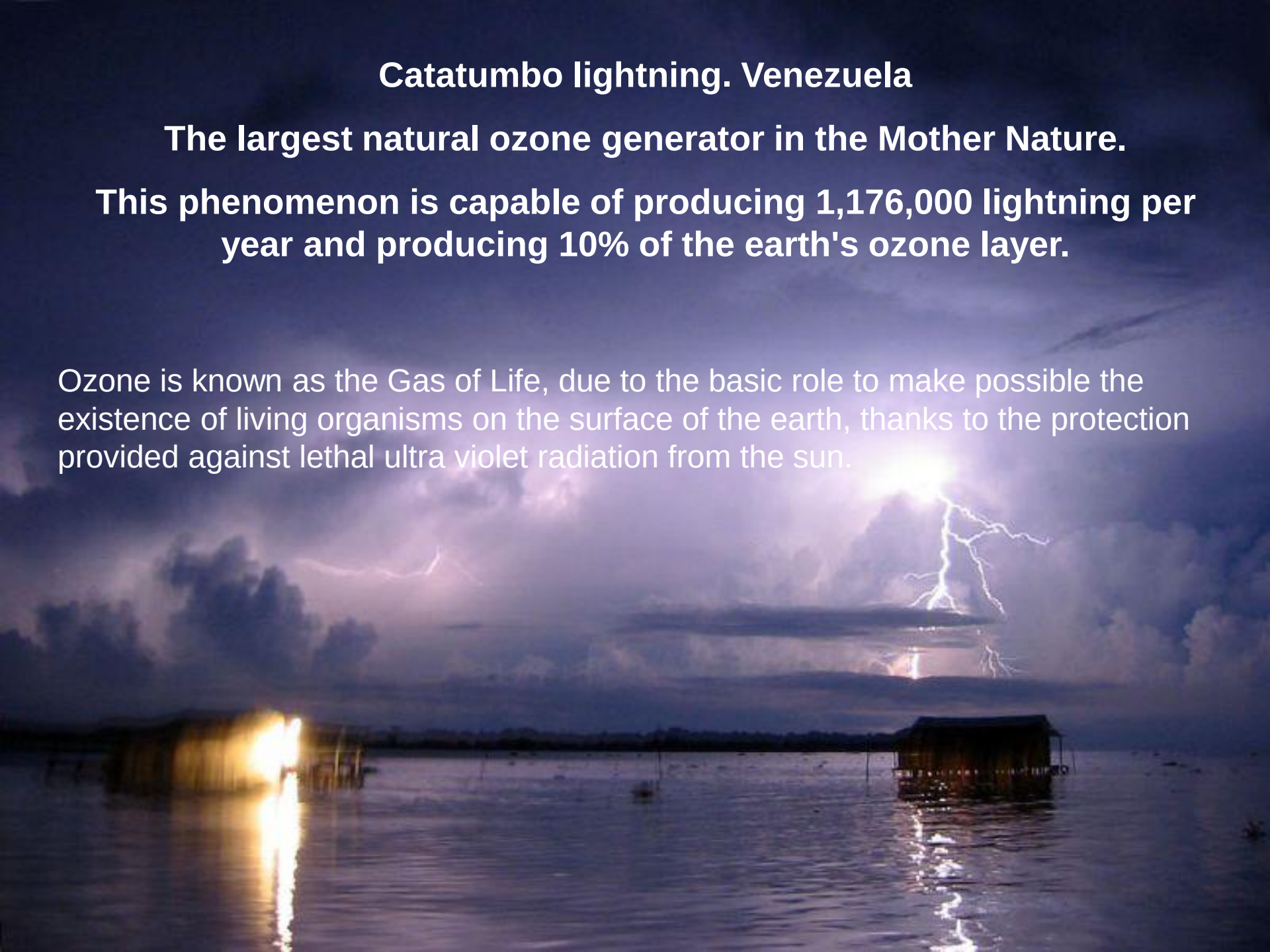
BASIC PRINCIPLES IN OZONE-THERAPY

Dra Adriana Schwartz



Catatumbo lightning. Venezuela

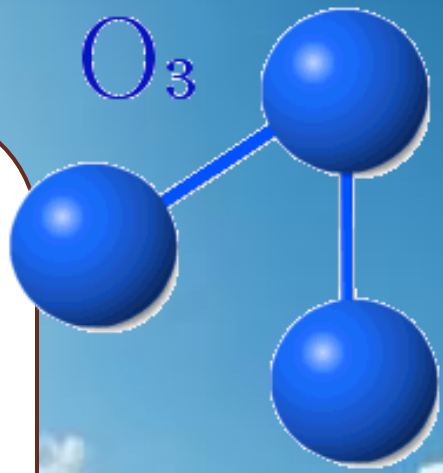
The largest natural ozone generator in the Mother Nature.

This phenomenon is capable of producing 1,176,000 lightning per year and producing 10% of the earth's ozone layer.

Ozone is known as the Gas of Life, due to the basic role to make possible the existence of living organisms on the surface of the earth, thanks to the protection provided against lethal ultra violet radiation from the sun.

SOURCE OF OBTENTION MEDICAL OZONE

- The ozone must be produced by a medically reliable and certified generator.
- The generator must allow the measurements of precise ozone concentrations (1 µg/NmL - 80 µg/NmL).
- The generator must produce ozone exclusively from medicinal grade, coming from a medical quality certified container.



O2

Characteristics of ozone

- Ozone is unstable oxidant. It is transform rapidly into oxygen. It can not be stored. Must be produced at the moment of being used.
- It is 1.6 more dense and ten times more soluble in water than oxygen.
- Ozone is a powerful disinfectant, which has a bactericidal power in 99,9 % on a wide specter of microorganisms, without developing resistance.
- Ozone is very active and its reaction with the tissues is 3500 times more powerful and rapid than any disinfectant liquid.
- Ozone metabolites penetrates very well in the microstructures, because the ozonides are 150 % smaller than any of the liquid disinfectant molecule;
- Ozone interacts with polyunsaturated fatty acids, which are present in a high percentage in the organism.
- Ozone can induce adaptation to oxidative stress or oxidative preconditioning.
- Under controlled doses can stimulate endogenous antioxidant mechanisms preparing the host to face physiopathological conditions mediated by reactive oxygen species.

Administration of ozone is contraindicated in

- Glucose-6-phosphate dehydrogenase deficiency (favism, acute hemolytic anemia)*
- Toxic Hyperthyroidism - Basedow Graves status
- Thrombocytopenia less than 50.000 and serious coagulation disorders
- Severe Cardiovascular instability
- Acute alcohol intoxication
- Acute Infarct of myocardium
- Massive and Acute Hemorrhage
- During convulsive states
- Hemochromatosis
- Patients receiving treatment with copper or iron.
- Ozone should never be inhaled.

MEASUREMENT UNITS

- The concentration's unit of measurement is **µg/NmL.**
- The µg/NmL units take into account the **pressure** and room **temperature**.
- The "N" of the µg/NmL means normalized milliliter therefore Standard Conditions of Temperature (0ºC) and Pressure (1 bar). This is the only unit recognized by the International Ozone Association - IO3A.
- The concentration expressed in µg/NmL must have a margin of error equal or better than ±10%.

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.

Formula for Calculating Dose

We strongly advise applying the *up-dosing system*, as Dr. Bocci stated, "*start low, go low*".

$$\text{DOSE} = \frac{\text{CONCENTRATION X VOLUME}}{1000}$$

- 1mg is equal to 1000µg
- 1 lt is equal to 1000 mL (cc)

VOLUME OF BLOOD TO BE EXTRACTED

- It is necessary to define the volume of blood to be extracted.
- This is done based on the weight of the patient being treated. Hemodynamic / hypovolemia disorders with a loss of 15 % of total circulating blood volume (CBV) are not considered.
- In case of AHT major, a withdrawal of 2 % or more than 1.5 % is conservative.
- A person of 85 kg has CBV of 65 mL / kg x 85kg = 5,525 mL.
- Ranges of a safe blood collection are: 1.2 mL / kg to 1.3mL / kg with the limit of 150 mL in individuals of 150 kg.

All therapeutic dosages are divided into three types, according to their mechanism of action:

- **a) Low doses**: These doses have an immunomodulatory effect and are used in diseases where there is suspicion that the immune system is very much compromised. For example, in cancer, for the elderly and for debilitated patients, etc.

- **b) Medium doses**: They are immunomodulatory and stimulate the antioxidant enzyme Defense System. They are most useful in chronic degenerative diseases such as diabetes, atherosclerosis, COPD, Parkinson syndrome, Alzheimer, and senile dementia.

- **c) High doses**: They have an inhibitory effect on the mechanisms which occur in autoimmune diseases such as rheumatoid arthritis and lupus. They are especially employed in ulcers or infected injuries and are, also, used to prepare ozonized oil and water.

Calculation of doses

- The concentration may vary placebos, therapeutic and toxic levels.
- This can be expressed in micrograms/mL or as milligrams/liter
- Eg. 20-30 mg/L is the same as 20-30 micrograms/mL and 10-20 micrograms/mL is the same as 10-20 mg/L
- Why ?

Because,

1mg is equal to 1000µg

1 lt is equal to 1000 mL (cc)

DOSE = CONCENTRATION X VOLUME
1000

Eg:

- Concentration of 20 microgram/mL
- Volumen of 300 mL
- Multiply 20 x 300 = 6000 micrograms
- As we know that 1000 microgram are equal to 1 miligram,
- Then, we divide 6000/1000 = 6.0 miligrams

- If you had expressed the concentration in mg/L, the result would be the same 20 mg/L is multiplied by 0.3L, liters are canceled and get the end result = 6.0 milligrams.
- 20 x 0.3 = 6.0 miligrams

Basic principles

- **Ozone concentrations for systemic uses** range from 10 µg/NmL to 40 µg/NmL, concentrations of 70 µg/NmL - 80 µg/NmL and above should be avoided because of the increased risk of hemolysis, reduction of 2, 3 DPG and anti-oxidant and a consequent inability in activating immune-competent cells.

- **Anticoagulant:** it is most advisable to use ACD-A *Anticoagulant Citrate Dextrose* Solution A, USP (2.13% free citrate ion), or Citrate Sodium 3.8% 10 mL per 100 mL of blood.

- **Heparin** is not advisable because it can induce thrombocytopenia and Platelet aggregation, and Citrate Sodium chelates Calcium. The quantity of ACD-A ranges from 7 mL -10 mL per 100 mL of blood.

- Warkentin, T.E. & Greinacher, A. Heparin-induced thrombocytopenia and cardiac surgery. *Ann Thorac Surg* 76, 2121-31 (2003).

