neurodermaitis(66%) and psoriasis(60%) (Криваткин С.Л, Криваткина Е.В., 1998).

Neurodermititis. Eczema

Ozone therapy is used in the treatment of some limited forms of neurodermititis.

Routes:

- Intravenous infusions of ozonized physiological saline or rectal insufflations with ozone/oxygen mixtures or major auto-hemotherapy
- Ozonized vegetable oil
- Aeration with ozone/oxygen mixture in a plastic bag

Management:

The course consists of 10-12 procedures of intravenous infusions with ozonized saline or rectal insufflations with ozone/oxygen mixtures done every second day. Major auto-hemotherapy is done twice a week up to 5-6 procedures. Ozonized vegetable oil is applied on the injured surface twice a day for 20 minutes until the eruption disappears. The aeration course consists of 5-8 procedures, done every second day for 20 minutes with ozone concentration being 5-20mg/l.

Positive result in the treatment of patients with eczema was noted in 86,8% of cases (complete clinical cure was achieved in 29,4% and significant improvement(70% eruption regress) –in 57,4% (Кошелева И.В., Иванов О.Л, 2000).

Acneiform Eruption

Routes:

- Minor auto-hemotherapy
- Major auto-hemotherapy
- Ozonated vegetable oil

Management:

In mild cases (isolated eruption) Minor Auto-hemotherapy is administered up to 8-10 procedures done every second day. In severe cases (massive eruption) Major Auto-hemotherapy is indicated up to 8-10 procedures done twice a week. Ozonized vegetable oil is to be applied on the injured surface twice a day for 20 minutes. Applications are to be done until the eruption disappears.

Furunculosis. Pyodermia

Routes:

- Major Auto-hemotherapy
- Minor Auto-hemotherapy
- Intravenous infusions with ozonated saline
- Subcutaneous microinjections with ozone/oxygen mixture around the focus of

inflammation

Management**:**

The course of treatment begins with Major Auto-hemotherapy up to 5 procedures done every second day, followed by intravenous infusions with ozonized saline which are alternated with Minor Auto-hemotherapy (6-8 procedures). Microinjections around the focus of inflammation are to be done every day till the rupture of the furuncle. The ruptured furuncle is to be irrigated with ozonized saline.

Herpes

Routes:

- Major Auto-hemotherapy
- Minor Auto-hemotherapy
- Ozonated vegetable oil

Management:

The course of treatment includes10-15 procedures of Minor Auto-hemotherapy done every second day and 4 procedures of Major Auto-hemotherapy done once a week. Ozonized oil is to be applied two times a day on the dry elements till the rupture of the papules. **Note.** In some cases there can be the exacerbation of the process at the very beginning of treatment. The exacerbation is less pronounced and is soon eliminated.

Psoriasis

Routes:

- Intravenous infusions of ozonated physiological saline or rectal insufflations with ozone/oxygen mixtures
- Major Auto-hemotherapy
- Minor Auto-hemotherapy
- Ozonized vegetable oil

Management:

Intravenous infusions with ozonated saline or rectal insufflations with ozone/oxygen mixtures are done every second day up to 10 procedures. Minor auto-hemotherapy includes 6 procedures done twice a week. Instead of intravenous infusions with ozonized saline, rectal insufflations with ozone/oxygen mixtures and minor auto-hemotherapy and a course of major auto-hemotherapy can be done. In includes 8-10 procedures, the first two procedures are to be done every second day, the remaining procedures are done twice a week.

Ozonated vegetable oil is to be applied on the injured surface twice a day for 20 minutes within a month to follow.

Mycosis

Routes:

- Ozonated vegetable oil
- Minor Auto-hemotherapy

Management:

The treatment consists of ozonated tampons applied on the nail plates twice a day for 30-40 minutes for a period of 3-6 months for fingernails and of 6-9months for toe-nails (until the new nail plate grows) A course of major auto-hemotherapy of 3-6 procedures is done every three months, the procedures are done every second day.

Ozone Therapy In Neurology

Chronical forms of cerebrovascular insufficiency (discirculatory encephalopathy)

Routes:

- Intravenous infusions of ozonated saline.
- Rectal insufflations with ozone/oxygen mixture

- Major Auto-hemotherapy

Management:

The course consists either of intravenous infusions of ozonated saline (the procedures can be substituted by rectal insufflations) or major auto-hemotherapy procedures. Intravenous instillated infusions are to be done daily up to 8 –10 procedures. Major Auto-hemotherapy procedures are to be done every second day up to 6 –8 procedures.

Rectal insufflations with ozone/oxygen mixture are to be done according to the scheme. The initial dose is 200ml, which is to be increased by adding 100ml more each day until the required dose (see Forms and Methods to Use Ozonated Materials).

The received results, that can testify to the efficiency of ozone therapy in this category of patients, are presented in the Table "The Results of Ozone Therapy in Patients with Discirculatory Encephalopathy".

The Results of Ozone Therapy in Patients with Discirculatory Encephalopathy

Severity of the Disease	Number of Patients	Results of Treatment		
		Positive	satisfactory	unacceptable
I	30	26	2	2
II	26	16	5	5
III	5	5	---	---
Results of Treatment (%)		78 %	11 %	11%

Neurologic manifestations of spinal osteochondrosis

Ozone analgetic effect has been successfully used in treating patients with vertebrogenic pain syndrome due to algopeptides direct oxidation, suppression of ischemia radices and blocking prostaglandin synthesis. Subcutaneous injections with ozone/oxygen mixtures into trigger points in combination with minor auto-

hemotherapy and intravenous infusions of ozonated saline provide positive result in the majority of patients with osteochondrosis of cervical, thoracic or lumbar spine.

Routes:

- Intravenous infusions with ozonated saline
- Rectal insufflations with ozone/oxygen mixture
- Minor Auto-hemotherapy
- Para vertebral injections of ozone/oxygen mixtures
- Subcutaneous injections of ozone/oxygen mixtures into trigger points and biological active points

Management:

The course consists of two alternated schemes of treatment

a. Intravenous infusions with ozonated saline or rectal insufflations are to be complemented the same day with subcutaneous injections along the nuchal bones line and with para-vertebral injections. Paravertebral injections are in the points of palpatory tenderness into the depth of 5 – 6 cm with the volume of 5 – 10ml.
b. Minor auto-hemotherapy procedures are done the same day with the subcutaneous injections of ozone/oxygen mixtures into biologically active points (V19 -V28, V40, V57, V60, VB30, VG4, E32, E44, RP9, F9). Subcutaneous injections into biologically active points are done into the depth of 1 –1,5cm with the volume of 1-2ml. The course consists of 8 -10 procedures.

Inflammmatory brain diseases (menigitis, encephalitis)

Routes:

- Intravenous infusions with ozonated saline
- Minor Auto-hemotherapy
- Major Auto-hemotherapy -ozone dose –1000-1200μg/100ml of blood

Management:

The treatment includes all the above listed procedures. Major Auto-hemotherapy is done every second day alternated with intravenous infusions of ozonated saline or minor auto-hemotherapy , upon the whole, 12-15 procedures.

Note: Ozone therapy is performed complementary to anti-inflammatory treatment.

Migraine, cephalgia

Routes:

- Intravenous infusions with ozonated saline, ozone concentration being 1200μg/l
- Rectal insufflations with ozone/oxygen mixture
- Major Auto-hemotherapy
- Minor Auto-hemotherapy
- Subcutaneous injections with ozone/oxygen triggers and biologically active points

Management:

The treatment consists of the above listed procedures. Intravenous infusions with ozonated saline or rectal insufflations with ozone/oxygen mixture are to be done daily or every second day up to 8-10 procedures.Minor auto-hemotherapy is done twice a week, up to 3 – 4 procedures.

Intravenous infusions with ozonated saline, rectal insufflations with ozone/oxygen mixture and minor auto-hemotherapy can be substituted with major auto-hemotherapy up to 8 – 10 procedures, the first two done daily and then 2 –3 times a week.

Subcutaneous injections with ozone/oxygen triggers and biologically active points of neck and collar zone are to be done daily though out the course of treatment.

The use of ozone therapy in 132 patients with various cephalgias resulted in significant improvement in the patient's self-assessed condition, revealed in the headaches with less intensity and of different character, as well as prolonged painless periods in 83% of patients with migraines, in 73% of patients with stress headaches and in 69% of cases with vertebrogenic cervicocranialgias (Мочалов А.Д., Котов С.А., 2000).

Mono- and poly-neuropathias of ischemic and compression type

Ozone therapy, though it does not eliminate the causes of compression of the nerve trunk, it stimulates the regeneration of the damaged nerve by improving the hemorheology and microcirculation, decreasing hypoxia and activating oxygen metabolism in the ischemic nervous tissue with aerobic processes.

Routes:

- Intravenous infusions with ozonated saline
- Rectal insufflations with ozone/oxygen mixture
- Major Auto-hemotherapy

Management:

The course consists of any of the above listed routes up to 8 –10 procedures. Intravenous infusions with ozonated saline are done daily or alternately. Rectal insufflations with ozone/oxygen mixture are done accordingly, starting with 200ml, which is to be increased by adding 100ml more each day until the required dose (see Forms and Methods to Use Ozonated Materials).

Major Auto-hemotherapy is to be done every second day.

