OZONIZED SALINE SOLUTION (SSO3) RUSSIAN METHOD

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Cancer Seminar

OZONIZED SALINE SOLUTION (SSO3)

- Technology of intravenous infusions of ozonized saline was developed by Russian ozone therapy school in Nizhny Novgorod city in the earliest 80thies of last century.

- The technology got official juridical status on state level and approved by the Ministry of health of Russian Federation in Traumatology, Dermatology, Obstetrics-Ginecology and Neonatology.

- Method assumes previous saturation of NaCl saline with oxygen-ozone mixture and its intravenous infusion to patient.

Oxygen-ozone mixture use in traumatology. Authors: Peretyagin S.P., Vorobiev A.V., Smirnov S.V. and others. № FS- 2007/029U 28.02.2007

Oxygen-ozone use in dermatology and cosmetology. Authors: Kocheleva I.V., Ivanov O.V., Vissarionov V.A. and others. № FS- 2005/058 4.10 2005.

Medical ozone use in obstetrics, gynecology and neonatology. Authors: Serov V.N., Fedorova T.A., Kachalina T.S. and others. № FS-2007 /014-U, 15.02.2007. Information letter, 2013.

History

- In October 1977 the academic A. Korolev from the scientific research center of the Academy of Medicine of Nizhny Novgorod, successfully developed the method of ozonated saline solution.
- In April 1979, for the first time in the world a cardioplegic ozonated saline solution was administered into the coronary system of a patient with congenital heart injury.

I.P.Shmakova, E.I.Nazarov et al. Methods of application of ozone in medicine (guidelines). The Ministry of Health of Ukraine Ukrainian Centre for Scientific medical information and license work, Kiev, 2004.

Utilization of ozonated cardioplegic solution in myocardium ischemia. Boiarinov G.A.; Morxov A.R.; Schbetz R. A.; Peretiagyn S.P.; Cardiología №2, 1983 C116-117