AGGREGATION EFFECT OF HEPARIN AND OZONIZATION OF PLASMA

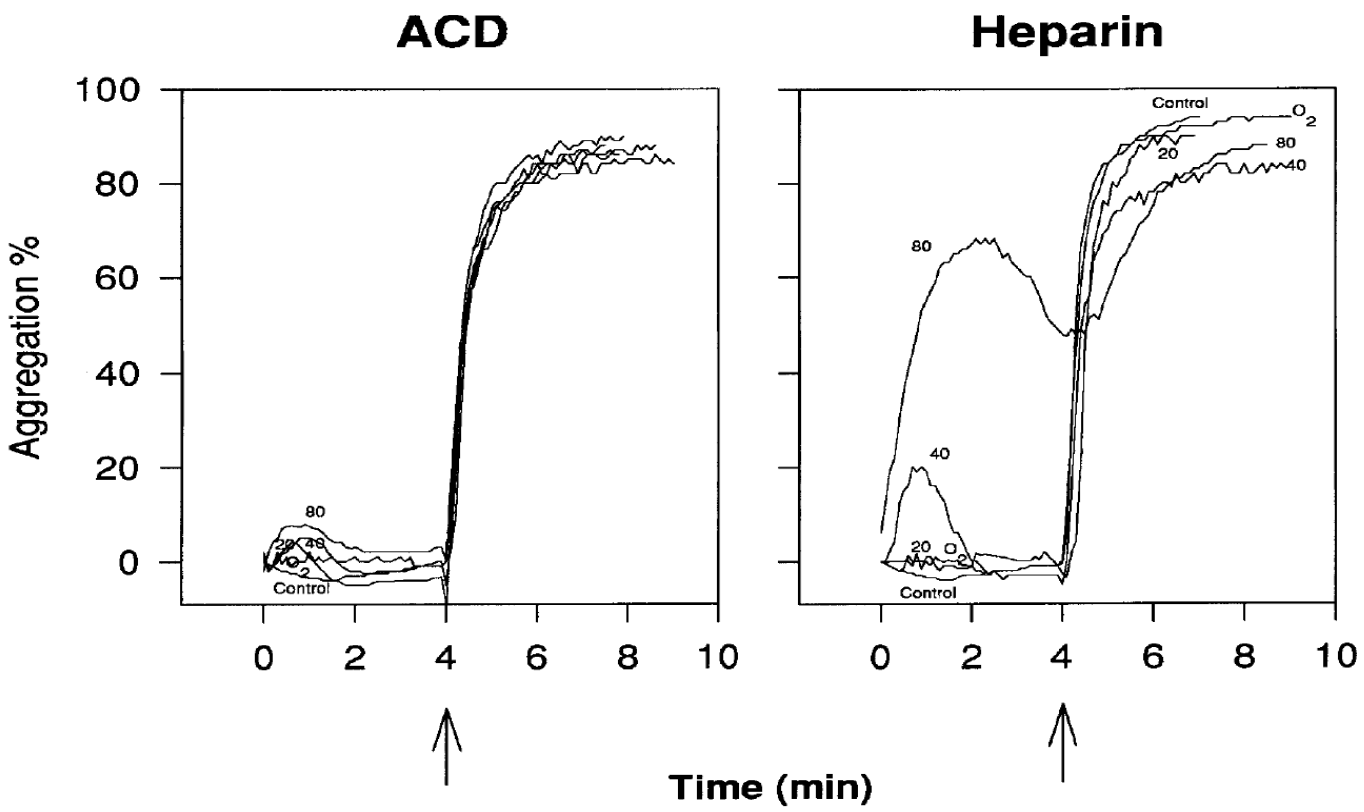
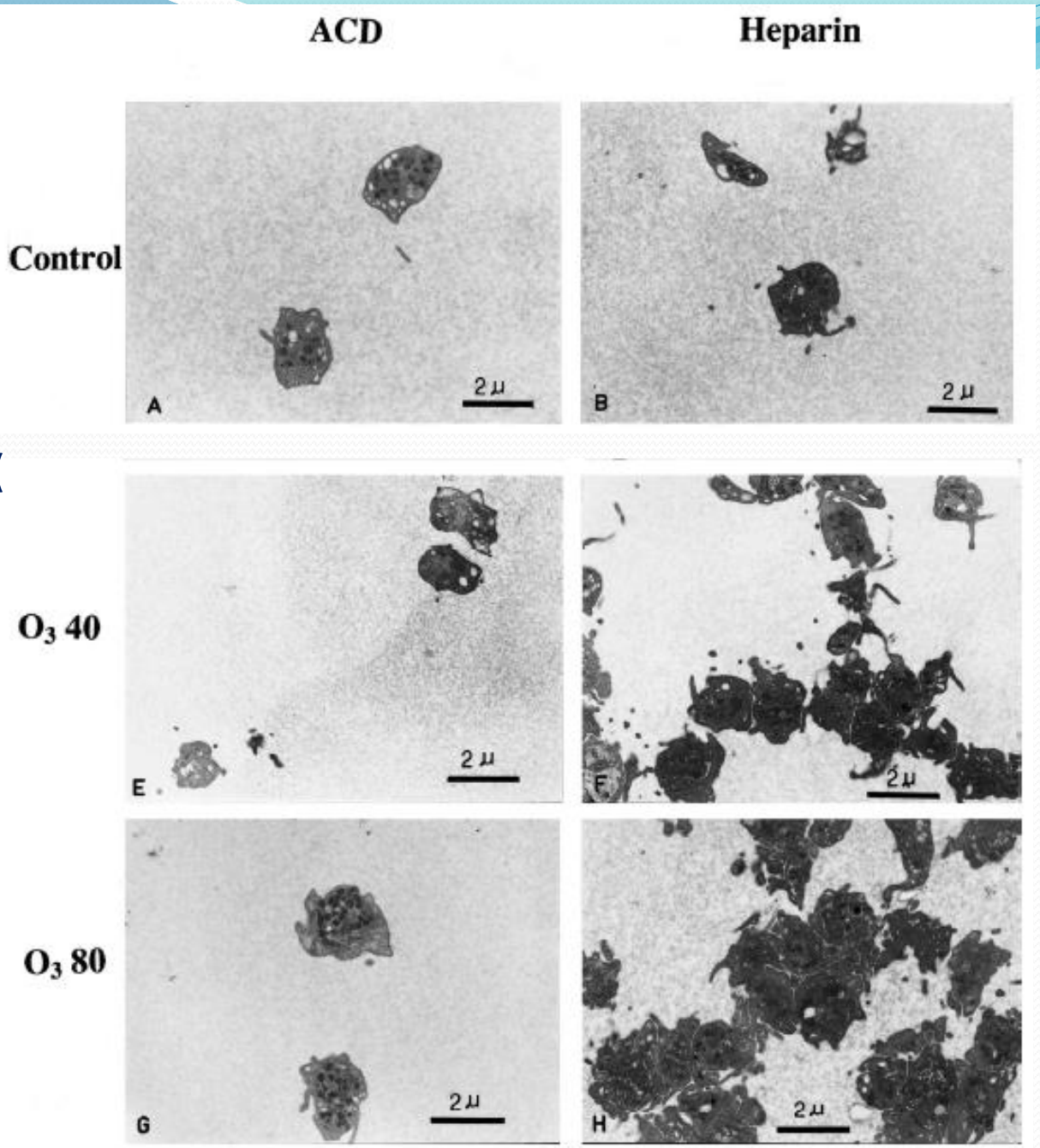


Figure 1. Representative tracings of platelet aggregation induced by progressively increasing O_3 concentrations (20, 40 and 80 μg/ml per ml PRP). O_3 causes immediate and dose-dependent aggregation only in heparinized PRP (right panel). Aggregation profiles of PRP in ACD are reported in the left panel. After 4 min, ADP induces full aggregation (arrow).

Effects of ozone and heparin on human platelets.
Transmission electron microscopic examination of human PRP´s either in ACD(left panel) or in heparin(right panel) Platelets exposed to O3 concentrations of 40 and 80 µg/mL per mL of PRP form aggregates on the right-hand side.



Bocci *et. al*. Studies on the biological effects of ozone: 9. Effects of ozone on human platelets. *Platelets* (1999) **10**, 110:116

Possible clinical responses to ozone

- It is feels more tired or feel initial relief, then gets worse, then improves and finally makes a plateau.
- At first there is no improvement, but after the 8th - 10th session begins to improve.
- There are a small number of patients who improve only after the end of a course of treatment of 20 sessions.
- The average response after the first 10 sessions

Possible clinical responses to ozone

Ozone therapeutic indications are based on the knowledge that low physiological doses of ozone may play important roles within the cell.

- Usually, the dose is not given per kg. weight, but at dose/response.
- Usually in malnourished or thinned patients very small volumes are given, like in children (50 mL). In elderly, usually 100 mL are used. 150 mL aere rarely used.
- On average volumes between 70 and 150 mL are reasonable.

Possible clinical responses to ozone

Dose and volume management

- Thin, active, anxious, hyperkinetic person do not support larger amounts of ozone (no more then 00 cc) and doses no more then (1.5 or 2.0)µg/mL

- Quiet, obese, sedentary patients allow larger volumes and higher concentrations (150-200cc)

- Stressed patients require a very less volume and less concentration.

Basic principles

- As a general rule, every five sessions the dose of ozone is increased and it is given in cycles that vary between 15 and 20 sessions.
- From the clinical point of view, a patient's improvement occurs between the fifth and tenth session.
- It is considered that after the twelve session the antioxidant defense mechanism has already been activated.
- The treatment is given daily, from Monday to Friday. It could also be administered two to three times a week.
- Cycles can be repeated every 5-6 months.

General principles to consider during treatment with Ozone

- Concentrations between 40 and 80 µg/mL are for local treatment of severely infected wounds.
- Concentrations between 20 and 40µg/ml for local treatment of bedsores, ulcers, proctitis, anal fissures not severely infected.
- Between 10 and 40 µg/mL are for Systemic treatment (IM, AHTMayor, AHMTMenor, IR, etc.

Recomended Doses and Concentrations of Ozone (µg/mL)

SISTEMIC				
	Concentration/Dosis			Observations and Volume
	Alta	Media	Baja	
Major Auto hemo-trasfusion	30-40 (3.0-4.0)	20-30 (2.0-3.0)	10-20 (1.0-2.0)	50-100 mL
Minor Auto hemo trasfusion	40-30	15-20	5-10	10 mL
Paravertebral	20	15	10	Aguja 22-27Gx1 ½, 5-20 mL
Subcutaneous	10	8	5	1-2 mL máximo 100 mL/sesión
Intra-articular	20	10	5	1-2 mL (dedo), 5-20 mL otros
Rectal insufflation	30 (6 µg)	25-20 (3.75-3.0 µg)	15-10 (1.5-1.0 µg)	200-150-100 mL

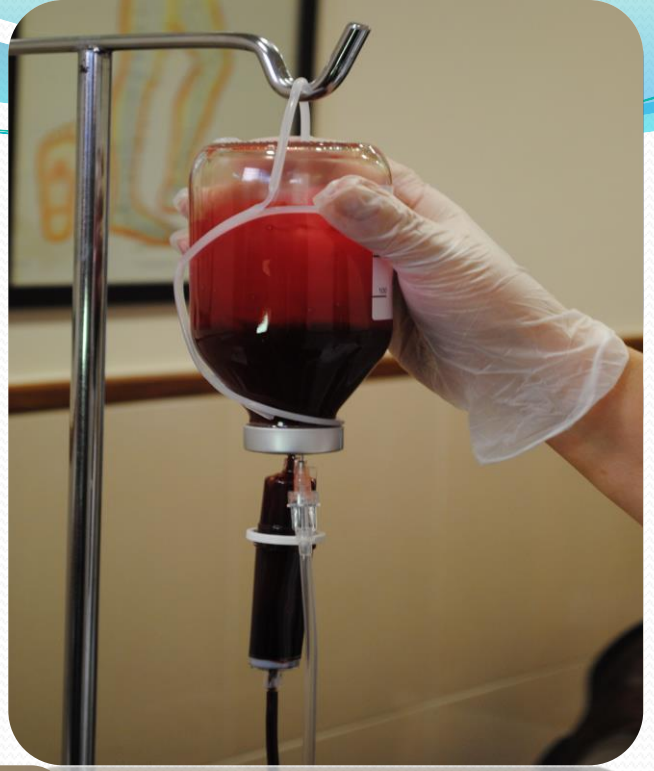
ISCO3. MADRID DECLARATION ON OZONE THERAPY 2nd Edition. International Meeting of Ozone Therapy Schools. Madrid, Spain, June 2015.