Positive clinical results due to ozone therapy have been obtained in 95% of cases with significant decrease of paresthesias improved sensitivity in enervation zone of the damaged nerve (Потехина Ю.П.,1997).

Cerebral circulatory embarrassment. Ischemic insults

Energy metabolic imbalance and significant decrease in the contents of macro-energetic compounds are considered to be the primary cause responsible for the changes taking place in neurons in ischemic stroke. The use of ozone therapy in patients with brain infarction appears to be highly recommended due to ozone optimizing effect on oxygen-transport blood function, increased oxygen utilization by brain calls due to activation of glycolysis, Krebs' cycle, -oxidation of fatty acids (Густов А.В. с соавт.,1999).

Routes:

- Intravenous infusions with ozonated saline
- Major Auto-hemotherapy -ozone dose-1mg/100ml of blood.

Management:

In the course of treatment one of the routes is to be chosen.

The first 3 – 4 intravenous infusions with ozonated saline are to be done daily, then every second day (3 –4 procedures) with the rest done twice a week. The course includes 10 – 12 procedures.

The first 2 major auto-hemotherapy procedures are done daily, the next 3 – every second day, the rest – twice a week, up to 8 –9 procedures for the course.

The patients with ischemic stroke showed positive changes in oxygen-transport blood system (43% increase in PO2 following the ozonated saline infusion and 26% increase after the course of ozone therapy), in blood coagulation system (10-15% decrease thrombocyte aggregation capacity with 8-10% fibrinolysis activation), the improvement in lipid spectrum (10-12% decrease in the total cholesterol. 7-10% in β-lipoproteins, 12-15% decrease in atherogenic coefficient). These changes brought positive results in the acute stage of the disease in 79% of cases and in 69% of cases in recovery phase (Густов А.В. с соавт., 1999).

Note. Ozone therapy is contraindicated in hemorrhagic strokes and in combined ischemic and hemorrhagic insults. Ozone therapy should not be administered in cases of ischemic strokes with unconfirmed diagnosis.[12]

OZONE IN DENTISTRY

Ozone was first investigated for dental applications in 1933 by a Zurich dentist named Fisch, who used ozone for the treatment of chronic periodontal infections and oral wounds. There have been many suggested dental applications for ozone that could potentially be of use in paediatric dentistry.[13]

Baysan et al., (2005). and Stubinger et al., (2006) - Proposed dental uses of ozone include: caries management, endodontic treatment, dental unit water sterilisation, and bleaching.[13]

In dentistry, ozone has been used either in gaseous (4.2×10^{-6} µg m)$^{-3}$; Heal Ozone, KaVo, Biberach, Germany) or in aqueous form for the elimination of caries pathogens, in the disinfection of root canals, as a rinse for avulsed teeth, and for enhancing epithelial wound healing. Currently, the established oral antiseptics for caries prevention, endodontic irrigation or adjunctive periodontal treatment include chlorhexidine digluconate (CHX) (0.2–2%), sodium hypochlorite (NaOCl) (2.25–5.25%), and hydrogen peroxide (H_2O_2) (3%). Regarding side-effects, it is known that CHX may cause mucosal desquamation, impaired wound healing and fibroblast attachment to root surfaces, tooth staining and altered taste sensation. NaOCl or H_2O_2 may result in hemorrhage, edema and skin ulceration in oral tissues. In proposing ozone as another potential antimicrobial for use in the oral cavity, it is important to compare possible toxic effects of ozone on resident oral cells with those of established agents.[14]

The main use of ozone in dentistry is relays on its antimicrobial properties. It is proved to be effective against both Gram positive and Gram negative bacteria, virus and fungi.

Caries

The ozone is used as an antimicrobial agent, since the application of ozone during 20 seconds leads to the destruction of 99,9% of microorganisms in the carious lesion. Due to the reactive potential of the ozone gas, and its high ability of oxidation, it is able to destroy bacterial membranes.[15]

Conventional removal of carious tissue and cavity preparation procedures do not guarantee the complete elimination of oral cariogenic bacteria perhaps entrapped within the dentin tubules or the smear layer and which may induce secondary caries or pulpal inflammation. For this reason, the use of ozone gas has recently been supported to improve cavity disinfection prior to restorative procedures. The antibacterial property of ozone is due to its strong oxidizing activity that involves rupture of the cell membranes and destruction of intracellular components through an oxidation reaction. It has been postulated that the elimination of cariogenic bacteria and the demineralization process promoted by ozone could arrest or even reverse dental caries development. In addition, the application of gaseous ozone was proven to be painless and atraumatic.[16]

The formation of a biofilm overlying tooth structure is essential for the initiation and progression of caries. Streptococcus mutans and Lactobacillus acidophilus are present in cariogenic biofilms and play a significant role in the carious process. The treatment of dentine surfaces to prevent biofilm formation and reduce bacteria growth may assist in the prevention of caries initiation and progression. The use of ozone therapy in the treatment of dental caries is equivocal and literature reviews suggest there is insufficient evidence to regard ozone treatment as a viable alternative to the current management and treatment of dental caries.[17]

(1)Rickard *et al*., (2004) - suggested that both the Cochrane review on ozone and the appraisal by the National Institute for Health and Clinical Excellence (NICE, 2005) concluded that evidence of efficacy was lacking at the time they did their

assessment. However, further research has been completed since the publication of these documents and some of the results indicate promise for the treatment of caries with ozone. One of the main problems in evaluating the efficacy for the use of ozone for treatment of caries has been the shortcomings in the study design.[13]

(2)Brazzelli *et al*., (2006). The complete Heal Ozone procedure involves the direct application of ozone gas to the caries lesion on the tooth surface, the use of a remineralising solution immediately after application of ozone and the supply of a 'patient kit', which consists of toothpaste, oral rinse and oral spray all containing fluoride.[13]

(3)Dahnhardt *et al*., (2006) - reported that the use of ozone resulted in an average reduction of DIAGNO dent score of 13% immediately after ozone treatment.[13]

(4)Azarpazhooh *et al*., (2008). - suggested that delivering ozone into a carious lesion will reduce the number of cariogenic bacteria. Ozone can also break down pyruvic acid to acetic acid. Essentially, the theory is that ozone diminishes the micro flora in a lesion and increases the lesional pH, thereby tipping the balance towards remineralisation. Thus ozone could possibly arrest the progress of the carious lesion and may, in the presence of fluoride, allow remineralisation to occur. This may either delay or prevent the need for traditional dental restorative treatment. In particular, studies into ozone and caries have frequently completed data analysis at the level of the lesion, which is not independent of the person, ignoring the clustering of multiple carious lesions within study participants. The teeth have been analysed independently as if they were all from different subjects, an approach which has been shown to lack validity.[13]

The majority of clinical studies into ozone and caries have used laser fluorescence (DIAGNO dent) readings and electric caries meter (ECM) scores. Although these devices have undergone extensive testing most dentists, would

probably agree that neither DIAGNO dent or ECM have replaced visual, tactile and radiographic detection as a routine method of caries diagnosis/monitoring.[13]

The clinical severity score (hard, leathery or soft) used in many studies as an indicator of tactile hardness of a lesion is subjective and could result in some level of measurement error too. Clearly, inherent difficulties arise in any area of research that requires the measurement of caries progression/arrest. Ozone application has been trialled in the management of four main categories of carious lesions:[13]

a. Incipient caries, [13]
b. Cavitated single surface lesions, [13]
c. Primary root carious lesions[13] and
d. Pit and fissure caries.[21]

Ozone has not been tested on interproximal carious lesions as these do not allow for the adequate sealing of the suction cap necessary for ozone application. Some impressive results have been reported on the use of ozone to arrest root caries, but this area of research will not be further discussed here as it is more pertinent to geriodontology than to the practice of paediatric dentistry.[13]

a. Incipient caries

(1)Abu- Naba'a *et al*.,(2003) - conducted a split mouth randomised clinical trial with 90 participants, each of whom had at least two permanent posterior teeth with non-cavitated pit/fissure caries. A total of 390 teeth were involved in this study – half of these teeth were used as controls and the other half received a 10 second application of ozone gas. In addition to this, some teeth from the control group and teeth from the ozone group received a resin fissure sealant. Readings were made at baseline and at 1,3,6,9 and 12 months. The unsealed teeth were all checked with clinical severity scores, DIAGNO dent and ECM, whereas, the sealed teeth only had the quality of the sealant checked. No radiographs were taken as part of the study.