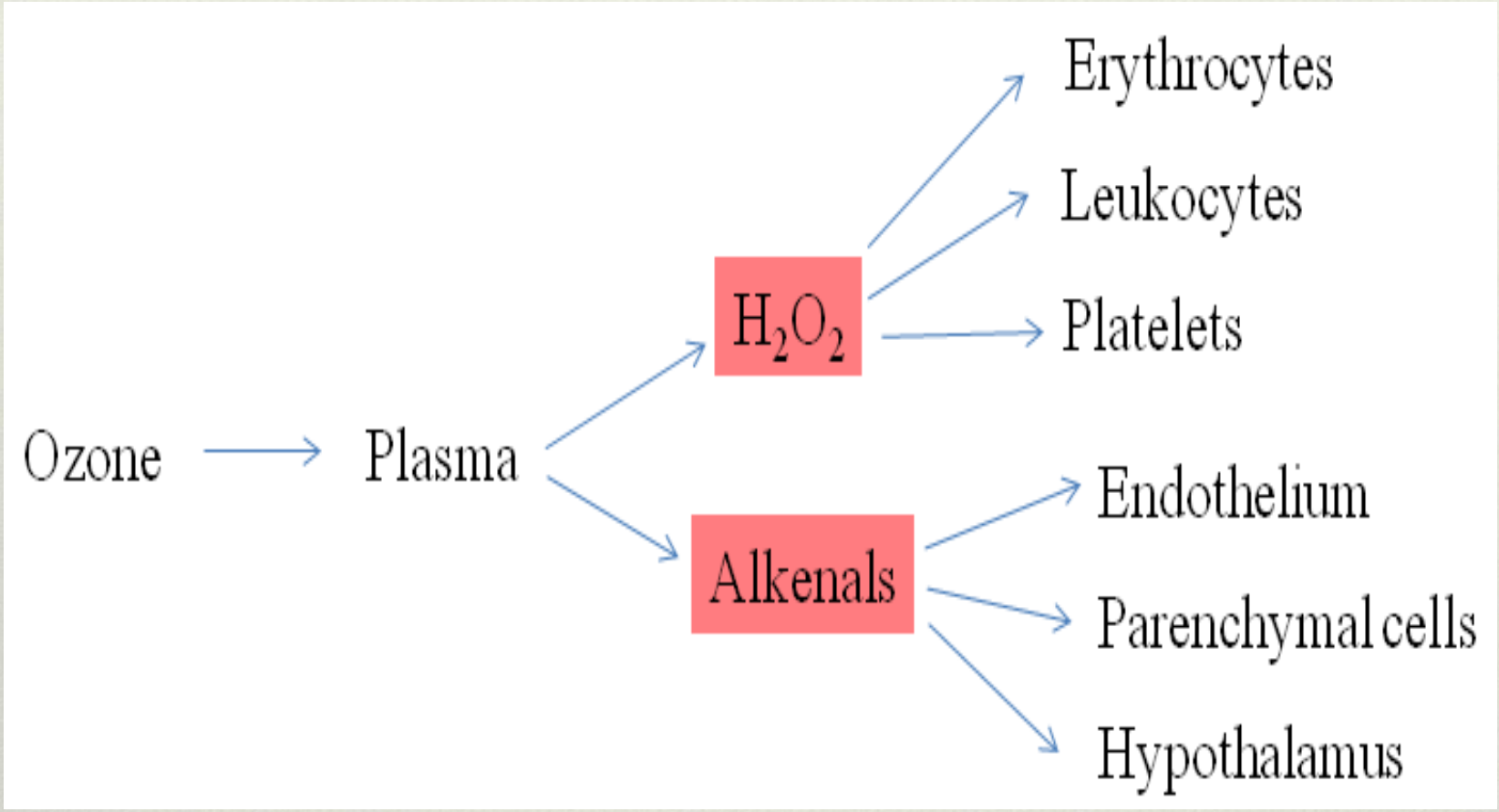
Mechanism of action

- The genomic mechanism of action of ozone was discovered much earlier in saline than in autohemotherapy.
- I refer to Korean and Russian studies published in 2004-2011-2013
- The response dependent of the activation of the nuclear transduction mechanisms signals Nrf2 (nuclear factor erythroid 2) which is a powerful protein located within each cell in the body and it is activated by an Nrf2 activator inducing the protein synthesis, e.g. SOD (superoxide dismutase), CAT (catalase), HO1 (heme-oxygenase 1), etc.)
- Ozone therapeutic indications are based on the knowledge that low physiological dose of ozone may play important roles within the cell.

Kim *et al.*, 2004. Ozone induced ↑Nrf2 in lungs and livers of B6C3F1 mice.

Qu *et al.*, 2011. ozonized saline activation of the Keap1-Nrf2- EpRE signaling pathway ↓ rat's liver injury induced by CCl_4

Cho *et al.*, 2013. (Nrf2(-/-)) and wild-type (Nrf2(+/+)) mice. Nrf2 deficiency exacerbates oxidative stress and airway injury by O_3.

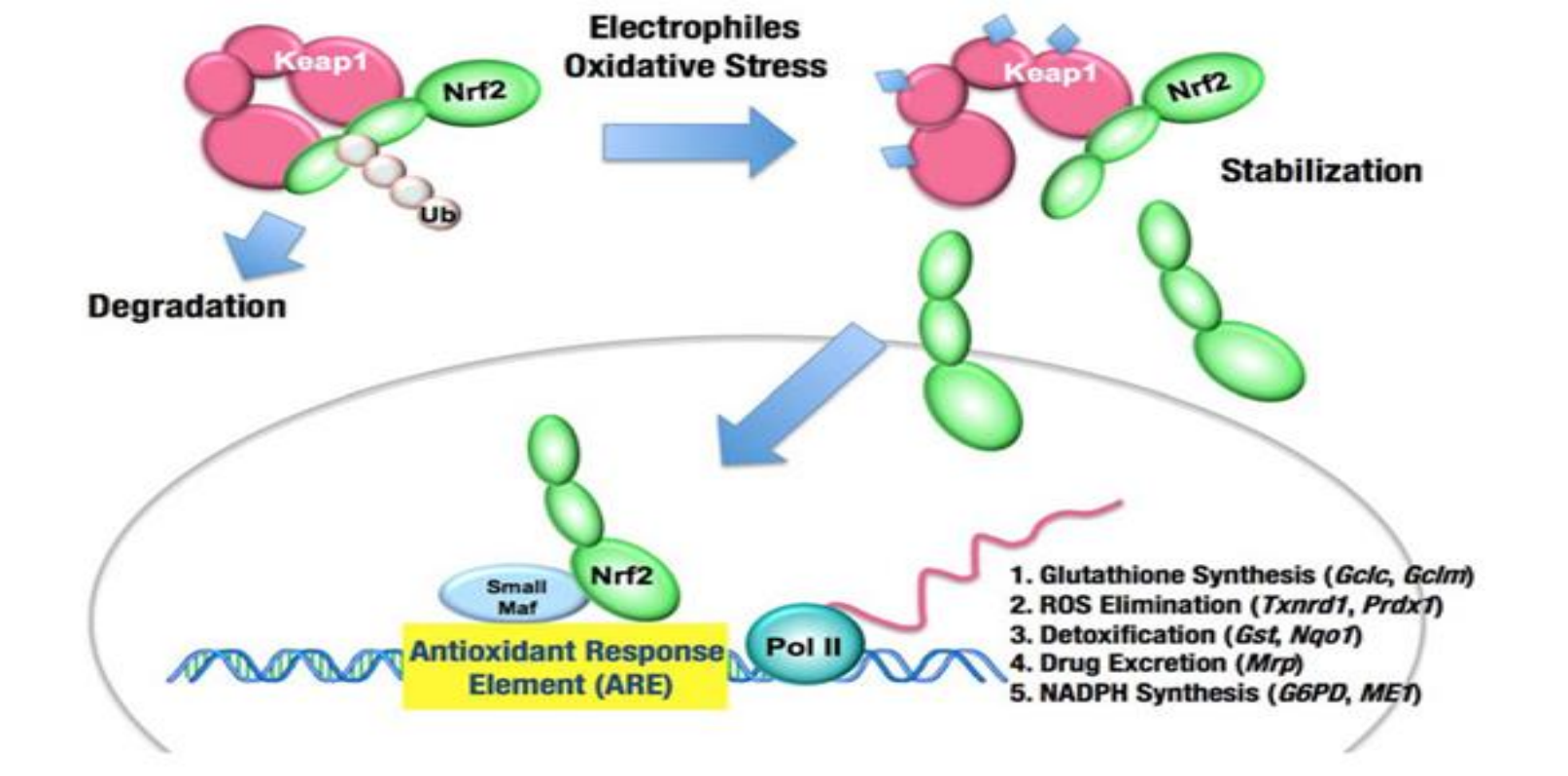


Ozone in contact with blood (serum components and cell membranes) generates oxidizing agents such as hydrogen peroxide and Alkenals.

