

Ozone Therapy in Multiple Sclerosis

Vincenzo Simonetti, Torino, Italy



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INTRODUCTION

I have been using ozone-therapy for 25 years and since 2000 I have been a member of the board of Italian Society of oxygen-ozone-therapy and I send you greetings for SIOOT.

Today I will tell you about using ozone-therapy in MS, that I have been treating for 20 years.

Are there any neurologist among you? Did any of you treat any MS patients with ozone-therapy?

Why didn't you treat them ?Maybe you have heard that you do not get good results?

Many slides that you will see later have bibliography.

INTRODUCTION

Until 2000 in Italy a lot of Doctors considered ozone-therapy effect as placebo:I think also here it was the same. Today thanks to all who believed and believe in the ozone it isn't like this any more.

In the last years other Doctors in many countries confirmed results similar to my protocol. In 2010 my patients convinced me to found a non-profit association: on www.associazionekaos.org you can see its purposes and also some videos of patients that witness.

INTRODUCTION

I use Ozone with low concentration and I had really good results in vascular diseases, diabetes, arthrosis and cancer; but for autoimmune diseases I suggest using high concentrations 50-55 γ /ml of ozone, because you need the immune-modulator effect.

In 2007 Lettieri showed that in case of myocardial infarction the area of necrosis was inversely proportional to the quantity of treated blood.

I think that in Multiple Sclerosis positive results are directly proportional to quantity of treated blood and to the concentration of ozone

INTRODUCTION

The reinfusion has to be done only after blood changed color: initially it is dark red and after reaction with ozone the color is bright red, and after this you can re-infuse slowly, if not you can have some problems like vascular and different results on patients.

The speed of reinfusion affects the vascular and neurovegetative systems during ozone major autohemotherapy, DOI: [10.4081/ozone.2016.6477](https://doi.org/10.4081/ozone.2016.6477)

Inflammation/Ipoxya and Dideases

All cronical deases, except those autosomal dominant, are consequence of cronical inflammation and/or ipoxya.

Every doctor should decrease inflammation and increase oxygenation.

Ozone decreases inflammation, increases tissue oxygenation and production of cellular energy, without side effects and without leaving traces in the environment.

Ozone can be applied with or without drugs support;

It can riduce toxicity of drugs and modulate their quantity

Ozone is essential for lifeA healthy lifestyle reduces inflammation, disease and drug consumption

Lifestyle and nutrition: determinants to keep us healthy

A healthy lifestyle reduces inflammation, disease and drug consumption

OZONE:EPIGENETIC FACTOR

> efficacy when in synergy with other epigenetic factors:

antiinflammatory nutrition

Vit. D

reducing stress

moderate aerobic physical activity

<Environmental pollution

ABUSE COFFEE or TEA

> Homocysteine

COFFEE: Caffeine and Chlorogenic acid

Black Tea: Theine and Chlorogenic acid

Chlorogenic acid :reduces SAMe available

SAMe: S-Adenosyl Methionine; methyl donor,

precursor to glutathione, necessary to nucleic acid,

polyamines, cell membranes, detoxifies the liver

1) Can black tea influence plasma total Homocysteine concentration?

J. Hodgson 2003 Amer.Soc.Clinical Nutrition

2) Consumption of high doses of Chlorogenic Acid, present in the coffee or of Black Tea increases total Homocysteine

M. Olthoff 2001 Amer.Soc.Clin.Nutrition 2001

3) Relationship between plasma total Homocysteine level, dietary caffeine and Vit B6 in pregnant women. NURS Health SCI 2014:Jun;16(16)164-70

MULTIPLE SCLEROSIS IN ITALY

- 110.000 cases
- 55 for 100.000 citizens
- 3.400 new cases a year
- One year actual cost for our National Health Service:

€ 5.000.000.000,00

On average € 45.000 for each patient

OZONETHERAPY COST

Maximum estimated cost

First year < € 3.000,00/patient

Subsequent < € 800,00/patient

Used drugs have high prices, and what is more there have important side effects.

COMPLEMENTARY MEDICINE AND MULTIPLE SCLEROSIS

- 67,3% of patients use it
- 90% is associated with traditional treatment
- 10% only complementary therapy
- Efficacy:
 - Positive for 67% of patients
 - Non influential for 32% of patients
 - Damaging for about 1% of patients

“In consideration of frequently use of these methods, it could be convenient to shed lighth on reason which prompt patients to try complementary therapies and to study their clinical potency.”