There was no statistical difference in the retention of the sealants. For the unsealed teeth, the recorded values for the control teeth were higher (i.e. worse) at the recall appointments than those of the ozone group, but this was not statistically significant.[13]

(2)Baysan and Beighton (2007) - investigated the effect of ozone application on the bacterial counts of non-cavitated occlusal carious lesions in vitro. Forty second application of ozone gas to non-cavitated occlusal lesions failed to significantly reduce the numbers of viable bacteria in infected dentine beneath the demineralised enamel.[13]

(3)Huth *et al*., (2007) - ran a split mouth clinical trial to assess the effect of a single 40 second application of gaseous ozone on non-cavitated fissure caries in permanent molars. Forty-one patients with 57 pairs of lesions were recruited. No remineralisation solutions were used in this study. The lesions were monitored with DIAGNO dent for a short period of time, up to 3 months in total. The ozone-treated teeth in patients deemed to be at high current caries risk showed either statistically significant caries reversal or reduced caries progression when compared to the untreated control lesions in these same patients. However, there was no statistically significant difference between the DIAGNO dent readings of the control and test lesions when the whole study population was considered.[13]

b. Cavitated carious lesions

Clinical application of gaseous ozone appears attractive for the treatment of cavitated occlusal and root caries lesions in cases where restorative treatment is not possible, e.g. anxious children. In theory, ozone can reduce the bacterial load in active carious lesions and thus may at least temporarily stop caries progression.[18]

(1)Dahnhardt *et al.*, (2006) - completed a controlled clinical study to (1) determine whether the treatment of dental caries with ozone was well-tolerated by apprehensive children, and to (2) ascertain whether ozone reverses caries in open single surface lesions. The 28 children in the sample were judged by the referring dentist as being un-treatable in the dental chair due to anxiety. The study population

contained 82 carious lesions, and for each child in which a lesion was treated with ozone, a control lesion was left untreated. Tactile hardness and DIAGNO dent values were assessed and the values in the test lesion were compared with the values in the control lesion after 2, 4, 6, and 8 months. The authors reported that 94% percent of the children were treatable and the vast majority "lost their dental anxiety". The hardness values improved significantly in the ozone-treated test lesions after 4, 6, and 8 months compared with the baseline reading, while the control lesions had no significant change in hardness at any of the recall intervals. No statistically significant changes were noted in the DIAGNO dent values of the teeth.[13]

c. Root caries

Root caries, involving both cementum and dentine, typically appears as a slowly progressing, chronic lesion. The histopathological changes seen in root dentine are similar to those seen in slowly advancing coronal caries, namely sclerosis with occlusion of the tubules and secondary dentine formation. The exposed cementum is usually 20 to 50 μm thick near the cemento-enamel junction, and brown discolouration with softening of the tooth structure may be found. Histologically, damage to the cementum is seen along a broad front, sometimes manifesting as a "delamination" along the incremental lines.[19] Ozone therapy can be considered as an alternative management strategy for root caries.[20]

(1)Baysan *et al.* (2000) - assessed antimicrobial effect of Kavo Heal ozone device on primary root caries lesions (PRCL) and evaluated the efficiency of ozone specifically on Streptococcus mutans and Streptococcus sobrinus. As a result, ozone exposure to either 10 or 20 s under experimental conditions reduced the total levels of micro- organisms in the PRCLs to < 1% of the control values. Application of ozone for a period of 10 s was also capable of reducing the numbers of Streptococcus mutans and Streptococcus sobrinus in vitro.[1]

(2)Holmes. (2003) observed effect of Kavo Heal ozone device on PRCL followed by professionally- applied remineralising solution containing xylitol, fluoride, calcium, phosphate and zinc. This treatment modality was applied to 89 patients, aged from 60 to 82 years. After 18 months 100 % of ozone-treated PRCL's had improved. In control group, where lesions were left without treatment, only one PRCL had improved. In 62 % of cases the status remained leathery, while in 37 % of PCRL's had worsened from leathery to soft.[1]

d. Pit and Fissure Caries

A number of published studies have reported on the efficacy of ozone on pit and fissure caries. Caries was treated in both permanent and deciduous teeth. The time between initial treatment and reassessment varied from 1 to 12 months, and some trials reviewed patients more than once. Treatment time with ozone varied between studies from 10 to 40 seconds. All patients received initial treatment with ozone, and in some circumstances. patients were re-treated at each review. Trial comparators were generally no treatment or placebo treatment with air applied through the HeaiOzone device. Representative studies and their findings are presented in the table.[21]

Treatment of Pit and Fissure Caries: Summary of Representative Studies

Author	No. of Patients	No. of Teeth	Success*	Duration of Study fmo)
Megighianetal. 2003"	60	200	90	1
Holmes. 2003'	193	579	99	4
Abu-Naba'a et al. 2003*	90	258	88	12
Stinson et al, 2003^	98	279	99	12
Holmes, 2003'"	376	2,364	99	12
Johnson etal. 2003"	105	114	81	1
Morrison and Lynch, 2003'-	145	240	89	3
Morrison and Lynch, 2003"	108	186	81	3
Hamid. 2004'-'	184	184	87	3
Hulhctai. 2005'^	41	114	80	3
*Based on a statistically significant improvement in clinical measures at $p < 0.05$				

Gasiform ozone has been investigated for the treatment of occlusal and root caries, whereas, the aqueous form, due to its biocompatibility and to its anti-inflammatory potential, has been suggested as an alternative treatment for periodontal disease. More recently, the application of ozone gas on dental hard tissues prior to adhesive procedures has been proposed.[22]

A particular recommendation of the ozone therapy is a consequence of the rapidity and complete painlessness of the method. Stimulation of the remineralization effect, hardening of already carious tissue and the disinfection effect in the not easily accessible fissures of permanent teeth – the consequence of all these factors is that ozone is more and more frequently and readily used in the treatment of young patients.[23]

Ozone in Prosthodontics

The wearing of removable dentures is not as common in the paediatric population, but there is certainly widespread use of acrylic removable orthodontic appliances. Ozone has been suggested as a disinfectant for acrylic and metal appliances, particularly because of its strong deodorizing power.[13]

(1)Oizumi *et al*., (1998) - found that gaseous ozone was a more effective microbicide than ozonated water, and suggested that direct exposure to gaseous ozone could be useful for disinfection of dentures.[13]

(2)Arita *et al*., (2005) - found no significant differences in the antimicrobial activity of ozonated water and commercially available denture cleaners.[13]

Antimicrobial efficacy of ozone as denture cleaners

Microbial plaque accumulating on the dentures is composed of several oral microorganisms, mainly *C. albicans*. Denture plaque control is essential for the prevention of denture stomatitis**.** Denture stomatitis can be controlled by topical application of ozonated oil over tissue surface and over denture surface.[2]

(1)Oizumi M *et al*., (1998) - Direct exposure to gaseous ozone was a more effective micro bicide compared with ozonated water. Therefore gaseous ozone can be clinically useful for disinfection of removable prosthesis. [2]

(2)Suzuki T *et al*., (1999) - Ozone can be applied for cleaning the surface of removable partial denture alloys with little impact on the quality of alloy in terms of reflectance, surface roughness, and weight.[2]

(3)Murakami H *et al*., (2002) - The use of ozone as denture cleaner is effective against methicillin-resistant S. aureus and viruses.[2]

(4)Nagayoshi M, *et al*., (2004) - There is also some evidence on the effectiveness of aqueous ozone application in adjunct to amino alcohol for decontamination of the implant surfaces.[2]

(5)Arita M *et al*., (2005) - The application of ozonated water may be useful in reducing the number of *C. albicans* on denture plates.[2]

Bonding strength of restorative materials

As ozone has been suggested for use as a cavity preparation disinfectant, an important consideration is whether the application of ozone affects the bonding strength achieved by restorative materials.[13]

(1)Schmidlin *et al.,* (2005) - found that gaseous ozone application had no effect on the shear bond strength of composite resin to bovine enamel and dentine samples.[13]

(2)Celiberti *et al*., (2006) - evaluated the effect of ozone application on the quality of resin sealants placed on prepared and sound molar fissures in vitro and also reported that no statistically significant difference was observed between the control and ozone treated samples in all tests.[13]

(3)Polydorou *et al.* (2006) studied antibacterial effect of Kavo Heal ozone device on Streptococcus mutans in comparison with the already proven activity of two dentin-bonding systems. Their findings show that an 80 s application of ozone is

a very promising therapy for elimination of residual micro- organisms in deep cavities and therefore of potentially increasing the clinical success of restorations. A 40 s application of ozone was found to reduce significantly the numbers of Streptococcus mutans, but not to extend of other treatments. A longer period of ozone activity could be advantageous as a result of its anticariogenic effect.[1]

(4)Onisor *et al*., (2007) - found that surface treatment with ozone may significantly decrease marginal quality of class V resin restorations in dentine without negatively influencing marginal quality in enamel.[13]

(5)Bitter *et al.,* (2008) - investigated the bond strength of fibre posts after the application of gaseous ozone to the root canal dentine. Adhesion of the self adhesive resin cement RelyX Unicem was significantly reduced after gaseous ozone application. However, pre-treatment with ozone did not affect the adhesion of the other bonding systems tested.[13]

(6)Al Shamsi et al., (2008) - reported no adverse effect on the bond strength of orthodontic brackets after pretreatment of enamel with ozone.[13]

Periodontics

Ozone has been proposed as an adjunct antiseptic in periodontitis therapy. P. gingivalis, T. forsythia, and P. micra could be eliminated by 2% CHX or by ozone gas at 53 gm^{-3}. Significantly greater antimicrobial effects were observed against planktonic cultures than against biofilm-associated bacteria. The rate of killing was influenced by the species of bacteria, and by the type and concentration of agent. There were no significant differences in the effectiveness of aqueous ozone (20 $lg\ ml^{-1}$) or gaseous ozone ($\geq 4\ gm^{-3}$) compared with 2% CHX but they were more effective than 0.2% CHX. Therefore, high-concentrated gaseous and aqueous ozone merit further investigation as antiseptics in periodontitis therapy. A safe system for applying gaseous ozone into the periodontal pocket that avoids inhalation still needs to be developed.[24]