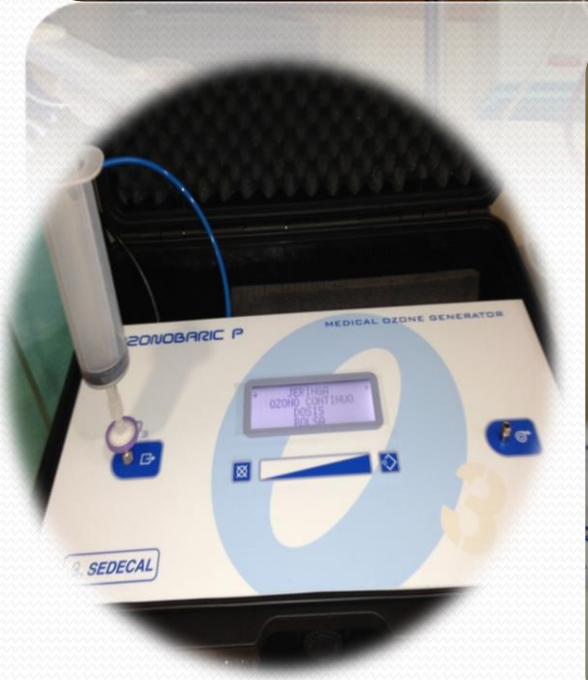
Safe range for the major autohemotherapy

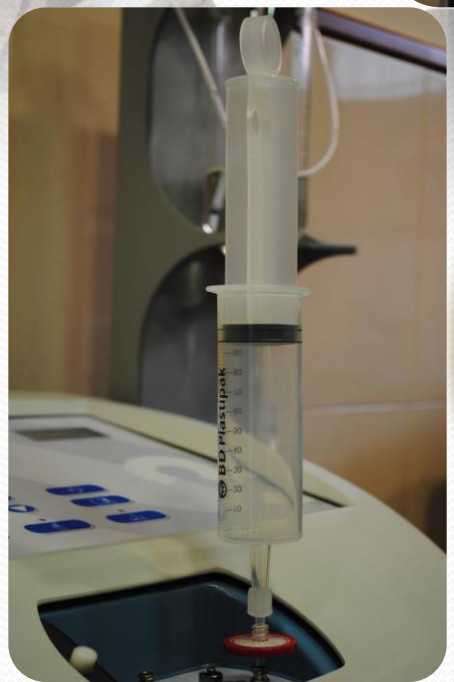
Volume and Concentration:

MAHTMajor 100 mL of blood

- Sessions 1 – 5: 20 µg/mL y 100 mL of blood
- Sessions 6 – 10: 25 µg/mL y 100 mL of blood
- Sessions 11 – 15: 30 µg/mL y 100 mL of blood
- Sessions 16 – 20: 40 µg/mL y 100 mL of blood




MEDICAL OZONE GENERATOR
SEDECAL


BD Plastipak

RECTAL INSUFFLATION

- The Rectal insufflation of ozone is a systemic route. The gas is quickly dissolved in the luminal contents of the bowel, where mucoproteins and other secretory products with antioxidant activity readily react with ozone to produce reactive oxygen species (ROS) and lipid peroxidation products. These compounds penetrate the muscular mucosa and enter the circulation of venous and lymphatic capillaries

- The range of dose is 10 - 30 µg/NmL
- The range of volume is 100 - 200 mL
- Concentrations higher than 40 µg/NmL can hurt the enterocyte.

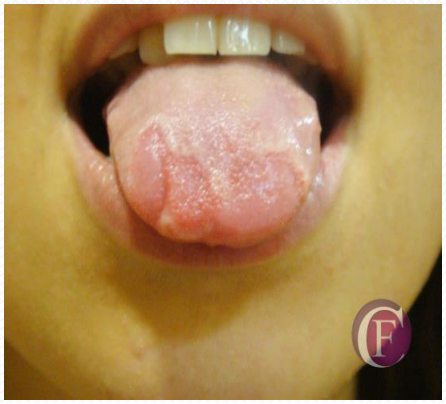
General principles to consider during treatment with Ozone

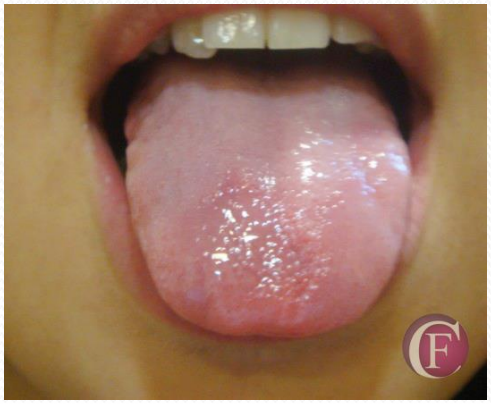
- Rectal insufflation
- 1º- 5° Session: 20 µg/ml and Vol. 100cc
- 6°- 10° Session: 25 µg/ml Vol. 150 cc
- 11º- 15° Session: 30 µg/ml, Vol. 200 cc
- 16°- 20°Session: 35 µg/ml, Vol. 200 cc

O3 Bagging and application of O3 oil

Ozonized water

- The concentration use of ozone in water is of 70-80 μ/ml, which serves to continuously irrigate the surgical field, with double effect:
- Disinfection of the surgical field and
- The trophic action of the damaged tissues, inducing the liberation of a cascade of numerous growth factors and chemical mediators, who guarantee the osteogenesis and the neoangionesis processes.





Interactions with ozone and diet suplementation control

- ACE Inhibitors, Ozone increases effects of the drug. Treatment with ozone in patients under anticoagulation therapy as Coumadin / heparin/ must be done under control of INR.

- Patients receiving treatment with copper or iron cannot receive ozone treatment.

- Synergic effect with other oxidative therapy (U.V., H_2O_2 etc.) should be expected.

- **Before, During and After Ozonetherapy**: Evaluate nutritional status and return to normal as required. Prepare the organism before administer ozone.

Interactions with ozone and diet suplementation control

- **During:** Maintain basal nutrient intake supplied by the diet. Do not administer antioxidants.

- **After:** Oral vitamins or antioxidants should be given before or after the ozone therapy but never during the treatment. Proceed to supplementation of the deficient nutrient (GSH, Vit. E, C. Se, Mn, Cu, Zn)

Psoriasis

Treatment Scheme: Cycle of 20 sessions, 4 cycles a year

- Rectal Insufflation: doses: 1,500µg – 4,500µg
- Local application of ozonated oil at 600 IP twice a day
- Micro- infiltrations in the psoriatic plaques twice a week 5-10 cc at 5-10 µg/mL
- If there is no improvement, increase the doses up to 4,000 µg.
- Consider the use of CGF+VIT D3

Psoriatic arthropathy

- Treatment squeme:
- O_3R: doses: 1,500µg – 4,500µg 20 sessions
- Intra-articular infiltration at 10-15 µg/mL; volumen of 5 cc twice a week.

Advantages of the use ozone vs corticoids

- Lower economic cost
- Less risk of infection
- Does not produce subcutaneous fat atrophy or depigmentation of the skin, which is a problem when repetitive applications of corticosteroids on very superficial structures are made, as in the case of De Quervein tenosynovitis or Morton's neuroma.
- Does not induce weakness of tendons and ligaments, which is the risk in repeated applications of corticosteroids or in torn tendons, this fact may cause the rupture of these structures. On the contrary, ozone produces a beneficial effect on tissue metabolism.

Advantages of the use ozone vs corticoids

- It does not produce deposit of crystals in the joints, which can generate a crystal arthropathy.
- It does not provoke avascular necrosis of the femoral head.
- No cognitive effects "steroid psychosis“
- Can be applied in diabetic patients.
- Can be applied in hypertensive patients.
- Can be applied in patients with kidney or liver failure.
- May be applied in immuno-depressed patients.
- Can be applied in patients with systemic infections.

Advantages of the use ozone vs corticoids

- Can be applied in patients with osteoporosis.
- Does not produce weight gain.
- Besides the anti-inflammatory and analgesic effect, ozone has a beneficial effect on tissue metabolism, which partly explains their long-term therapeutic effects.
- Can be applied in patients with allergy to corticoids or local anesthetics.
- Can be applied in joints or infected tissues, in fact can be a very effective treatment for such problems.
- Can be applied at multiple sites in a single session.
- You can be repeated many sessions of infiltration. In the case of corticosteroids should be applied only 2 to 3 sessions.
- Have a beneficial effect on systemic metabolism.
- Corticoids are immunosuppressant.
- Can be applied in patients with gastro duodenal ulcers or at risk of bleeding in the digestive tract.

Disadvantages of ozone infiltration

- It can be very painful if is applied too quickly or at high concentrations, it may produce a vasovagal reaction, fainting and even cardiac arrest in extreme cases.
- There is possibility of inadvertent application in a blood vessel, if we do not do systematic aspiration with the syringe while infiltrating, with the consequent of gas embolia due to ozone applied directly into the bloodstream.
- There are reports of fatal accidents by neglected people who were not prepared to administer CPR immediately.

Disadvantages of ozone infiltration

- There may be an exacerbation of pain, if we apply higher doses at first, or should apply in areas where there is resistance at the time of injection, or not to be in the right space, so we must be very careful when applying ozone.

- Staff working with ozone is exposed to risks from chronic or acute inhalation of ozone, unless they have the necessary security measures, as good quality and well calibrated equipment, well-ventilated work environment and prevent leaks of ozone in the workplace, hoses and connections in good condition, work with carbon mask, etc.

Caution!

The fact that ozone is a molecule with antibacterial properties does not mean you should not carry out all aseptic and antiseptic measures necessary for any injection procedure, in the same way as we do when we inject corticoids it should be used disposable sterile needles and syringes to prevent any infections or legal medical problem.

Hyperbaric oxygen (HBO)

Physiology

- By improving the metabolism of oxygen, the cell gets more ATP, works better and perform better its functions of ion transport through membrane.
- Release the same ROS, but less ozonides and aldehydes which definately can be obtained with ozone.
- HBO released mainly H_2O_2 and singlet oxygen

Hyperbaric oxygen (HBO)

- It has poor effects on enzymes, especially on SOD and catalase, and much poorer on the myeloperoxidase and less vaccine effect than ozone.
- Myeloperoxidase by being regulated by HBO is useful in inflammatory processes, but this is better achieved with ozone through TNF, IL 1, IL 10 and others.
- HBO did not significantly stimulate the secretion of hormones, as ozone does.