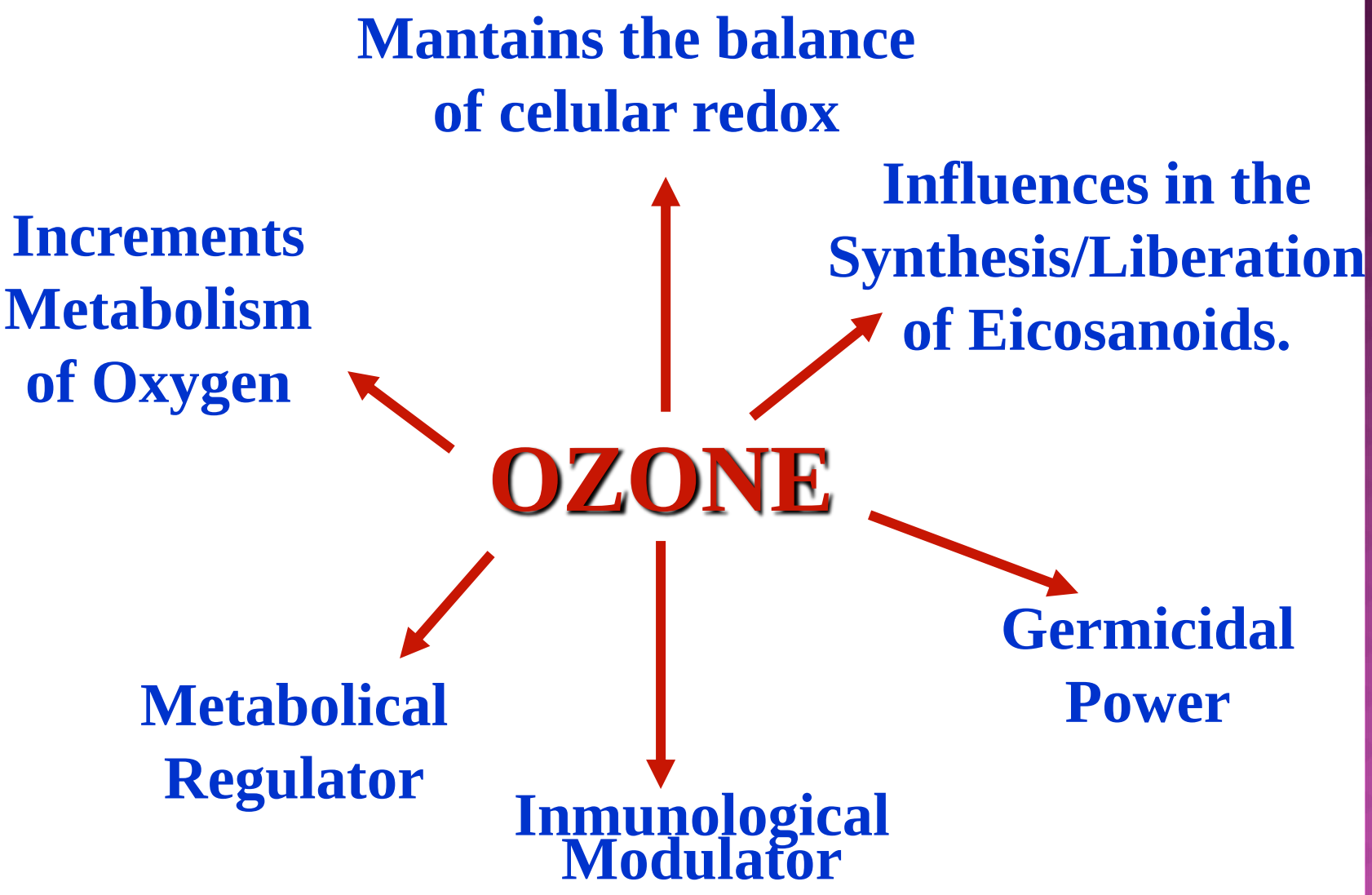
Hydrogen peroxide triggers biochemical pathways in blood cells, while alkenals, after the infusion of ozonated solution into the donor, act on a variety of cells.

- This mediators oxidize cysteine residues of the molecule Keap1 which are going to stabilize NRF2 and releases it.

- Once released it migrates into the cell nucleus and bonds to the DNA at the location of the EpRE (electrophile-responsive element) which is the master regulator of the entire antioxidant system located in all human cells.