(1)Nagayoshi *et al.* (2004) - tested the efficacy of ozonated water on survival and permeability of oral micro- organisms and dental plaque. They confirm that ozonated water (0.5–4 mg/l) was highly effective in killing of both gram positive and gram negative micro-organisms. Gram negative bacteria, such as Porphyromonas endodontalis and Porphyromonas gingivalis were substantially more sensitive to ozonated water than gram positive oral streptococci and Candida albicans in pure culture. Furthermore ozonated water had strong bactericidal activity against bacteria in plaque biofilm. In addition, ozonated water inhibited the accumulation of experimental dental plaque in vitro.[1]

(2)Stubinger *et al.*, (2006) - suggested that the antimicrobial properties of ozone and reported stimulation of the host defence system potentially make ozone a therapeutic agent for the treatment of gingivitis and periodontitis.[13]

(3)Huth *et al.* (2006-2007) - in their study declared that the aqueous form of ozone, as a potential antiseptic agent, showed less cytotoxicity than gaseous ozone or established antimicrobials (chlorhexidine digluconate-CHX 2%, 0.2%; sodium hypochlorite-NaOCl 5.25%, 2.25%; hydrogen peroxide-H_2O_2 3%) under most conditions. Therefore, aqueous ozone fulfils optimal cell biological characteristics in terms of biocompatibility for oral application.[1] The results of in vitro studies suggest that aqueous ozone may actually have an anti-inflammatory capacity, showing decreased inflammatory cytokine expression at the cell level. When tested on human oral epithelial cells and gingival fibroblast cells, aqueous ozone was more biocompatible than antiseptics such as chlorhexidine, hydrogen peroxide and sodium hypochlorite.[13]

(4)Muller *et al.* (2007) compared the influence of ozone gas with photodynamic therapy (PDT) and known antiseptic agents (2% Chlorhexidine, 0.5 and 5% Hypochlorate solutions) on a multispecies oral biofilm in vitro. The following bacteria were studied – Actinomyces naeslundi, Veillonella dispar, Fusobacterium nucleatum, Streptococcus sobrinus, Streptococcus oralis and Candida albicans. Gasiform ozone was produced by vacuum ozone delivery system Kavo Heal ozone.

They concluded that the matrix-embedded microbial populations in biofilm are well protected towards antimicrobial agents. Only 5 % Hypochlorate solution was able to eliminate all bacteria effectively. Usage of gasiform ozone or PDT was not able to reduce significantly or completely eliminate bacteria in the biofilm.[1]

(5)Kronusová. (2007) used ozone in following cases: prevention of dental caries in fissures of the first permanent molars in children, application of ozone in prepared cavity, after tooth extraction, in case of postextractional complications, in patients with chronic gingivitis, periodontitis and periodontal abscesses, herpes labialis, purulent periodontitis, dentition difficilis etc. Almost all patients with gingivitis showed subjective and objective improvement of their status, as well as patients with periodontal abscess, where no exsudation was observed. Application of ozone after tooth extraction was found also quite useful – only 10 % of patients suffered from such complication as alveolitis sicca, but even in these cases the clinical course was shorter and more moderate.[1]

Endodontics

Endodontic treatment aims to clean and disinfect root canals that are more or less strongly infected by bacteria and seal them sufficiently to prevent reinfection. Preparing the root filling through mechanical instrumentation of the root canal walls is, on its own, inadequate to achieve this end,1 since there are always regions of the complex canal anatomy that are inaccessible by mechanical means. Therefore, sufficient cleaning must include irrigation with a disinfecting solution as a so-called chemical debridement. 2 Apart from its disinfecting effect, the solution also serves to rinse off and remove any dentin chips.[25]

Endodontic (root canal) treatment of infected teeth has long been a treatment of choice and the standard of care in dentistry for an infected tooth. Endodontic treatment involves cleaning out the main canal of a tooth with instrumentation, irrigation and chemicals (hydrogen peroxide, chlorhexidine, and ethylenediaminetetra

acetic acid (EDTA), Sodium hypochlorite and ozone water). These canal are then filled with a material called guttapercha before the tooth is finally restored with a crown. This procedure is intended to sterilize the tooth from all the invading bacteria that caused the tooth and the surrounding bone to become infected. Standard of care endodontic procedures are employed during diagnostics and treatment. Then OOT (Oxygen Ozone Therapy) is used for disinfection of the root canals and dentinal tubules. The following steps should be added before the final fill of the canal:

- The files are coated with ozonated olive oil for lubrication and disinfection.
- The canals are prepared and then irrigated with ozonated water and dried.
- Before placing the root canal filling, the canals are provided with a slow insufflation of gas (45- 60 seconds) with an ozone concentration of 45-50 mcg/ml.[26]

There are three aspects to the success of endodontics:

- The mechanical preparation
- Chemical disinfection
- Three-dimensional obturation.[27]

Ozone gas in a concentration of ~4 g m^3 (HealOzone; KaVo, Biberach, Germany) is being used clinically for endodontic treatment.[28]

The need for endodontic treatment of traumatised teeth in children, including teeth with open apices, does mean that a highly biocompatible endodontic irrigant would be of great interest in paediatric dentistry. However, conflicting results have been reported on the antimicrobial activity of ozone in the root canal system.[13]

(1)Nagayoshi *et al.*, (2004) - found that ozonated water was inferior to 2.5% sodium hypochlorite in antimicrobial action against enterococcus faecalis and streptococcus mutans in bovine dentin in vitro.[13]

(2)Estrela *et al*. (2007) studied antimicrobial effects of ozonated water, gaseous ozone and antiseptic agents (2.5 % hypochlorite and 2 % chlorhexidine) in infected human dental root canals. All these substances had no antibacterial effect against Enterococcus faecalis over a 20 minute contact time in the infected root canals.[1]

(3)Cardoso *et al.,* (2008) - reported that ozonated water did not neutralize endotoxin, but was reported to be effective against candida albicans and enterococcus faecalis in the root canal system.[29]

Bleaching

In root canal treated teeth, crown discoloration is a major aesthetic problem, especially in anterior teeth. Conventional walking bleach requires much more time and results are not often satisfactory. Also, capping the tooth with ceramic crown is not always a good idea. But, now ozone has the answer to all these questions. After placing the bleaching agent the crown is irradiated with ozone for minimum of 3-4 minutes. This ozone treatment bleaches the tooth within minutes and gives the patient a happy and healthier-looking smile.[30]

(1)Azarpazhooh *et al.,* (2008) - Ozone has been suggested as having applications in tooth bleaching. Industrial uses of ozone include bleaching of paper pulp, flour, starch and sugar However, there is no published evidence of bleaching efficacy of teeth by ozone.[13]

(2)Manton *et al.,* (2008) - found the application of ozone with carbamide peroxide solution did not significantly affect bleaching effectiveness compared with peroxide alone. In fact, the application of ozone prior to carbamide peroxide bleaching significantly decreased bleaching effectiveness.[13]

Ozone therapy in oral and maxillofacial surgery

(1)Sanseverino ER *et al*.,(1989) - Ozone has a positive influence on bone metabolism and reparative process of the bone.[2]

(2)Filippi. (1995) was observed the influence of ozonized water on the epithelial wound healing process in the oral cavity. It was found that ozonized water applied on the daily basis can accelerate the healing rate in oral mucosa. This effect can be seen in the first two postoperative days. The comparison with wounds without treatment shows that daily treatment with ozonized water accelerates the physiological healing rate.[1]

(3)Steinhart H *et al*., (1999) - Ozone therapy is also found to be beneficial for the treatment of the refractory osteomyelitis in the head and neck in addition to treatment with antibiotics, surgery and hyperbaric oxygen.[2]

(4)Agapov VS *et al*., (2001) - In patients with chronic mandibular osteomyelitis, it was observed that medical ozone exposure promoted more complete and rapid normalization of nonspecific resistance and T-cellular immunity, thus accelerating clinical cure and reducing the incidence of complications.[2]

(5)Agrillo A *et al.*, (2006-2007) - It has been documented that dental extraction becomes possible in a patient with avascular bisphosphonate-related jaw osteonecrosis or in those who received pyrophosphate analogous when treated with ozone therapy. Compared with other therapeutic choices like antibiotics, surgical treatment, the new treatment protocol recommends the use of ozone therapy as therapeutic support in the treatment of bisphosphonate related osteonecrosis of the jaws.[2]

(6) Vescovi P *et al*., (2010) - Ozone therapy in the management of bone necrosis or in extraction sites during and after oral surgery in patients treated with Bisphosphonates may stimulate cell proliferation and soft tissue healing.[2]

(7)Petrucci MT *et al.*, (2010) - When a combination therapy of a course of antibiotics, surgery and ozone therapy was given to patients with Osteo necrosis of jaw in patients with multiple myeloma there was a decrease in both the incidence of osteoradionecrosis of the jaw and the extent of lesions.[2]

Ozonated water in decontamination of avulsed teeth before replantation

(1)Ebensberger U *et al.*, (2002) - A high level of biocompatibility of aqueous ozone on human oral epithelial cells, gingival fibroblast cells, and periodontal cells has been found. Two-minute irrigation of the avulsed teeth with non-isotonic ozonated water not only provides mechanical cleansing, but also decontaminate the root surface, with no negative effect on periodontal cells remaining on the tooth surface before replantation.[2]

(2)Stubinger *et al.,* (2006) - Non isotonic ozone water has been shown to not have any negative effects on the root surface at an exposure time of less than 2 minutes, which means that there may be promise in its application for root surface irrigation prior to replantation of avulsed teeth or during tooth transplantation procedures.[13]

Uses in oral medicine

Soft tissue lesions like Herpes, Aphthae, Removable denture ulcers, Cuts, Cheilitis, Candidiasis, Cysts and Traumatic wounds can be treated with either Ozonated water or oils. The disinfectant and healing properties help in the healing of these lesions.[31]

Ozone proved to be effective against all bacteria when tested, while mycobacteria were shown to be the most susceptible to the oil.