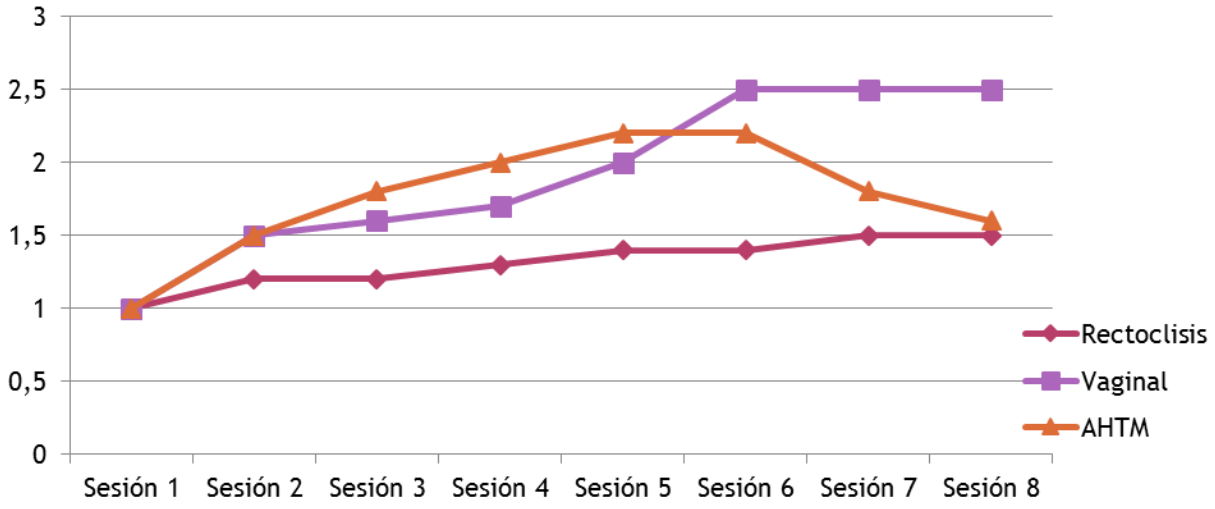
Indication of HBO

- Acute osteomyelitis. The Chronics are best solved with MAHT
- Diving accidents
- Brain-vascular disease.
- Ozone, as well as HBO are very good at Hemorrhagic Ischemic Vascular Brain Accident, but the elderly do not easily withstand HBO.
- Delayed bone consolidation.

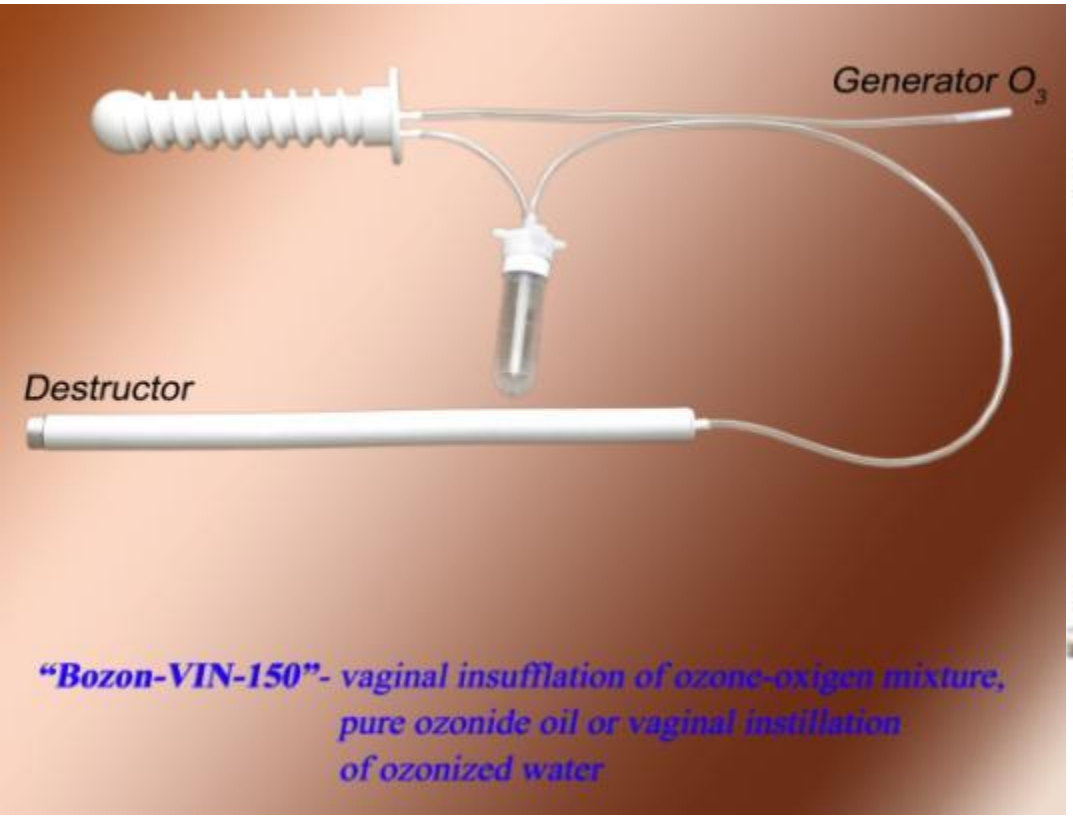
Disadvantages of Hyperbaric oxygen (HBO)

- High costs claustrophobia
- Elders do not tolerate high pressures
- Contraindicated in glaucoma, emphysema, sinusitis, use of pacemakers
- Risk of explosion and death of patients and staff

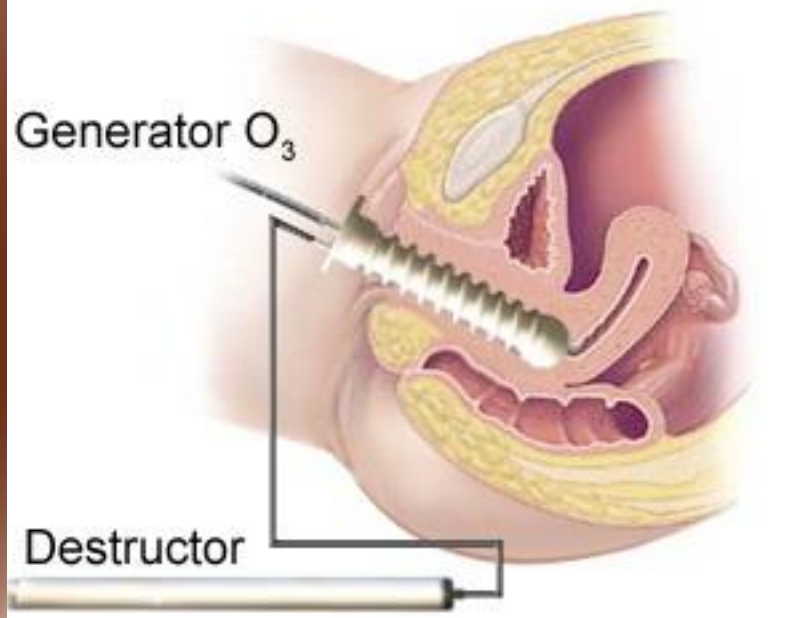
COMPARATIVE DYNAMICS OF CAPILLARY BLOOD FLOW SPEED, DURING MAJOR AUTOHAEMOTHERAPY, RECTOCLISIS AND VAGINAL INSUFFLATION.

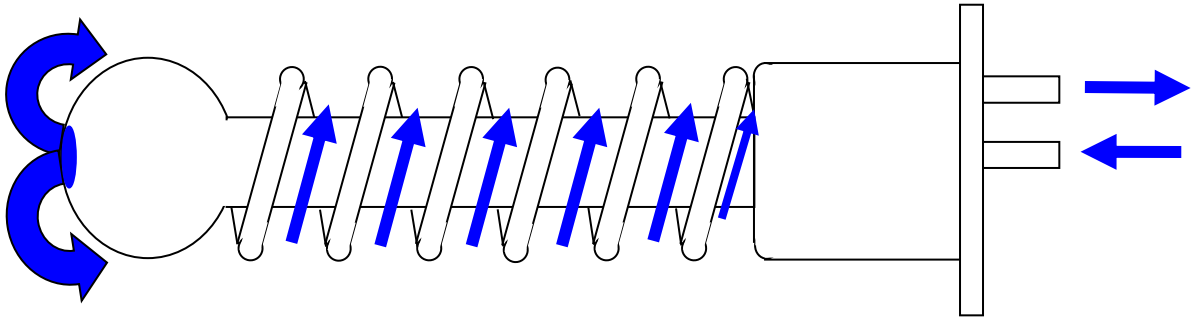


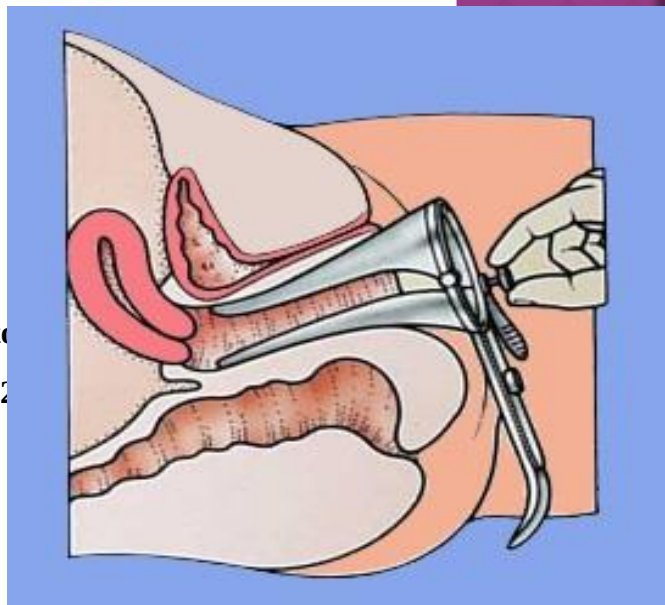
Vertical coordinate shows the rate of capillary flow (cm/seg)
Horizontal coordinate shows the number of sessions
Rectal insufflation: 0.4 L O2-O3 concentration 30 mg/L
Vaginal insufflation: 20 µcg/mL, 200 mL/min 10 min
AHTMajor: dose 2mg

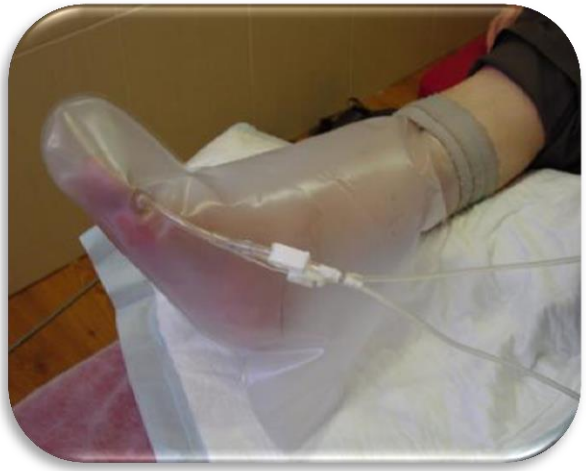


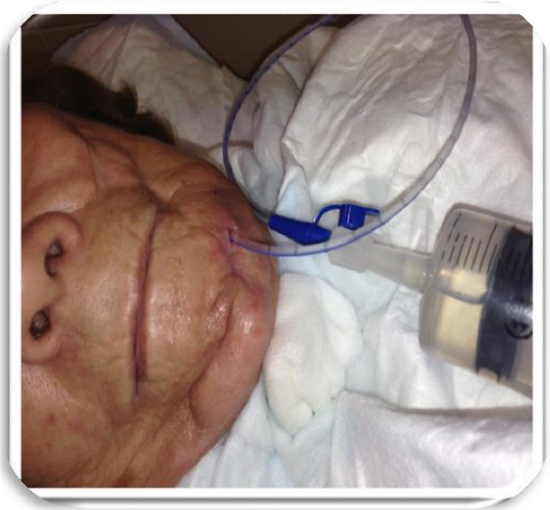
"Bozon-VIN-150"- vaginal insufflation of ozone-oxigen mixture, pure ozonide oil or vaginal instillation of ozonized water