Biological Effects of Ozone



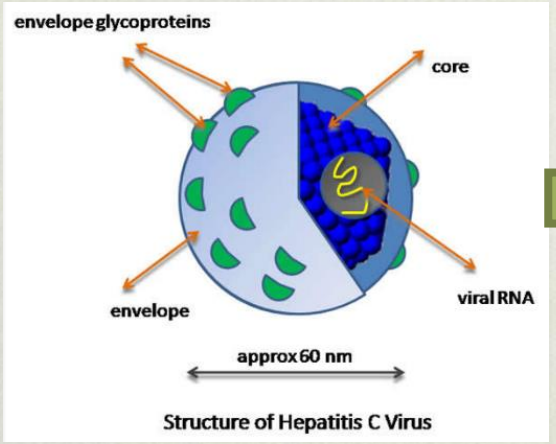
Virucidal action of the SSO3

- The action of ozone on the viral particles could change the structure of the virions so that they remain structurally intact but dysfunctional enough to not being pathogenic.

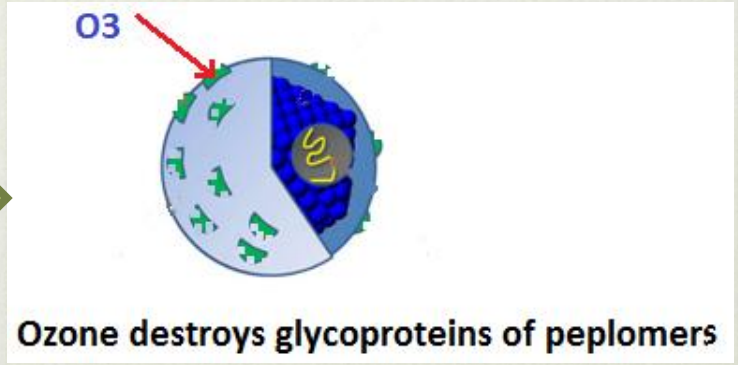
- The attenuation of the functionality of the viral particle through slight modifications of the viral envelope, and possibly of the viral genome itself, modifies its pathogenicity and allows the host to increase its immune response.

- The creation of dysfunctional viruses by ozone offers a unique therapeutic possibilities.

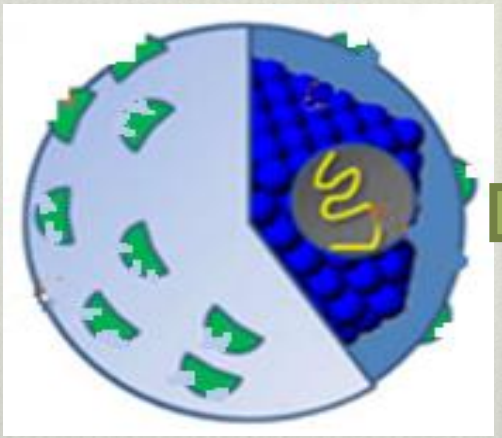
- Considering the fact that there are many mutational variants in any affected individual, the creation of an antigenic spectrum of disabled virions could provide a host-specific stimulation of the immune system, therefore, the design may obey of what can be called: a vaccine of autologous host-specific.

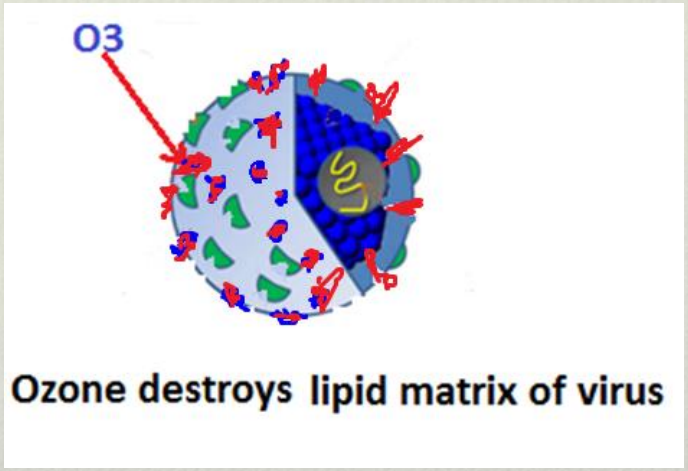


Structure of Hepatitis C Virus



Ozone destroys glycoproteins of peplomers





Ozone destroys lipid matrix of virus

The use of ozonated saline compels to ask two questions:

1. If the mixture of ozone with saline generates H2O2 and NaCl substrates that may cause complications in the body,

2. If the dose of ozone that the patient receive with this procedure is sufficient to obtain an appropriate therapeutic response.

1st Question

- According to Prof Bocci, bubbling ozone in saline solution at 50 μg/mL during 10 min the concentration of hydrogen peroxide in saline is about 2.5 μg/mL
- And bubbling ozone in saline at 70 μg/mL during 4 minutes the concentration of hydrogen peroxide in a saline solution is 0.062 μg/mL
- The concentration of ozone in the saline solution reaches 5 μg/mL This is mean that the hydrogen peroxide concentration is about 1 % of the concentration of ozone.

Research

A simple calculation shows that in weight units, the concentration of hydrogen peroxide comprises 85 μg/mL <0.00001%.