(1)Clavo *et* al (2004) - concluded that the ozone therapy can produce an improvement in blood flow and oxygenation in some tissues and appears to have had some positive effect during the treatment of patients with advanced head & neck tumors.

(2)Macedo and Cardoso (2005) - described a case report of the application of ozonated oil on herpes labialis and mandibular osteomyelitis and demonstrated faster healing time than conventional protocols.[32]

Ozone for treatment of Peri-implantitis

(1)Karapetian VE *et al.,* (2007) - For the prevention of peri-implantitis an adequate and steady plaque control regimen must be ensured. Ozone, a powerful antimicrobial kills the microorganisms causing peri-implantitis. In addition, ozone shows a positive wound healing effect due to the increase of tissue circulation. Gasiform ozone or ozonized water shows an increased healing compared to wound healing without ozone therapy.[2]

Decontamination of tooth brush

Ozone application was found to remove the toothbrushes bristles microbiota following conventional brushing.[2]

Cracked tooth syndrome

According to the clinical situation and symptoms, a conservative attempt can be used with ozone application. After revealing the crack and evaluation of the case apply ozone gas for 60-120 seconds and restore with a long term temporary filling, i.e., glass ionomer cement. Put the tooth slightly offoccusion and reassess periodically.[33]

Hypersensitive teeth

Noncarious hypersensitivity is due to contributing factory among which are erosion, abfraction, bite pressure, recessed gum, etc. after final diagnosis and elimination of the cause, ozone application might alleviate almost instantly the pain felt by the patient from Hypersensitive teeth in some causes. Apply ozone for 40-60 seconds on sensitive areas then apply remineralizing agent.[33]

Smear layer present over the exposed surface prevent the penetration of ionic calcium and fluorine deep in to the dentinal tubules. Ozone removes the smear layer, open up the dentinal tubules, broadens their diameter and calcium and fluoride ions flow easily, deeply and effectively to plug the dentinal tubules. Thus, ozone can

effectively terminate the root sensitivity problem within seconds and also result last longer than those by conventional method.[34]

Use of topical ozone to treat recurrent aphthous ulceration

Recurrent aphthous ulceration is a common mucosal disorder that can be painful and debilitating for patients. This type of ulceration has been associated with systemic disease and it has been suggested that a variety of immunological, microbial and genetic factors may all play a role in its aetiopathogenesis. A wide variety of treatment strategies for aphthous ulceration has been discussed in the literature. This case report demonstrates the beneficial use of topical application of ozone using the Healozone appliance (Kavo) in a patient with long standing aphthous ulceration involving the lateral border of the tongue. The topical application of ozone provided an effective means of producing resolution of clinical symptoms related to aphthous ulceration for this patient. Further clinical investigation is required in order to determine the potential of this treatment modality in the treatment of recurrent aphthous ulceration.[35]

OTHER USES OF OZONE

Antibacterial Effect of Ozone on Plaque biofilm

Both caries and periodontal disease are caused primarily by plaque biofilm. Ozone might be useful to control oral infectious microorganisms in dental plaque. Ozonated water strongly inhibited the accumulation of dental plaque. Ozonated oil is used as a safe therapeutic alternative in patients with Acute Necrotizing Ulcerative Gingivitis. Healing and bactericidal properties makes it useful as a subgingival irrigant. The antimicrobial property of ozone is not only effective in reducing the number of cariogenic bacteria, but also causes significant reduction in the microorganisms present in the root canal. However it was not successful in completely eliminating these bacterias embedded in the biofilm. (Polydorou O *et al*., 2011, Knight GM *et al*., 2008, Nagayoshi M *et al*.,2004, Bezrukova IV *et al*.,2005, Johanson E *et al*.,2009).[2]

Ozonated water is effective in killing gram-positive, gram-negative bacteria and oral Candida albicans causing periodontal disease. Ozonated water had nearly the same antimicrobial activity as 2.5% sodium hypochlorite and also the metabolic activity of fibroblasts was high when the cells were treated with ozonated water. The aqueous form of ozone, as a potential antiseptic agent, showed less cytotoxicity than gaseous ozone or established antimicrobials like chlorhexidine digluconate, sodium hypochlorite or hydrogen peroxide under most conditions. Therefore, aqueous ozone fulfils optimal cell biological characteristics in terms of biocompatibility for oral application. (Fukuizumi T *et al*.,2004, Kshitish Detal., 2010). Ozone may be considered as an adjunctive to conventional treatment strategy due to its powerful ability to inactivate microorganisms.[2]

Ozone effects on bacterial organisms

Werner von Siemens developed the first ozone generator in 1857.

(1) Mudd JB *et al*., (1969) - Surrounding the bacterial cytoplasm is a phospholipid proteinaceous cytoplasmic membrane, itself englobed by a structurally-stabilizing peptidoglycan shell. In acid-fast bacteria (e.g.,*mycobacterium tuberculosis*), up to one half of the capsule contains complex lipids. Ozone acts on bacterial cell membranes via the oxidation of their lipid and lipoprotein components, whose multiple chemical bonds then assume new angular configurations incompatible with viable bacterial architecture. There is evidence for interaction with proteins as well.[2]

(2)Cech T *et al*., (1986) - Higher organisms have developed mechanisms for protecting DNA and RNA, and for repairing them when disrupted, which could provide a partial explanation for why, in clinical treatment using ozone at doses prescribed, ozone is toxic to pathogens and not to the patient).[2]

(3)Rilling S *et al*., (1987) - Pioneering clinical applications first came during the First World War when externally applied ozone/oxygen mixtures were administered to battlefield wounds. Ozone fought infections, and via its vasoactive properties, encouraged wound repair. Equipment failures, however, due to ozone oxidative action on rubberized treatment envelopes, impeded progress in this area until the development of ozone-resistant plastics many decades later. [2]

(4)Ishizaki K *et al*., (1987) - In one study exploring the effect of ozone on E. coli, ozone penetrated through cell membranes, reacting with cytoplasmic contents, cleaving the circular plasmid DNA, thus impairing bacterial procreation.[2]

Today, there are over 3000 ozone-based municipal water purification systems worldwide, a constantly growing number. This represents a clear testimony to ozone's potent antimicrobial properties. Exposed to ozone, all bacterial species fare poorly. Bacterial envelopes are composed of invaginating multilayers whose components are ozone-reactive.[2]

Given adequate time of exposure and intensity of concentration, any and all bacterial species – except perhaps the super hardy *Deinococcus radiodurans* and

similar organisms - invariably succumb to ozone action, a fact that endows ozone therapy with one of its most solid scientific foundations.[2]

(5)Thanomsub *et al.* (2002) tested the effects of ozone treatment on cell growth and ultrastructural changes in bacteria (Escherichia coli, Salmonella sp., Staphylococcus aureus and Bacillus subtilis). It was discovered that ozone at 0.167 mg/min/l can be used to sterilize water, which is contaminated with up to 105 cfu/ml bacteria within 30 minutes. Destroying of bacterial cell membrane was observed, subsequently producing intercellular leakage and eventually causing cell lysis. Nevertheless, these ozone concentrations have no significant effect on the cell viability in bacterial cultures at higher concentrations of 106 and 107 cfu/ml.[1]

(6)Hems *et al.* (2005) evaluated the potential of ozone as an antibacterial agent using Enterococcus faecalis as a test species. Ozone was used both gasiform (produced by Purezone device), and aqueous (optimal concentration 0.68 mg/l). It was concluded that ozone in solution was antibacterial against planctonic Enterococcus faecalis after 240 s treatment. However it was not effective against Enterococcus faecalis cells in a biofilm unless they were displaced into the surrounding medium by agitation. Gaseous ozone was not effective on the Enterococcus faecalis biofilm.[1]

(7)Viebahn R (2007) - essentially this consisted of an oxygen chamber subjected to an intense electrical field.[2]

Effect of ozone therapy in randomized clinical studies. (2011).[36]