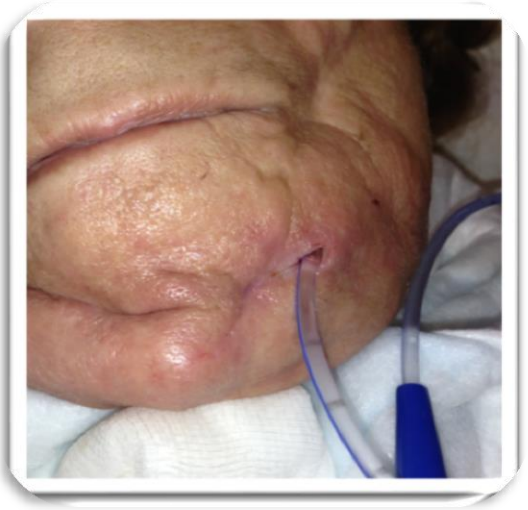




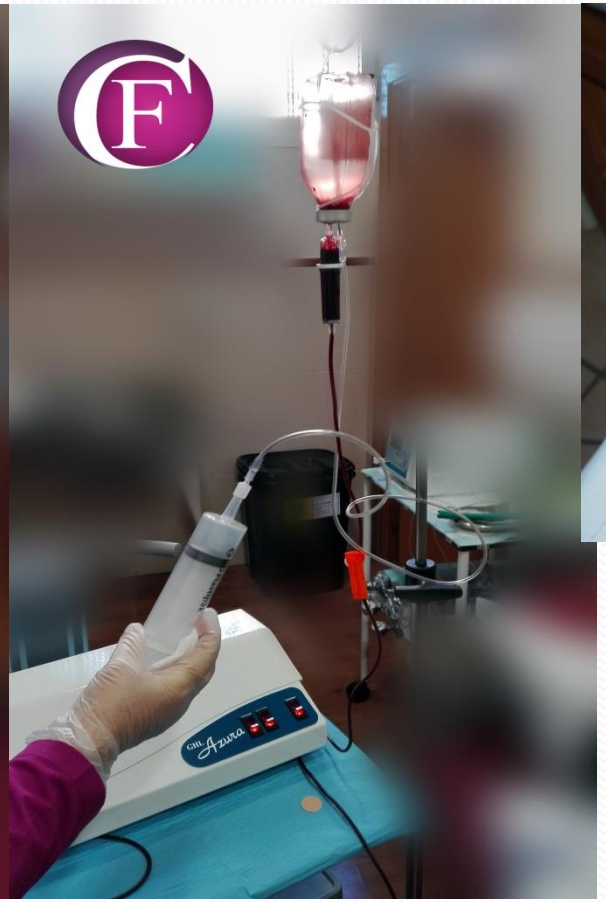


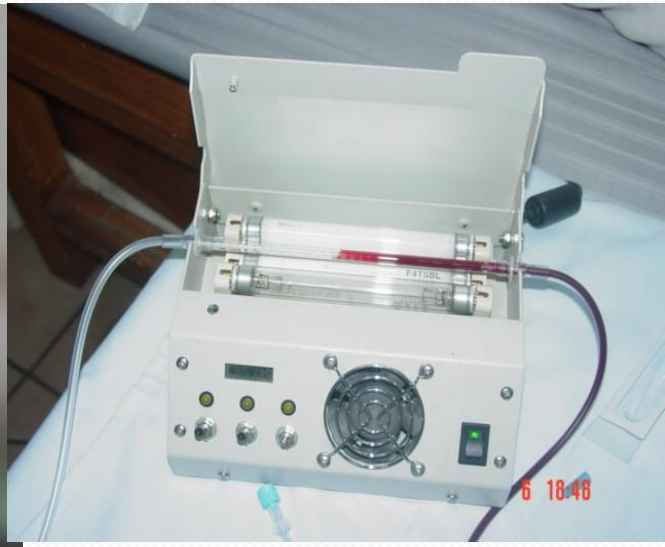


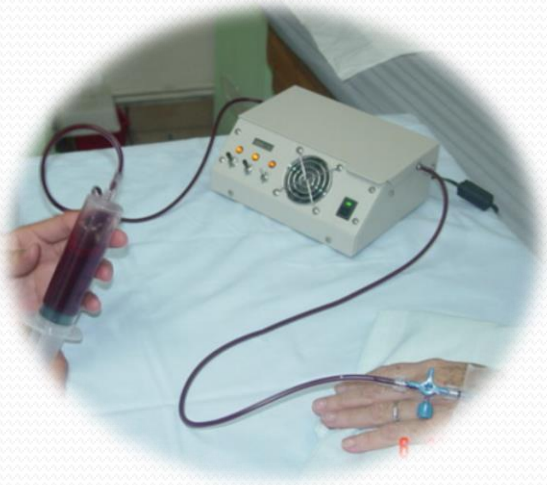




UV-LIGHT + OZONE







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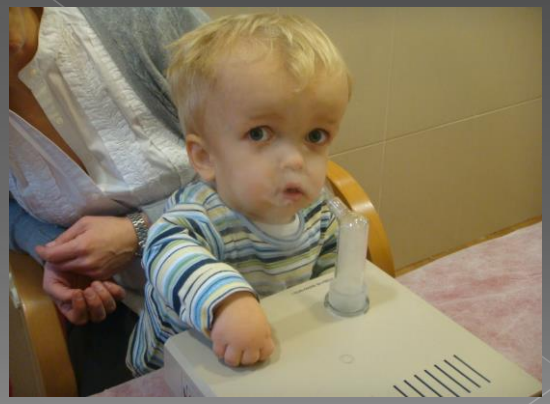
OZONE SAUNA

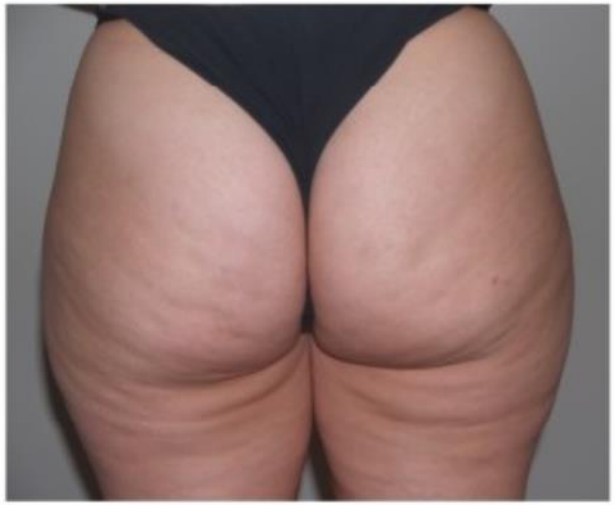
THERPEN INHALATION & FACIAL MESOTHERAPY

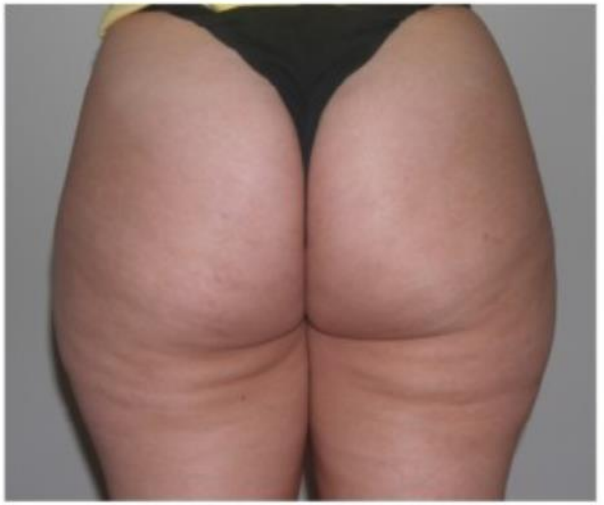


Ozone in celulitis

In celulitis: never use a volume larger than 200 mL per session, one subcutaneous injection every (5-10) cm in skin fold and in a volume of (2-3) mL per point. Concentration of 15 µg/NmL to 20 µg/NmL with a 27 G (0.3 mm) needle. Cycles of 15 - 20 sessions, twice a week.

The infiltration has to be done slowly to avoid pain and a possible embolia.





Facial Bioestimulation

- Mesotherapy:

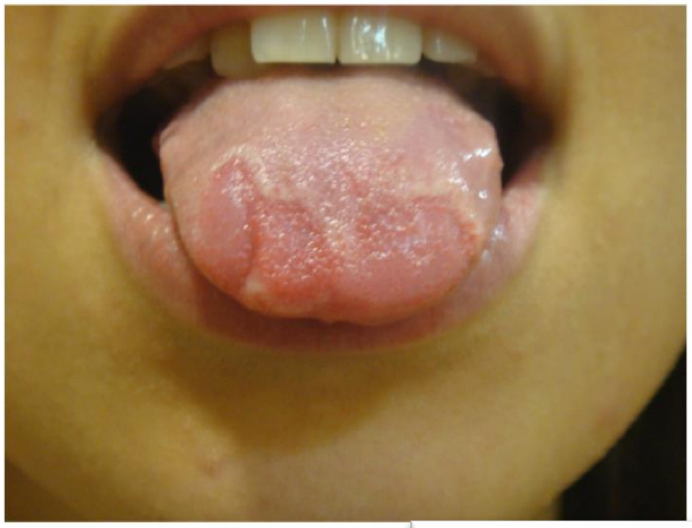
20 cc volume

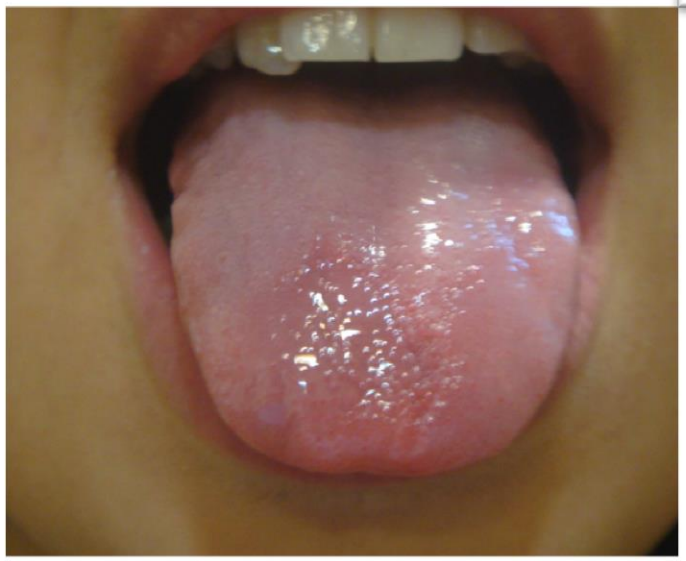
3-5 µ/ml of concentration.

Once a week 10 sessions.