- Russian chemists have also shown that the concentration of sodium hypochlorite in the ozonized saline is less that 0.001 μg/mL

- According to research made by Professor Claudia N. Kontorshchikova: In ozonated 0.9% saline solution (0.55 mg/L of O2-O3) on average were found 0.004 mM/L of chloride ions.

Maslennikov, O. V., KONTORSHCHIKOVA, C. N., & GRIBKOVA, I. A. (2008). Ozone therapy in Practice. Health Manual, Ministry Health Service of The Russian Federation The State Medical Academy Of Nizhny Novgorod, Russia.

Ozonization Method of Saline Solution. Peretiagyn S. P.; Struchkov A.A.; Peretiagyn N. C. ; Kulechina N. B.; published 20.12.06, Patent 2289413 Russia, МКИ A 61 K 33/40Бюл. № 35 (заявка № 2004126456/15 от 31.08.04)

Research

- Analysis of hydrogen peroxide in samples of ozonized 0.9% NaCl solution, made by methods of analytical chemistry, revealed no accumulation of hydrogen peroxide in concentrations exceeding 0.002% in any of the ozonation schemes, although they found even much lower concentrations, on the order of 0.0004%
- The value of pH in ozonated physiological solution were found to be 7.3±0.2

Research

- At that same time prof Razumovski stated:

"The descomposition of ozone in aqueous solutions of NACL is not accompanied by formation of products other than oxygen. In particular, no noticeable amounts of hypochlorites and chlorates are observed. This particularly significant for medicinal application of ozonized isotonic solutions".

Razumovskii, M.L. Konstantinova, T.V. Grinevich, G.V. Korovina, V.Ya. Zaitsev, 2010, published in Kinetika i Kataliz, 2010, Vol. 51, No. 4, pp. 517–521 and Razumovskii et al. Phys. Chem 434, 163 (2010) ISSN 0023-1584, Kinetics and Catalysis, 2010, Vol. 51, Nº 4 pp. 492-496 Pleiades Publishing Ltd., 2010. Original Russian Text.

I.P.Shmakova, E.I.Nazarov et al. Methods of application of ozone in medicine (guidelines). The Ministry of Health of Ukraine Ukrainian Centre for Scientific medical information and license work, Kiev, 2004.

Conclusions to the 1st question

- It is clear that the concentration of hydrogen peroxide and the sodium chloride is not conspicuous or even noteworthy.
- Thus there is no reason that the ozonated saline solution be dangerous to patients' health.
- Clinicians, who have been using intravenous drop-infusions of ozonated physiological solutions report on good, positive results of treatment.

Second question

To the question of if it is effective or not the Russian method for the treatment of diseases that ozone therapy usually treat are effective or not.

❖That depend of the doses.

❖The ozonation is carried out at very low concentrations of ozone and these are calculated according to patient weight.

❖As a rule, in the Russian method, the concentrations used ranging between 1 and 3 mg/L

❖Higher levels lead to pronounced activation of the processes of free radical oxidation and misbalance between lipid peroxidation and antioxidant defense system (C.Kontorschikova,1999).

Método de solución salina ozonizada/Peretiagyn S. P.; Strukov A.A.; Peretiagyn N. C.; Kulechina N. B.; Publicado 20.12.06, Patente. 2289413 Rusia, МКІ A 61 K 33/40 Biu. № 35 (заявка № 2004126456/15 от 31.08.04)

- Ozone dissolution significantly depends on the water quality, temperature and pH medium.

$O_3 + H_2O = 2OH` + O_2$ - chain formation

$O_3 + OH` - HO_2` + O_2$

$O_3 + H\,O_2` = OH` + 2\,O_2$ - development

$OH' + OH` = H_2\,O_2$ – break

$O_3 + H_2\,O_2 = OH` + H_2\,O_2` + O_2$

$OH` + H\,O_2` = H_2\,O + O_2$

- Maximal ozone amount in water sample is observed within 8 -15 minutes. An hour later in the solution there can be found only oxygen free radicals.

Doses

- **Low ozone dose:** 1 μgr/Kg; dose the patient receives 0.4 μgr/mL
- **Medium ozone dose:** 2 μgr/Kg; dose the patient receives 0.8 μgr/mL
- **High ozone dose:** 5 μgr/Kg. dose the patient receives 2.0 μgr/mL
- Calculation of the ozone gas concentration to prepare ozonated saline:

(Please note that the dissolved ozone concentration is 25% of the ozone gas concentration)

- **Dose Formula:**

Indications of the doses

- **Low dose:** are used to stimulate the immune system, diseases of the cardiovascular system, gynecology and obstetrics to prevent toxemia in the first trimester of pregnancy and fetal hypoxia in the third quarter.
- **Medium dose:** are used for detoxification endo-toxemia and chronic inflammatory diseases of different etiologies.
- **High doses:** used in the treatment of infectious diseases, dermatology and burns.

Calculation of Low Dose

For example: If the patient weighs 80 kg, multiply as follows:
Low ozone dose: 1 µgr/Kg * 80 Kg = 80 µgr

Formula: 80 = ozone gas concentration * 25% x 200 mL

The ozone concentration in saline is 25% (0.25) of the ozone concentration in the gas.