Author (year)	Type of study	Microbiology	Ozone effect[3]	P	No. patients	No. teeth	*In vivo / In vitro*	Mean age	Sex	Con-trol group
Kshitish et al. 2010 (6)	Randomized, double-blind split-mouth clinical trial	*A. actinomyce-temcomitans, P. gingivalis, T. forsythensis, Herpes simplex virus, Epstein-Barr virus, Cytomegalovi-rus, C. albicans*	Greater reduction of plaque, gingi-val and bleeding indexes versus chlorhexidine. Reduction of *A. actinomycete-mcomitans* and *C. albicans*	0.05	16	_	*In vivo*	_	_	_
Estrela et al. 2006 (7)	_	*S. Aureus*	Effective in eliminating *S. aureus*	_	_	_	*In vitro*	_	_	Yes
Hauser-Gerspach et al. (9)	_	_	Not effective in reducing the presence of mi-croorganisms	_	40	At least 2 per patient	*In vivo*	5.1±1.5	23 males 17 females	_
Baysan et al. 2007 (10)	Randomized clinical trial	*Streptococci, Lactobacilli, Actinomyces*	No decrease in bacteria in dentin after ozone therapy	<0.001	_	104	*In vitro*	_	_	Yes
Manton et al. 2008 (11)	Randomized clinical trial	_	Not effective in increasing white-ning effect	_	_	60	*In vitro*	_	_	_
Holmes 2003 (12)	Randomized, double-blind clinical trial	__	Arrested progres-sion of caries	<0.01	89	_	*In vivo*	60	_	Yes

Ozone's antiviral actions

Viruses are parasites at the genetic level, separated into families based on their structures, types of nucleic genome and modes of replication. Recently, there has been ever increasing interest in ozone's potential for viral inactivation in vivo. Long established is ozone's in vitro neutralization of viruses and it stands to reason that this capacity would be studied in living systems. In vivo ozone applications, however, present special challenges. All viruses are susceptible to ozone; yet differ widely in their susceptibility.[2]

(1)Riesser V *et al*., (1977) - Analysis of viral components showed damage to polypeptide chains and envelope proteins impairing viral attachment capability, and

breakage of viral RNA. Other researchers suggested that, in ozonation, it is the viral protein capsid that sustains damage.[2]

(2)Roy D *et al.*, (1982) - Poliovirus resistance was 40 times that of coxsackie virus.[2]

Viruses, unlike mammalian cells, have no enzymatic protection against oxidative confrontation. Lipid-enveloped viruses are especially sensitive to ozone challenge, implicating that lipid alteration is a salient mechanism for their viral death. Viruses containing lipid envelopes include the Hepadnaviridae (Hepatitis B), the Flaviviridae (hepatitis C, West Nile virus, yellow fever); the Herpesviridae, a large family grouping the Simplex,Varicella- Zoster, Cytomegalovirus, and Epstein-Barr viruses; the Orthomyxoviridae (influenza); the Paramyxoviridae (mumps, measles); the Coronaviridae (SARS); the Rhabdoviridae (rabies); the Togaviridae (Rubella, encephalitis); the Bunyaviridae (Hantavirus); the Poxviridae (smallpox); the Retroviridae (HIV), and the Filoviridae (Ebola, Marburg), among others. Indeed, once the virion's lipid envelope becomes fragmented, its DNA or RNA core cannot progress in its life cycle. Viruses that do not have an envelope are called "naked viruses." Made of a DNA or RNA nucleic acid cores, and a nucleic acid protein coat, or capsid, they are generally more resistant to ozone challenge than lipid-coated virions.[2]

Some naked viruses include: Adenoviridae (respiratory infections), Picornaviridae (poliovirus, coxsackie,echovirus, rhinovirus, hepatitis A), Caliciviridae (hepatitis E, Norwalk gastroenteritis), and Papillomaviridae (Molluscum contagiosum). Ozone interacts with the viral proteins of naked viruses, forming protein hydroxides and peroxides, leading to viral demise.[2]

There are several known actions of ozone on human body, such as anti-microbial, immunostimulating, antihypoxic, analgesic, detoxicating, bioenergetic and biosynthetic (activation of the metabolism of carbohydrates, proteins & lipids) etc.[2]

Anti-microbial action

The anti-microbial effect of ozone as a result of its action on cells by damaging its cytoplasmic membrane due to ozonolysis of dual bonds and also ozone-induced modification of intracellular contents because of secondary oxidants effects. This action is non-specific and selective to microbial cells; it does not damage human body cells because of their major antioxidative ability. Ozone is very efficient in antibiotics resistant strains. Its anti-microbial activity increases in liquid environment of the acidic pH. In viral infections the ozone action lies in the intolerance of infected cells to peroxides and change of activity of reverse transcriptase, which takes part in synthesis of viral proteins.[32]

Immunostimulating action

Ozone influences cellular and humoral immune system. It stimulates proliferation of immunocompetent cells and synthesis of immunoglobulins. It also activates function of macrophages and increases sensitivity of micro-organisms to phagocytosis. When administered at low concentrations, the organisms own resistance is mobilized, i.e. ozone activates the immune system. As a response to this activation through ozone, the body's immune cells produce special messengers called cytokines. These molecules in turn activate other immune cells, setting off a cascade of positive change throughout the immune system, which is stimulated to resist diseases. This means that the application of medical ozone is extremely useful for immune activation in patients with a low immune status and/or immune deficit. Ozone causes the synthesis of biologically active substances such as interleukins, leukotrienes and prostaglandins which is beneficial in reducing inflammation and wound healing. [32]

Antihypoxic action

Ozone brings about the rise of pO_2 in tissues and improves transportation of oxygen in blood, which results in change of cellular metabolism activation of aerobic processes (glycolysis, Krebs cycle, b-oxidation of fatty acids) and use of energetic resources. It also prevents formation of erythrocytes aggregates and increases their contact surface for oxygen transportation. Its ability to stimulate the circulation is used in the treatment of circulatory disorders and makes it valuable in the revitalizing organic functions. [32]

Analgesic & detoxicating action

Ozone causes secretion of vasodilators such as NO which is responsible for dilatation of arterioles and venules.[32]

Bioenergetic & biosynthetic action

It activates mechanisms of protein synthesis, increases amount of ribosomes and mitochondria in cells. These changes on the cellular level explain elevation of functional activity and regeneration potential of tissues and organs. Miscellaneous actions of ozone are circulatory enhancement, disruption of tumor metabolism and stimulation of oxygen metabolism.[32]

Ozone is a potent oxidizer

Ozone has been proven to be one of the most powerful oxidants we can use in dentistry.[37]

Enhanced healing associated with ozone use

Ozone also can play a key part in the healing process.[37]

Ozone in Sterilization

Ozone has been used for years as a drinking water disinfectant. Ozone is produced when O_2 is energized and split into 2 monatomic (O_1) molecules. The monatomic oxygen molecules then collide with O_2 molecules to form ozone, which is O_3. Thus, ozone consists of O_2 with a loosely bonded third oxygen atom that is readily available to attach to, and oxidize, other molecules. This additional oxygen atom makes ozone a powerful oxidant that destroys microorganisms but is highly unstable (ie, half-life of 22 minutes at room temperature).[38]

A new sterilization process, which uses ozone as the sterilant, was cleared by the FDA in August 2003 for processing reusable medical devices. The sterilizer creates its own sterilant internally from United States Pharmacopeia grade oxygen, steamquality water, and electricity; the sterilant is converted back to oxygen and water vapor at the end of the cycle by passing through a catalyst before being exhausted into the room. The duration of the sterilization cycle is about 4 hours 15 minutes, and occurs at 30˚C to 35˚C. Microbial efficacy has been demonstrated by achieving a sterility assurance level (SAL) of 10^{-6} with a variety of microorganisms to include the most resistant microorganism, Geobacillus stearothermophilus. The SAL is defined as the probability of a single unit being non sterile after it has been subject to the sterilization process.[38]

APPLICATION OF OZONE IN MEDICAL FIELD

Modalities of ozone administration

It is clear that ozone can be administered with great flexibility but it should never be directly injected as a gas mixture in the circulatory vessels because of the risk of provoking oxygen embolism, given the fact that the gas mixture never contains less than 95% oxygen. Schematically, the methods of ozone administrations can be classified as follows. The ozonated autohemotherapy (O3-AHT), distinguished in:

a. Major (M-O3-AHT), and
b. Minor (M-O3-AHT), in relation to the blood volume; as well as
c. Extravascular Blood Oxygenation- Ozonation (EBOO).
d. The quasi-total body exposure (QTBE) to O2-O3.
e. The various forms of ozone administration into different tissues:
    1. Subcutaneous (SC);
    2. Intramuscular (IM);
    3. Intradiscal (ID);
    4. Intracavitary (peritoneal and pleural spaces);
    5. Intravaginal, intrauretral and vesical;
    6. For dental applications, mainly as ozonated water.

a. In the Major (M-O3-AHT), a predetermined volume of blood (from 100 up to 225 mL, on the basis of the patient's body weight) to which has been added either sodium citrate 3.8% (1+ 9 mL blood) or heparin (20 IU/ mL of blood) can be exposed to an equal volume of gas mixture (95%O2-5%O3), with the ozone concentration (from 20 up to 80 μg/mL of gas per mL of blood, i.e.: 0,42-1,68 mM) precisely determined by using an ozone resistant, disposable 500 ml glass bottle under vacuum. This simple, inexpensive (all the necessary disposable material costs about 15 US$) procedure has already yielded therapeutic results in chronic limb ischemia superior to

those achieved by conventional medicine . It is also useful as a supporting help in chronic infection diseases and probably in autoimmune disorders.

b. The Minor (M-O3-AHT), is also precise and it consists in treating usually 5 mL of blood with an equal volume of gas mixture (O2-O3) with an ozone concentration of 80- 100 mg/L of gas per mL of blood (total ozone dose = 0.4-0.5 mg). In this case the blood is vigorously mixed with the gas mixture for about 1 min and immediately injected in the gluteus muscle with the gas foam. It has different aims because it acts as an immune enhancer and inducer of heme-oxygenase 1 (HO 1). It is easy to perform, inexpensive, safe and well-tolerated. It supports the M-O3-AHT in chronic infection diseases especially useful in herpetic infections.