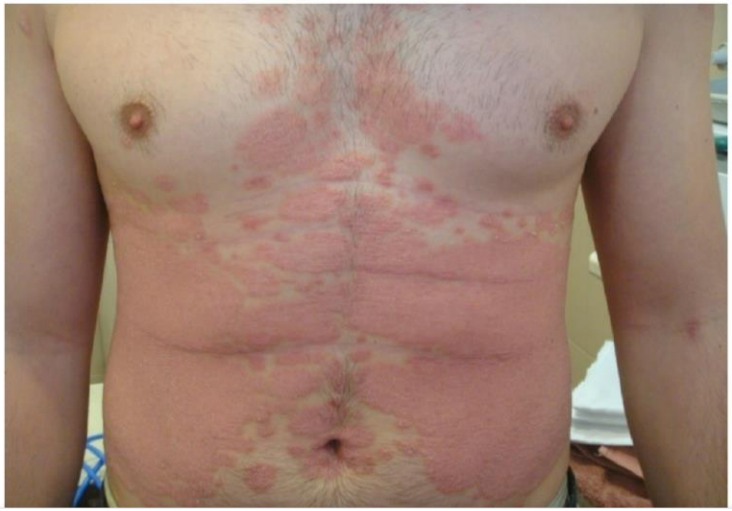
- Post infiltration apply ozonized oil 400 IP
- And make a massage with a vacuum O3 bells.

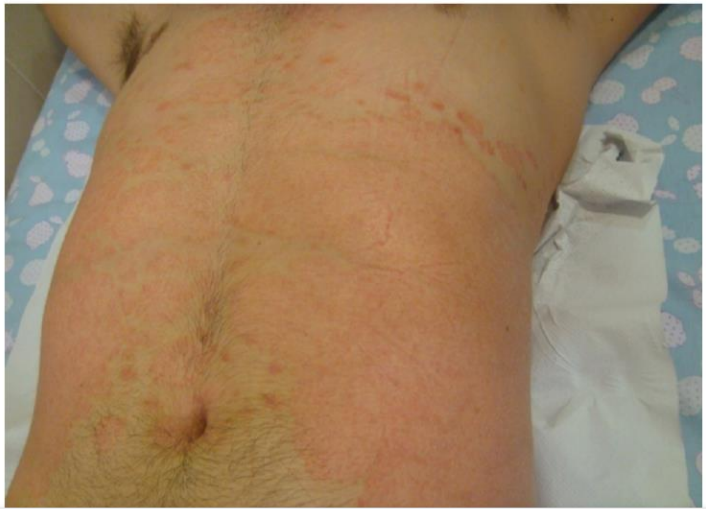
Muguet tongue (Oral Candidiasis)