80 = ozone gas concentration * 25% * 200; 80 x 0.25 = 20

❖ 80 x 20 = 1600 mg/1000 = 1.6 µgr/NmL Ozone gas concentration (or 1.6 mg/NmL) Ozone concentration which is going to set on the generator = 1.6 µg/NmL

Therefore, if we are continuously bubbling at a concentration equal to 1.6 mg/L, the concentration of ozone disolved in saline solution will be: **1.6 x 0.25 = 0.4 µgr/mL (0.4 x 200= 80µgr)** Dissolved ozone concentration in saline = 0.4 *µg*/mL and the one the patient will receive.

Calculation of Medium Dose

- **Medium ozone dose**: **2 µgr/Kg** * 80 Kg = 160 µgr
- **Formula: 160 = ozone gas concentration * 25% * 200 mL**
- 160 x 0.25 = 40
- 80 x 40 = 3200/1000 = 3.2 µgr/NmL Ozone gas concentration.
- Ozone gas concentration = 3.2 µgr/NmL (to be set it on generator)
- 3.2 x 0.25 = 0.8 µgr/mL dissolved ozone concentration in saline.
- Dissolved ozone concentration in saline = 0.8 *µg*/mL is going to be the one the patient will receive.

Calculation of High Dose

- **<u>High ozone dose</u>: 5 µgr/Kg** * 80 Kg = 400 µgr
- 400 = ozone gas concentration * 25% * 200
- 400 x 0.25 = 100
- 80 x 100= 8000/1000 = 8 µgr/NmL Ozone gas concentration to be set on the generator.
- 8 x 0,25 = 2 µgr/mL dissolved ozone concentration in saline. This is what the patient will receive.

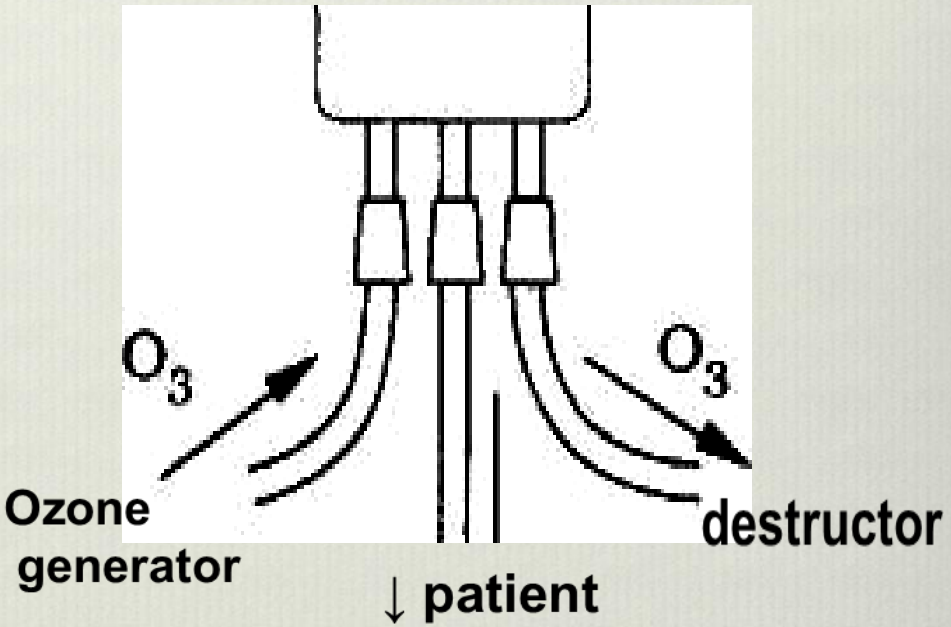
Measurement units

- The µg/NmL units take into account the pressure and room temperature.
- The "N" of the µg/NmL means normalized mililiter therefore Standard Conditions of Temperature (0ºC) and Pressure (1 bar).
- Each ozone generator should detect these differences and have the capacity to self-adjust.
- Gamma (symbol: γ), is was used as a synonym and abbreviation of microgram but now is obsolete.

- **International Scientific Committee of Ozone Therapy. Madrid Declaration on Ozone Therapy. 2th ed. Madrid: ISCO3; ISBN 978-84-606-8312-4; 2015. 50 p. Schwartz-Tapia A, Martínez-Sánchez G, Sabah F, Alvarado-Guémez F, Bazzano-Mastrelli N, Bikina O, Borroto-Rodrígez V, Cakir R, Clavo B, González-Sánchez E, Grechkanev G, Najm Dawood A H, Izzo A, Konrad H, Masini M, Peretiagyn S, Pereyra, V R, Ruiz Reyes D, Shallenberger F, Vongay V, Xirezhati A, Quintero-Marino, R. Madrid Declaration on Ozone Therapy. 2th ed. Madrid: ISCO3; ISBN 978-84-606-8312-4; 2015. 50 p.**