c. The EBOO is a procedure to be used in emergency conditions such as PAD stage 4, because of complexity and invasiveness due to blood collection and infusion from two contralateral veins and blood circulation through an ozone-resistant gas exchanger. Finally, by using a peristaltic pump, blood returns to the circulation via a contra lateral vein. About 5L of blood can be oxygenated-ozonated within one hour during which the blood/ozone quantities can be varied but always precisely determined. It has a precise rationale and normally procures a rapid improvement. However, it is expensive and must be performed by technicians specialized in extravascular blood circulation.

d. The QTBE to O2-O3 for avoiding the inhalation of ozone exclude the head and the neck of the patient. On the other hand, the extensive cutaneous exposure to O2-O3 does not need any venous puncture and, owing to the vast expanse of the skin (about 1.5 m2) allows a generalized and beneficial effect. The usual exposure time in a perfectly insulated ozone-resistant cabinet is 20-30 min: the final ozone concentration during treatment is below 1 μg/mL delivered at both controlled and modifiable temperature (37-40°C) and Relative Humidity (≤100%) depending upon the pathology and the state of the patient. Ozone, while is never absorbed as such

through the skin because it always reacts with the aqueous-lipidic cutaneous surface, allows the well-demonstrated absorption of LOPs. There is no doubt that it has a pharmacological effect that, although less predictable than M-O3-AHT, exerts beneficial effects in cardiovascular, infectious diseases and in aging.

e. Administration of ozone into different tissues

1. In the past, O2-O3 mixture was injected into subcutaneous tissue. The ozone concentration should never exceed 20μg/mL and the gas volume 20 mL because it elicits a transient pain and the risk of embolism must be avoided. Total multiple injections (up to 50) of 1 Ml each with an ozone concentration of 2-3 μg/mL are performed as a therapy for lipodistrophy.

2. Mono lateral or even bilateral injection of 5-10 mL of gas with an ozone concentration of up to 20μg/mL is performed into the trigger points of the paravertebral muscles corresponding to the metamers of the herniated disc usually interesting from L4 to S1. This "chemical acupuncture" is the indirect approach for treating lumbar disc herniation and alternate daily treatments for about 3 weeks yield a therapeutic results in about 68% of the patients. Otherwise,

3. The injection of gas (2-5 mL) with an ozone concentration of 30μg/mL is directly performed into the herniated nucleus pulposus under radioscopic control. The percentage of cure is almost 80%.

4. In the case of mesothelioma, peritoneal carcinomatosis or peritonitis, endo peritoneal or endo pleural injection of up to 2500 mL of gaseous mixture with an ozone concentration of 10-20 μg/mL can be performed. This modality is rarely used in Western Countries and must be performed by a specialist [Bocci V, Zanardi I, Travagli V:A rational innovative treatment for peritoneal carcinomatosis. Cancer Invest. 2011, submitted].

5. Insufflation of variable volumes of gas (50-200 mL) with an ozone concentration ranging between 10-15 μg/mL of gas can be done into the vaginal, uretral and vesical cavity for different types of infections or in the case of post-

radiation micro hemorrhage of the bladder. Vaginal washing with ozonated water (20 µg/mL) and ozonated oil pessaries are efficacious.

6. Primary root carious lesions are successfully treated in children by using a dental hand piece with a removable silicon cup for exposing the tooth's lesion to the gas without any leakage.[1]

Routes of Ozone Administration.[39]

Parenteral	Topical or locoregional
Intra-arterial (IA)[a]	
Intramuscular (IM)	Nasal[b]
Subcutaneous (SC)	Tubal[b]
Intraperitoneal (Ipe)	Auricular
Intrapleural (IPL)	Oralb
Intra-articular (IPL)	Vaginal
(a) Periarticular	Urethral and intrabladder
(b) Myofascial	Rectal
Intradiscal (ID)	Cutaneous
Intraforaminal (IF)	Dental
Intralesional (Iles)[c]	

[a]No longer used for limb ischemia. Hepaticmetastasis could be embolized via the hepatic artery.
[b] To be performed during 30--40 sec apnea.
[c] Intratumoral or via a fistula

Administration can be through any route with modifications:

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

- Ozone in Saline – Can be used topically or given IV or SQ.
- Intra-articular administration – For joint healing and prolotherapy.
- Prolo/Sclerotherapy – Very good, less painful than other agents.
- Acupuncture – With ozone, more effective than B12.
- Ozonated olive oil – Ozone is bubbled through oil until it has thickened. This will produce ozonides that are not irritating and thus is applied topically even to eyes.
- Inhalation – Ozone that has been bubbled through olive oil and humidified will not irritate respiratory epithelium.
- Subconjunctival injection – For ulcers and keratitis sicca.
- Gingival and tooth apex injection – Can eliminate infection.
- Urinary bladder insufflation – For chronic inflammation.
- Disc protrusions – Prolotherapy, which can be injected at interspinous space and around facets, stabilize joints and accelerate healing.
- Auricular – Can be direct, hsumidified, or bagged with a homemade device made from IV bags and tubing.[40]

APPLICATION IN DENTISTRY

Three basic forms of application to oral tissue are

(1)Ozonated water,
(2)Ozonated olive oil and
(3)Oxygen/Ozone gas[34]

The oils have been used for periodontal and surgery healing work. The ozonated oils can eliminate and prevent infection, resolve pain within about 30 minutes and they promote accelerated healing.

Dental Caries: Ozonated oils play no part in the treatment of caries. The ozonoid oil product is not sufficiently active enough to destroy deep micro-biological niches and biomolecules that lead to demineralisation in enamel, nor deep micro-biological niches in dentine tooth structure. Ozonated oils may help to reduce pain and infection is gross caries with pulpal exposure, but this has not been tested or reported. The oil-base will interfere with dentine and enamel bonding systems.

Ozone gas delivered from the LT-CMU3 Unit or a similar ozone generating device that has CE and MD Marks, are the only ozone units that should be used in these cases. The CE and MD Marks are part of a world-wide mark of Quality Assurance.

Gum Tissue Infections:

(1) Bacterial: Clean the affected area with cooled boiled or sterile water or hydrogen peroxide mouth rinse. Apply a thin layer of the ozonated oil over the affected skin surface. Seek dental help if necessary. The patient should be instructed to re-apply every 3-4 hours after re-cleaning the affected surface. There is no need to cover with a dressing.

(a)Dry Socket: Dry socket is a superficial bone and soft tissue infection, usually following the removal of a tooth or teeth (especially 8's) but this can occur in any site in the mouth after surgery. It is painful and can take a long period of time to settle and heal with routine antibiotics.

To treat with ozone oils, clean the affected area with cooled boiled or sterile water or hydrogen peroxide mouth rinse.

A small syringe with a blunt end, for example the Ultradent 1.2ml syringe with a fine acid etchant delivery tip, is filled with ozonated oil. The syringe tip is introduced into the dry socket to its full depth if possible and the oil is expelled into the socket as the syringe tip is withdrawn. The patient should be sent home with a supply of the oil, syringes, delivery tips and instructed in oral hygiene care and the case reassessed at regular time intervals.

(b)Periapical Sinus: After the nerve tissue is irreparably damaged by trauma or caries, it will die. If this goes undetected, an area of infection at the tip of the root will develop. The drainage pathway is towards the buccal plates and sulcus. Treatment should be combined with RCT (Root Canal Therapy).

During RCT, the sinus can be irrigated with ozonated oils. A small syringe with a blunt end, for example the Ultradent 1.2ml syringe with a fine acid etchant delivery tip, is filled with ozonated oil. The syringe tip is introduced into the sinus to its full depth, and the oil is expelled into the sinus as the syringe tip is withdrawn. The case should be reassessed at regular time intervals.

(2) Fungal: eg Denture Sore Mouth: Clean the affected gum tissue surface with cooled boiled or sterile water or hydrogen peroxide mouth rinse. Clean the denture with soap and water, rinse, and dry. Apply a thin layer of the ozonated oil over the fitting surface (the surface that touches the gum tissue) of the denture and replace. The patient should be instructed to re-apply every 3-4 hours after re-cleaning the affected surface.

(3) Viral: eg Lip Herpes

Clean the affected skin surface with cooled boiled or sterile water or hydrogen peroxide.

Apply a thin layer of the ozonated oil over the affected lip surface. The patient should be instructed to re-apply every 3-4 hours after re-cleaning the affected surface.

(a)Mouth & Tongue Ulceration: Clean the affected skin surface with cooled boiled or sterile water or hydrogen peroxide mouth rinse. Apply a thin layer of the ozonated oil over the ulcer site and surrounding skin edge. The patient should be instructed to re-apply every 3-4 hours after re-cleaning the affected area.

(b)Aphthous Ulcers: Either ozone gas from the LT-CMU3 unit can be delivered onto the ulcer surface, or ozonised oils can be placed onto the ulcer surface directly. Clean the affected skin surface with cooled boiled or sterile water or hydrogen peroxide mouth rinse. Apply a thin layer of the ozonated oil over the affected skin surface. Seek medical help urgently. The patient should be instructed to re-apply every 3-4 hours after re-cleaning the affected surface.