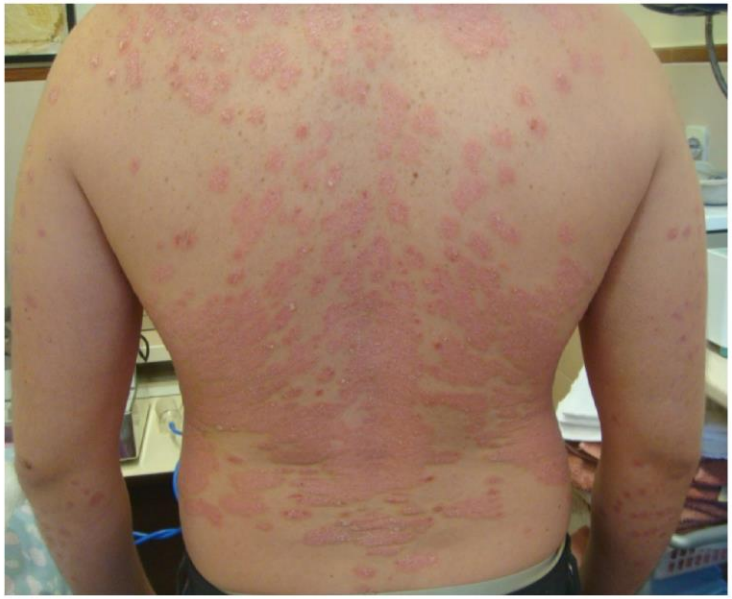


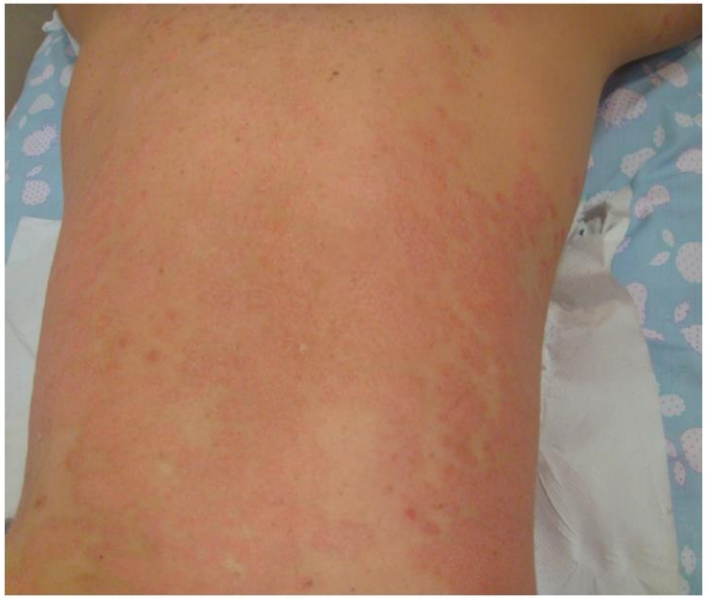


Psoriasis



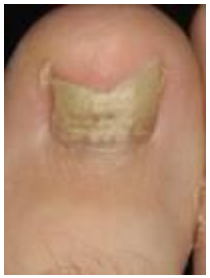


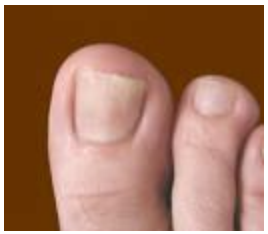


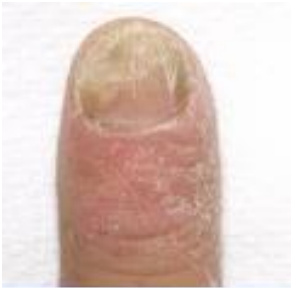


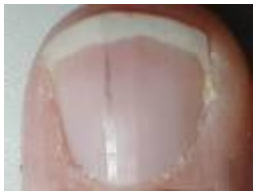
OleoSan®
Derived from Ozone

Efecto Germicida

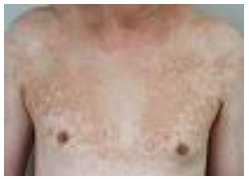




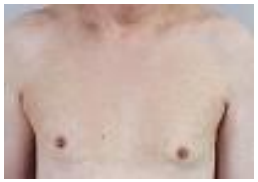




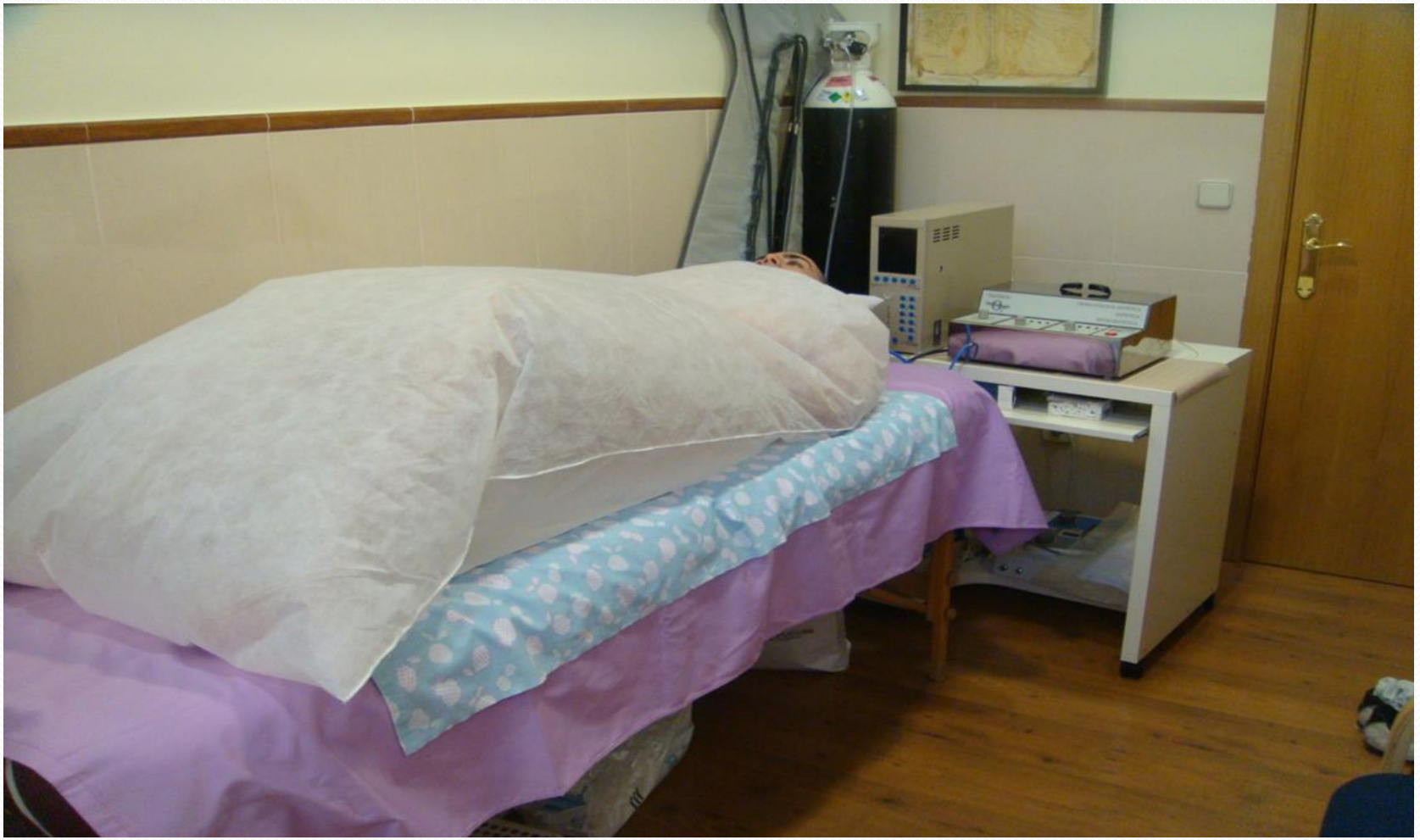
Before OleoSan

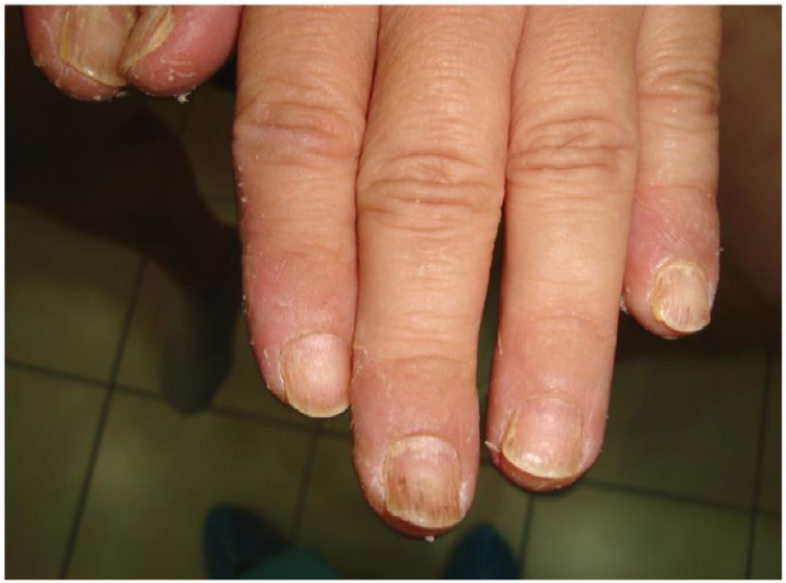


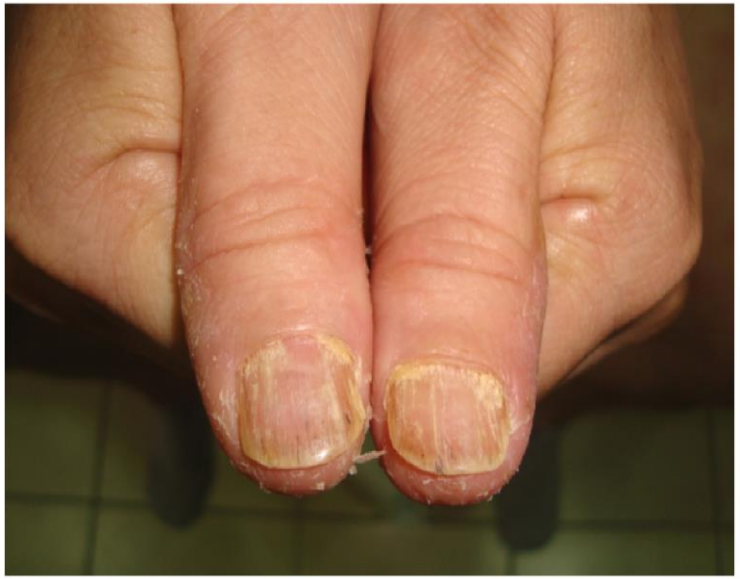
After OleoSan

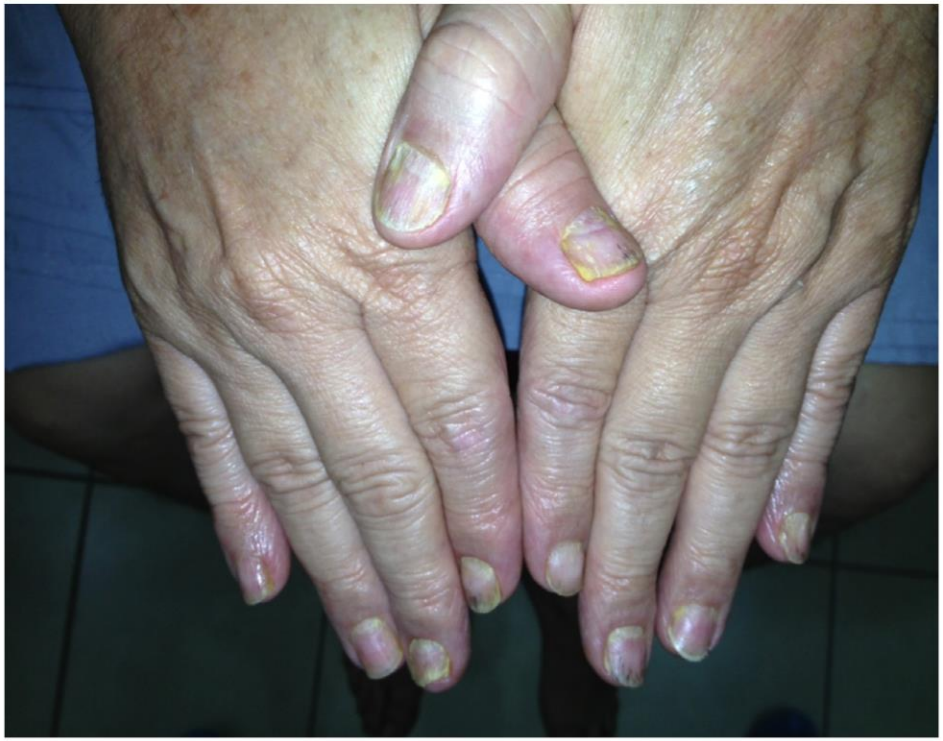


Body O3 Bagging in psoriasis

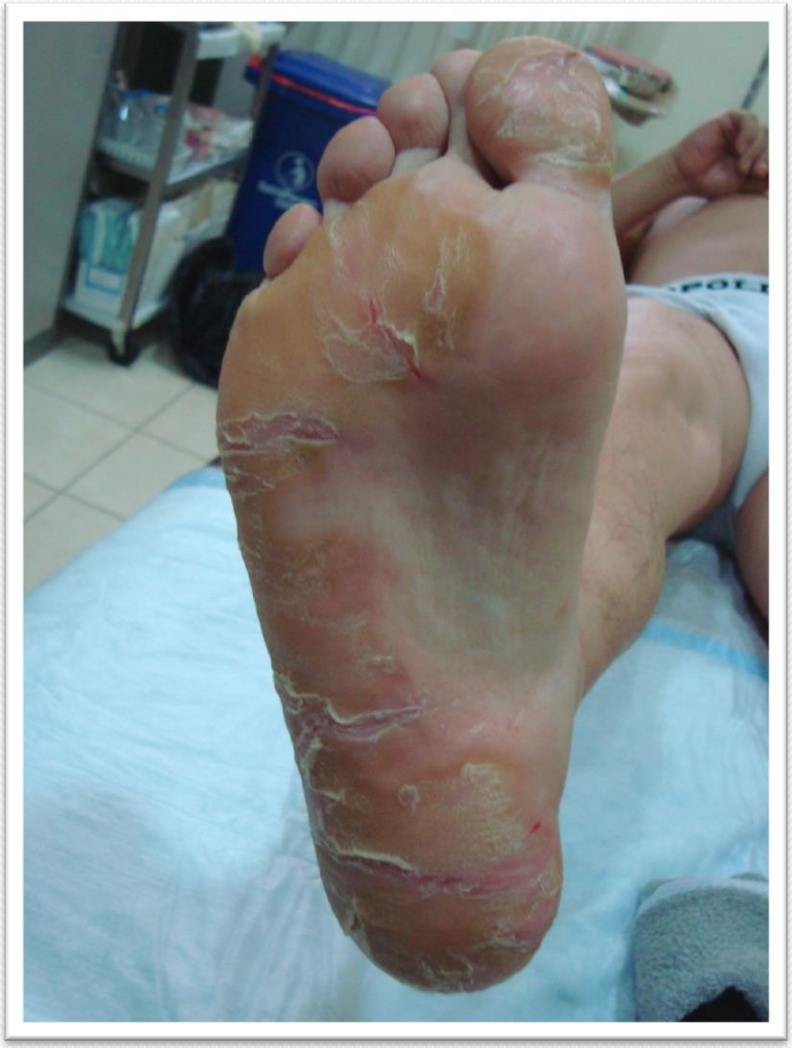


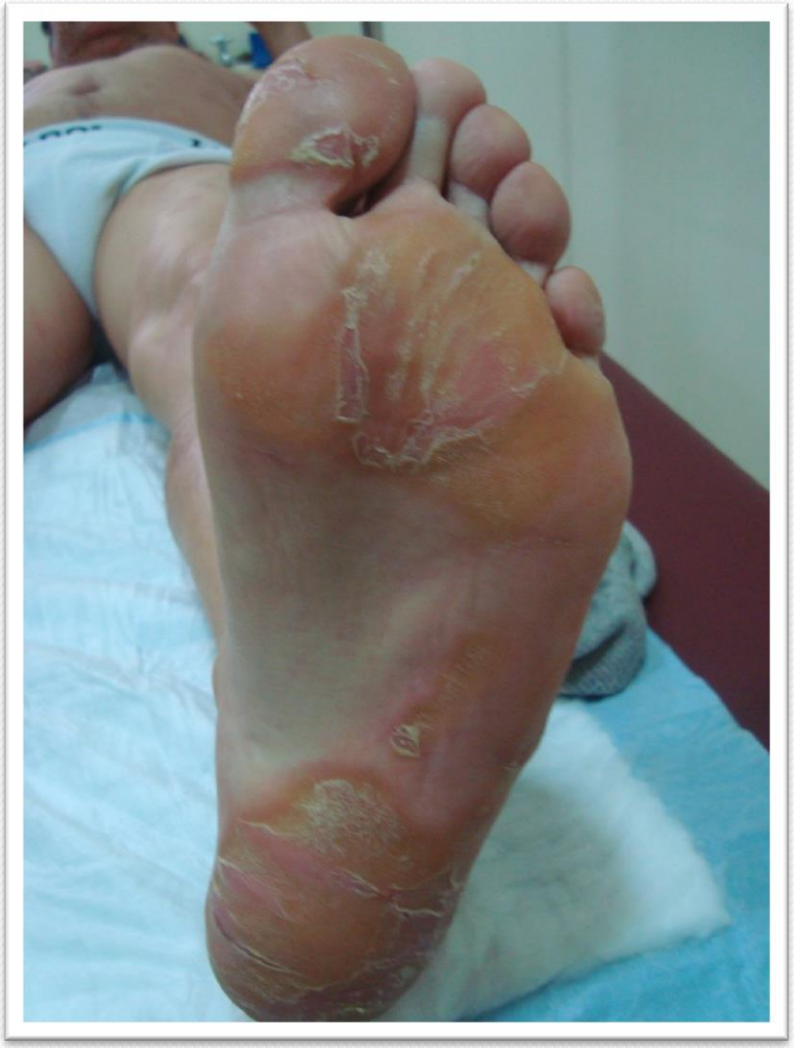




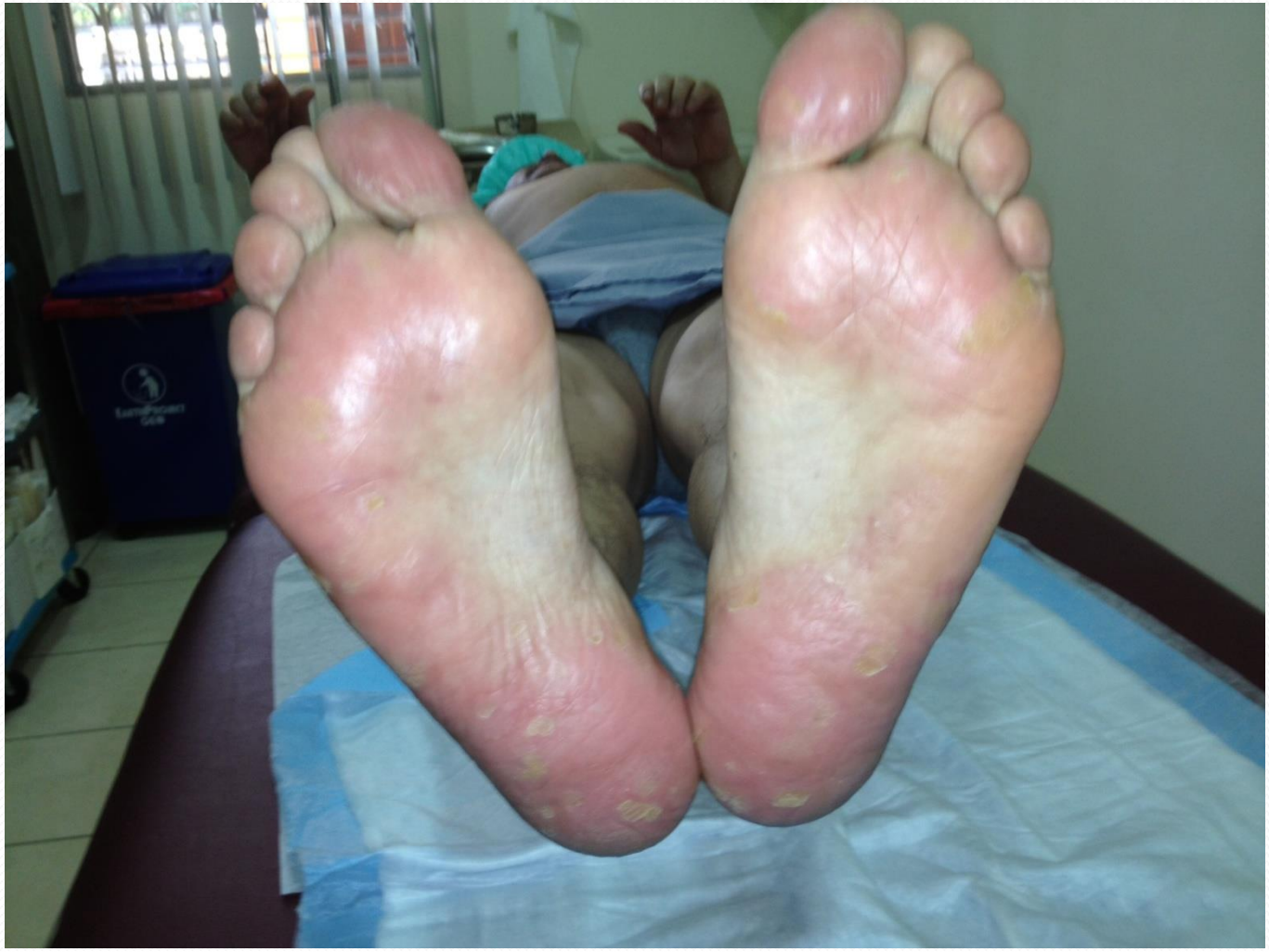


PSORIASIS

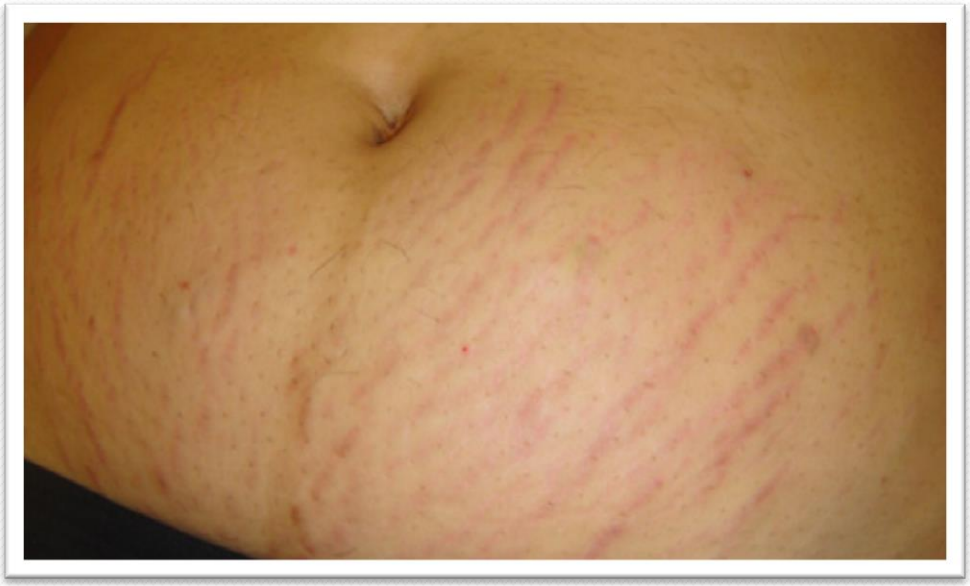