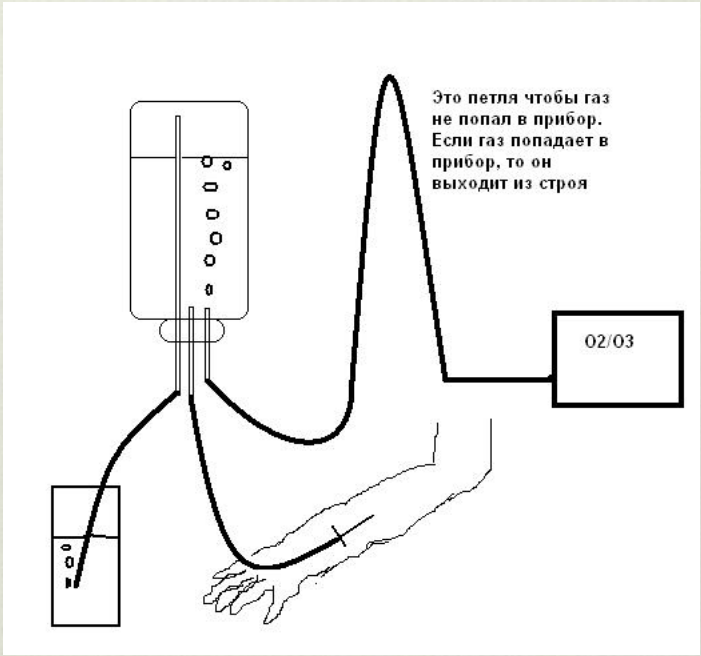
“Three needle system”

- The procedure involves inserting three needles in the bottle with 200 ml of saline solution: a long needle that connects to the ozone destroyer and takes out the pressure inside the bottle, the second needle, which is short, to the generator and the 3rd is connected to the patient.

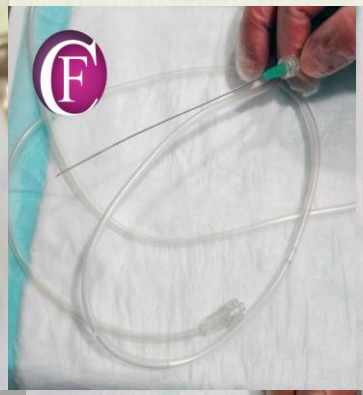


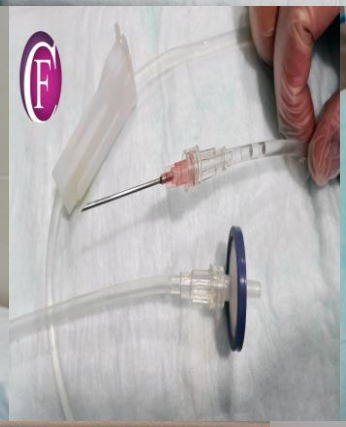
“Three needle system”

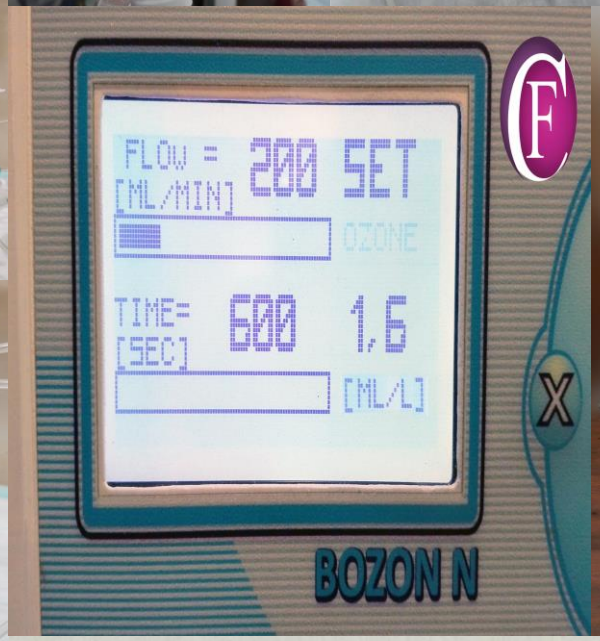
- Bubbling during 10 min then infuse the solution intravenously during 15-30 min under a constant bubbling.
- The infusion of the solution has to be of room temperature to increase its stability and capacity for ozone saturation.
- Once the solution is prepared, should be infused as soon as possible, because is known that ozone is quickly decomposed.
- The barbotage should be stopped by disconnecting the instillator when about 50 mL of solution left in the flask, in order to avoid embolism. The infusion beig kept on.