Superficial Burns: Clean the affected skin surface with cooled boiled or sterile water or hydrogen peroxide mouth rinse. Apply a thin layer of the ozonated oil over the affected skin surface. Seek medical help urgently. The patient should be instructed to re-apply every 3-4 hours after re-cleaning the affected surface.

Periodontal Pockets: These oils should be used in conjunction with thorough scaling and debris prophylaxis. They are not an alternative to routine professional oral hygiene care. All periodontal pockets should be charted and measurements noted. Points of bleeding and pocket depth should be recorded. After professional prophylaxis, a small syringe with a blunt end, for example the Ultradent 1.2ml syringe with a fine acid etchant delivery tip, is filled with ozonated oil.

The syringe tip is introduced into the periodontal pocket to its full depth, and the oil is expelled into the pocket as the syringe tip is withdrawn. At no time should the oil be injected into the soft tissue. The aim is to fill the pocket with the ozone oil

or gel as an adjunct to debris removal. The patient should be instructed in oral hygiene care, and the case reassessed at regular time intervals. Ozonated oil can be re-applied at 1week intervals in all cases, or in severe cases, more frequently.

Root Canal Therapy: Ozone, ozonated water and ozonised oils can be used during root canal therapy to clean and sterilize the canal systems. Once access has been created, and the canal system opened, ozone gas delivered by the LT-CMU3 unit is used to sterilize the canal system. 120 – 240 seconds of ozone should be used. If RCT is being staged over more than one visit, a small syringe with a blunt end, for example the Ultradent 1.2ml syringe with a fine acid etchant delivery tip, is filled with ozonated oil.

The syringe tip is introduced into each canal and the oil is expelled into the canal as the syringe tip is withdrawn. The access is then sealed. At recall, no more than 5-7 days after the previous appointment, the canals are opened, re-cleaned and if suitable, filled.

Surgery Sites / Surgical Suture Lines: Clean the suture line with cooled boiled or sterile water, or hydrogen peroxide solution. Apply a thin layer of the ozonated oil over the affected skin surface with a suitable instrument, such as a 'Micro-Brush'. The patient should be instructed to re-apply every 3-4 hours after re-cleaning the affected surface. There is no need to cover, such as with a perio-pack, unless protection from further trauma is required.[41]

THE GOALS OF OZONE THERAPY

Setting the standard-of-care and therapeutic goals on sound evidence-based science is critical. Therapeutic goals are inclusive and not exclusive of standard-of-care.

- Elimination of pathogens.
- Restoration of proper oxygen metabolism.
- Induction of a friendly ecologic environment.
- Increased circulation.
- Immune activation.
- Stimulation of the humoral anti-oxidant system.[32]

INDICATIONS AND CONTRAINDICATIONS

Indications of ozone therapy

1. Arterial circulatory disorders
2. Immunodeficiency and immunodysbalance
   - Additive therapy in carcinoma patients
   - Diseases caused by viruses (eg. Hepatitis)
3. Inflammatory conditions
4. Rheumatic diseases
5. External ulcers and skin lesions[32]
6. Dentistry
   - Prophylaxis and prevention of caries.
   - Remineralization of pit and fissure caries.
   - Remineralization of root caries and smooth surface caries.
   - Restoration of open cavitation along with conventional conservative measures.
   - Bleaching of discoloured root canal treated teeth.
   - Endodontic treatment.
   - Desensitization of external sensitive tooth necks.
   - Soft tissue pathoses.
   - Implantology.
   - Dry socket.[34]

Contraindications of ozone therapy

- Pregnancy.
- Glucose-6-phosphate-dehydrogenase deficiency (favism).
- Hyperthyroidism.
- Severe anemia.
- Severe myasthenia.
- Acute alcohol intoxication.
- Recent myocardial infarction.
- Hemorrhage from any organ.
- Ozone allergy.[32]

ADVANTAGES AND DISADVANTAGES

Advantages

- Non-invasive or minimal intervention technique.
- Induction of a friendly ecologic environment.
- Improves metabolism of infected tissues by means of its oxidizing effect.

Disadvantages

- The problem of maintaining the ideal tightness between the cap and the ozoned tooth.
- The device does not administer ozone when there is a risk of untightness.
- More time (may be even 10 minutes) needed for a proper preparation of the cap.[33]

OZONE PROTOCOLS

Protocols:[42]

Condition	Technique					
	Insufflation				Cupping	Sauna
	Ear	Vagina	Rectum	Urethra	w/funnel	
AIDS	no	yes	Yes	No	no	**Yes**
Arthritis	no	yes	Yes	No	no	**Yes**
Lymphoma	no	yes	No	No	yes	**Yes**
Brain cancer	**yes**	no	No	No	no	Yes
Breast cancer	no	**yes**	No	No	yes	**Yes**
Colon cancer	no	yes	**Yes**	No	no	Yes
Cervical cancer	no	**yes**	No	No	no	Yes
Lung cancer	no	no	No	No	yes	**Yes**
Prostate cancer	no	no	Yes	**Yes**	no	**Yes**
Cancer, other types	no	yes	Yes	No	yes	**Yes**
Previous stroke	yes	yes	Yes	No	no	**No**
Previous heart attack	yes	yes	Yes	No	yes	**low heat**
Pregnancy	yes	**no**	Yes	No	**yes**	No
Circulatory problems	no	yes	Yes	No	no	**Yes**
Heart Disease	yes	yes	Yes	No	**yes**	**low heat**
Multiple Sclerosis	**yes**	yes	Yes	No	no	**low heat**
Alzheimer's	**yes**	no	No	No	no	Yes

Asthma	yes	no	No	No	**yes**	**Yes**
Bacterial infection	yes	yes	Yes	No	yes	**Yes**
Bladder infection	no	no	No	**Yes**	yes	No
Viral infection	yes	yes	Yes	No	no	**Yes**
Herpes	no	yes	Yes	Yes	yes	**Yes**
Cervical dysplasia	no	**yes**	No	No	no	No
Candida and CFS	**yes**	yes	Yes	No	no	**Yes**
Cataracts	**yes**	no	No	No	no	No
Glaucoma	**yes**	no	No	No	no	No
Macular degen.	**yes**	no	No	No	no	No
Retinitis pigmentosa	**yes**	no	No	No	no	No
Colitis, Crohn's, IBS	no	yes	**Yes**	No	yes	Yes
Diabetes	no	yes	Yes	No	Bagging	**Yes**
Diverticulitis	no	no	**Yes**	No	yes	**Yes**
Emphysema	no	no	No	No	**yes**	**Yes**
Fibromyalgia	yes	yes	Yes	No	yes	**Yes**
Hepatitis	no	yes	Yes	No	**yes**	**Yes**
Lupus	yes	yes	Yes	No	no	Yes
Rheumatoid Arth.	yes	yes	Yes	No	no	**Yes**
Sinusitis	**yes**	no	No	No	no	No
Tinnitus	**yes**	no	No	No	no	No

OZONE TOXICITY

Overwhelming evidence shows that the bronchial– pulmonary system is very sensitive to ozone and this gas should never be inhaled. The respiratory tract lining fluid is constituted by a very thin, watery film containing a minimal amount of antioxidants that makes mucosal cells extremely vulnerable to oxidation. Pulmonary embolism, which occurred during direct intravenous administration of O_2/O_3, an application prohibited by the European Society of Ozonetherapy since 1983.[7]

Marchetti and Monaca (2000) There has been a reported case of death due to air embolism during the use of ozone in the treatment of psoriasis.[32]

Lo Giudice (2004) Reported that a 45-year-old woman complained of acute bilateral visual loss after intra-discal and peri-ganglionic injection of ozone-oxygen gas mixture for lumbar disk herniation.[32]

Corea (2004) reported a case of vertebrobasilar stroke after treatement with ozone-oxygen for lumbar disc herniation. Ozone inhalation can be toxic to the pulmonary system and other organs. Complications caused by ozone therapy are infrequent at 0.0007 per application.[32]

Known side effects are epiphora, upper respiratory irritation, rhinitis, cough, headache, occasional nausea, vomiting, shortness of breath, blood vessel swelling, poor circulation, heart problems and at times stroke. Because of ozone's high oxidative power, all materials that come in contact with the gas must be ozone resistant, such as glass, silicon and Teflon. However, in the event of ozone intoxication the patient must be placed in the supine position and treated with vitamin E and n-acetylcysteine. Hepatitis C and HIV infections have also been reported following ozone autohaemotherapy.[32]

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This Book markedly emphasizes the nuances of Ozone in dentistry along with shedding light on medical applications. A sincere effort been made to describe the comprehensive aspect supported with studies on Ozone. Minimal Invasive procedures a part of recent trends in dentistry have demanded the use of OZONE. Its wide array of use in multifactorial dental infections without any known severe side effects have led to its importance. Ozone gas is immunostimulating, potent analgesic, detoxicating, antimicrobial, bio-energetics and has biosynthetic properties as it causes activation of the metabolism of carbohydrates, proteins and lipids. Ozonated water and olive oil forms an ideal delivery system as they have the capacity to entrap and then release oxygen/ozone. The use of OZONE, which has no effects on environment also is future of green dentistry for greener tomorrow.

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