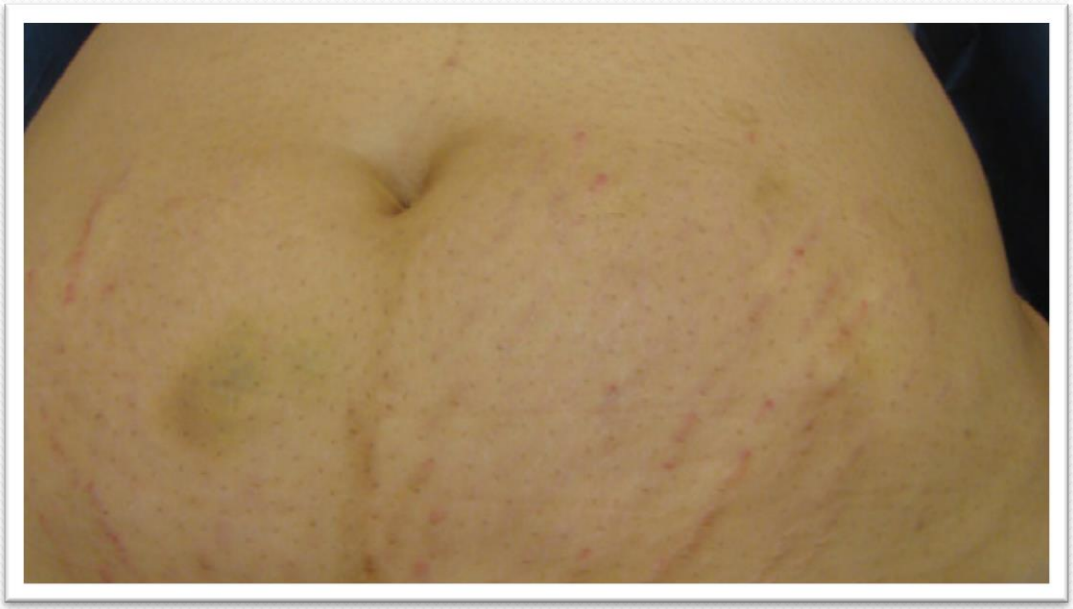


20 days after ozone treatment

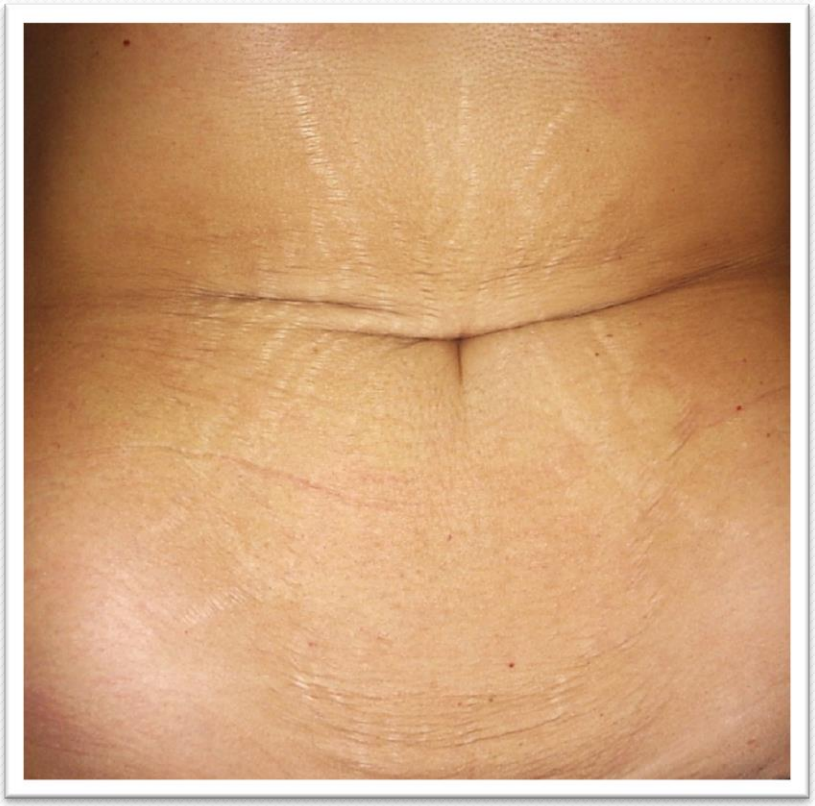


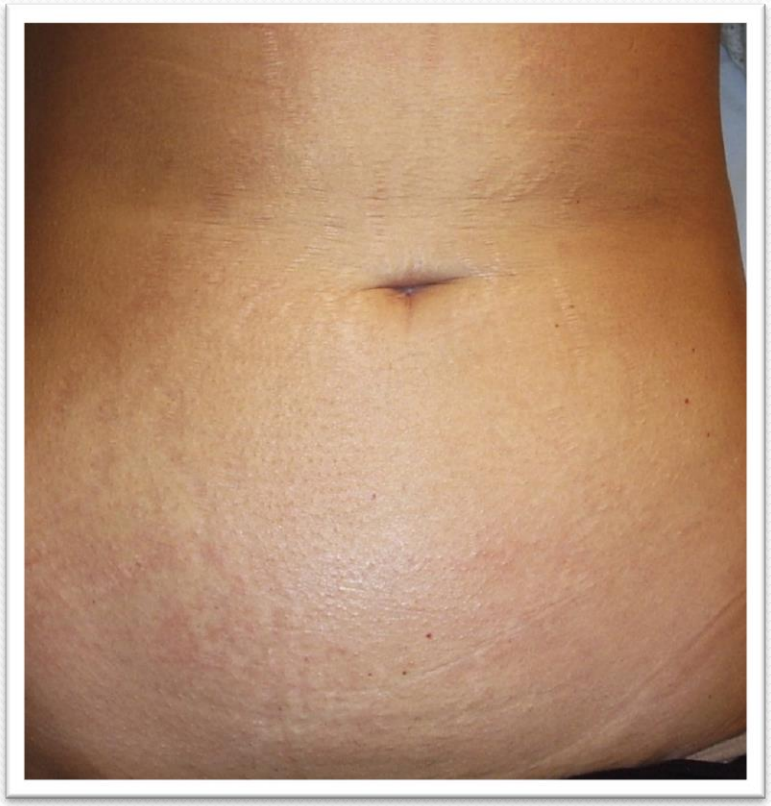
stretch marks





Stretch marks (two month after treatment





CONCLUSIONS

- Ozone in contact with blood (serum components and cell membranes) generates oxidizing agents that oxidize cysteine residues Keap1 molecule.
- Some of the oxidizing agents are H2O2, 4-hydroxynonenal and other aldehydes.
- Oxidation of cysteine residues in Keap1 ubiquitination prevents its degradation.
- Activation of Nrf2 pathway, by interacting with the recognition site EpRE, regulates expression of proteins on life.
- Low doses of controlled ozone, these can stimulate endogenous antioxidant mechanisms, preparing to face the host pathophysiological conditions mediated by reactive oxygen species.

THANK YOU VERY MUCH