Salina Fisiológica Grifols® 0,9%
250 ml



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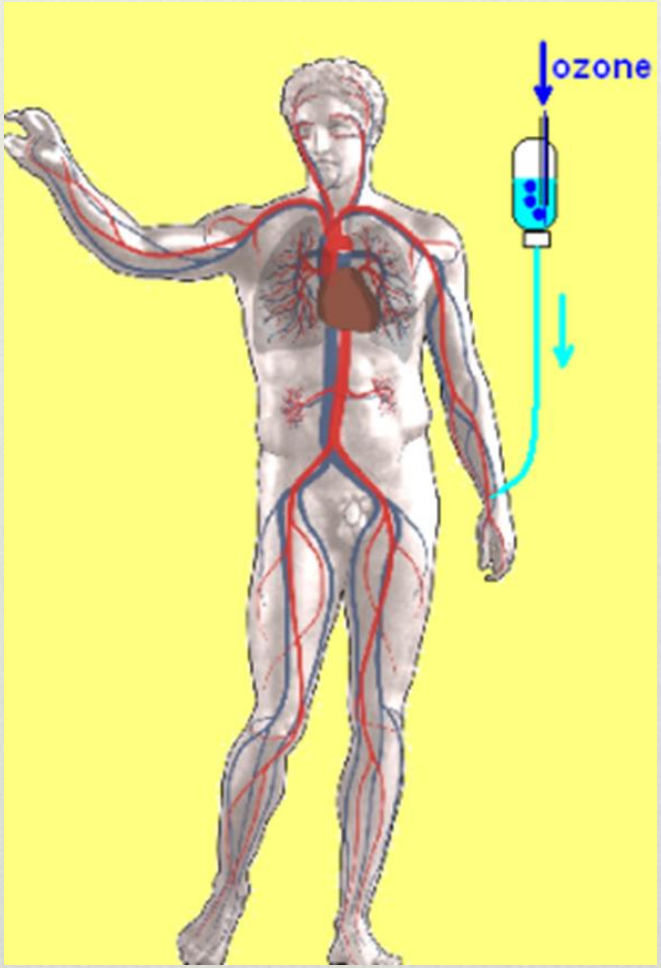
Degradation of the ozone

- The procedure involves taking into account the temperature of the solution.
- After 5 min iv infusion, the ozone concentration in the solution falls by 17%
- After 10 min falls by 29%;
- After 15 min falls by 37%,
- After 20 minutes it falls by 43% and
- After 25 min falls by 46%

“Three needle system”

- Dripping of 80-120 drops/min
- The number of procedures for a treatment cycle is 6 to 10.
- Procedures are conducted daily or every other day.



Recommended Range of Concentrations (mg/mL) of ozone

- 0.1 to 0.4 mg (early toxicosis of pregnancy)
- 0.5 to 1 mg (patients post myocardial infarction, abortion, gestosis)
- 1.1 - 2 mg (different surgeries, cardio sclerosis, hypertension)
- 2.1 - 3 ug (osteomyelitis, vascular ulcers, diabetes, trophic sores, acute thrombophlebitis, duodenal and stomach ulcers, post myocardial infarction, hypertension, cardio sclerosis)
- 3.1 - 3.5 mg (burns, infections, endo- and myocarditis)
- 5.1 - 10 mg (septic conditions)

What is the difference between SSO3 and Major AHTM?

- Since the Saline Solution is a plasma expander, therefore, SSO3 represents a greater amount of blood being treated than major AHMT and therefore, we may need to use less number of sessions.

- Perhaps this is the crucial point of the effectiveness of the Russian method.

What is the quantity of blood processes by ozone in Major AHT and IV Saline Solution?

If we take into account:

The speed of the flow of blood in the cubital vein which is (0.1 – 0.2) L/min,

The time that procedure takes = 30 min,

The volume of ozonized blood:

(0.1-0.2)L/min x 30min = 3-6 L of blood

Which physical law is applied to ozonized saline solution?

- **Henry's Law,** which states that a gas is dissolved in a liquid (at constant temperature) in direct proportion to its pressure (either partially or not). If we speak of partial pressures then it is assumed that the gas is a mixture of two or more gases.

- If we introduce in a bottle, a pure water and oxygen at 1 bar, this gas dissolves in water up to saturation. If we increase the pressure, oxygen begins to dissolve again until the new level of saturation. Thus, the amount of gas is dissolved directly proportional to the pressure.

- This does mean that the liquid dissolves more or less depending on the pressure and has nothing to do with the time it does.

Which physical law applied to major AHTM?

- Ozone does not diffuse or dissolves in the blood but reacts with it. Diffusion and dissolution are different concepts in physics.
- Henry's statement refers to inorganic liquids and blood is an organic and living fluid, the reaction is much more complex since it reacts immediately with biomolecules such as uric acid, unsaturated fatty acids, etc. resulting hydrogen peroxide, lipid peroxides, ozonides, etc.
- The reaction of ozone in blood does not follow Henry's Law.

Disadvantages

- Large doses or high concentrations of ozone cannot be administered due to the risk of causing phlebitis.
- If the bottle is disconnected from the generator then it can progressively and gradually lose the ozone concentration in the solution.
- The generator is trapped at least for about 30 min per patient.
- Not suitable for auto immune diseases.

Conclusions

- The method proved to be effective, safe and easy to perform.
- It's cheaper then others method.
- It can be applied to people with religious restrictions to blood transfusions.
- There is no threat or risk onto the eyes of the health administration.
- It has a wide scientific backup
- It is very effective in viral diseases.

Conclusions

- For some diseases, like the autoimmune, these doses of SSO3 are insufficient. In these cases it's most appropriate to apply the major autohemotherapy because what we need is high suppressive doses.

- Nevertheless, there is a huge list of diseases for which the Russian method is entirely appropriate and effective like: Virus and infectious diseases, degenerative and cardiovascular diseases, in obstetrics/gynecology and cancer. All of them needs the application of low doses.

From my dear Madrid
Thank you for your attention