CAUSES OF MS

- ✓ 184 Genetic polymorphisms until today
- ✓ Infective Hypothesis: Epstein Barr Virus
- ✓ Self-immune
- ✓ Stress worsens MS evolution: Weygandt: PNAS 21/11/2016
- ✓ CCSVI (Chronic Cerebro-Spinal Venous Insufficiency Zamboni 2006):
Confirmed by NAIMS:NATURE 18/11/2016
- ✓ Disequilibrium microbiota active inflammatory processes
- ✓ Vitamin D prevents T cell migration in the brain
- ✓ Vit D < μ 50 gr/ml > frequency and evolution MS

**OZONE THERAPY AND
MULTIPLE SCLEROSIS:
WHY?**

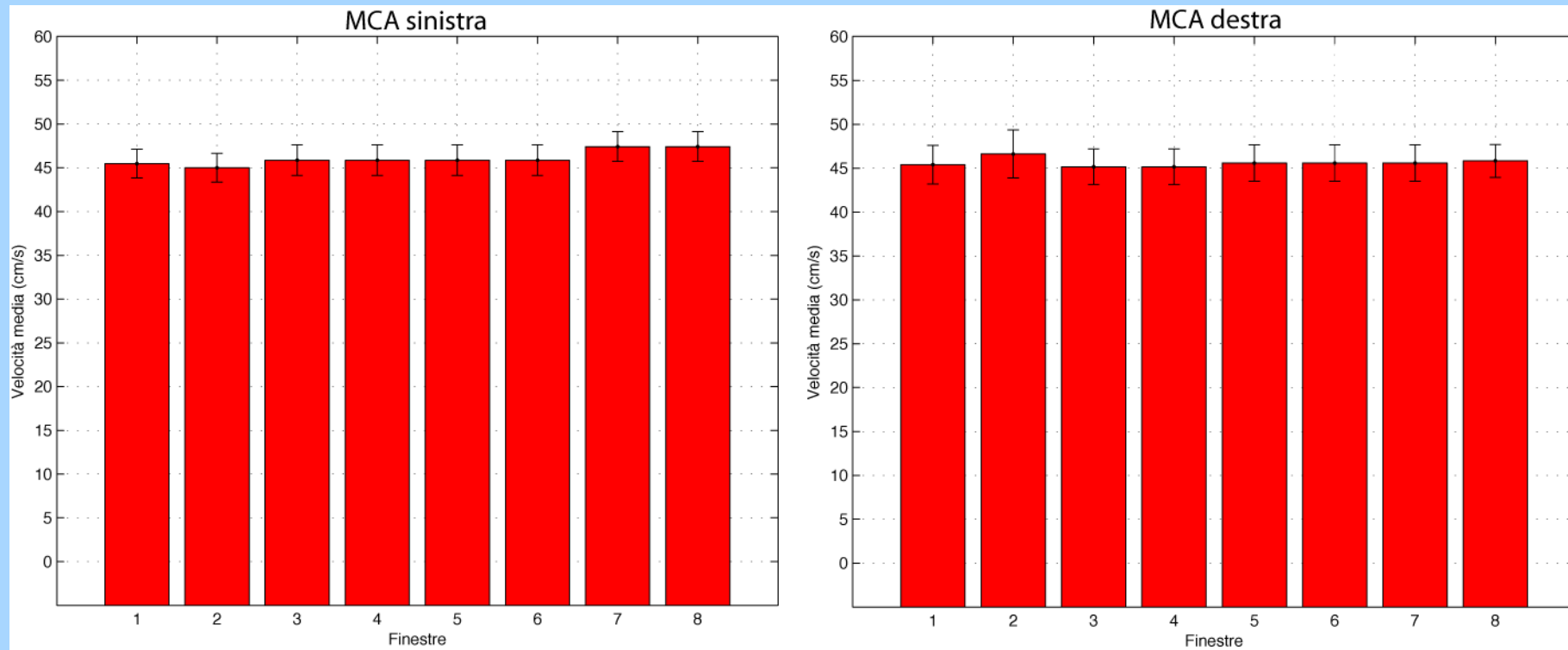
NIRS Test: After 1 hour from starting reinfusion O₂Hb increases in the frontal lobes, despite the constancy of carotid flow: a clear sign of an increase of microvascular perfusion and increased reactivity of hemoglobin

**F.Molinari,V.Simonetti,M.Franzini,F.Vaiano,L.Valdenassi,S.Pandolfi,W.Liboni
J Immunopat. Pharmacol. 2014 27:379-89**



TCD SIGNALS DURING THERAPY

F.Molinari,V.Simonetti,M.Franzini,F.Vaiano,L.Valdenassi,S.Pandolfi,W.Liboni
J Immunopat. Pharmacol. 2014 27:379-89

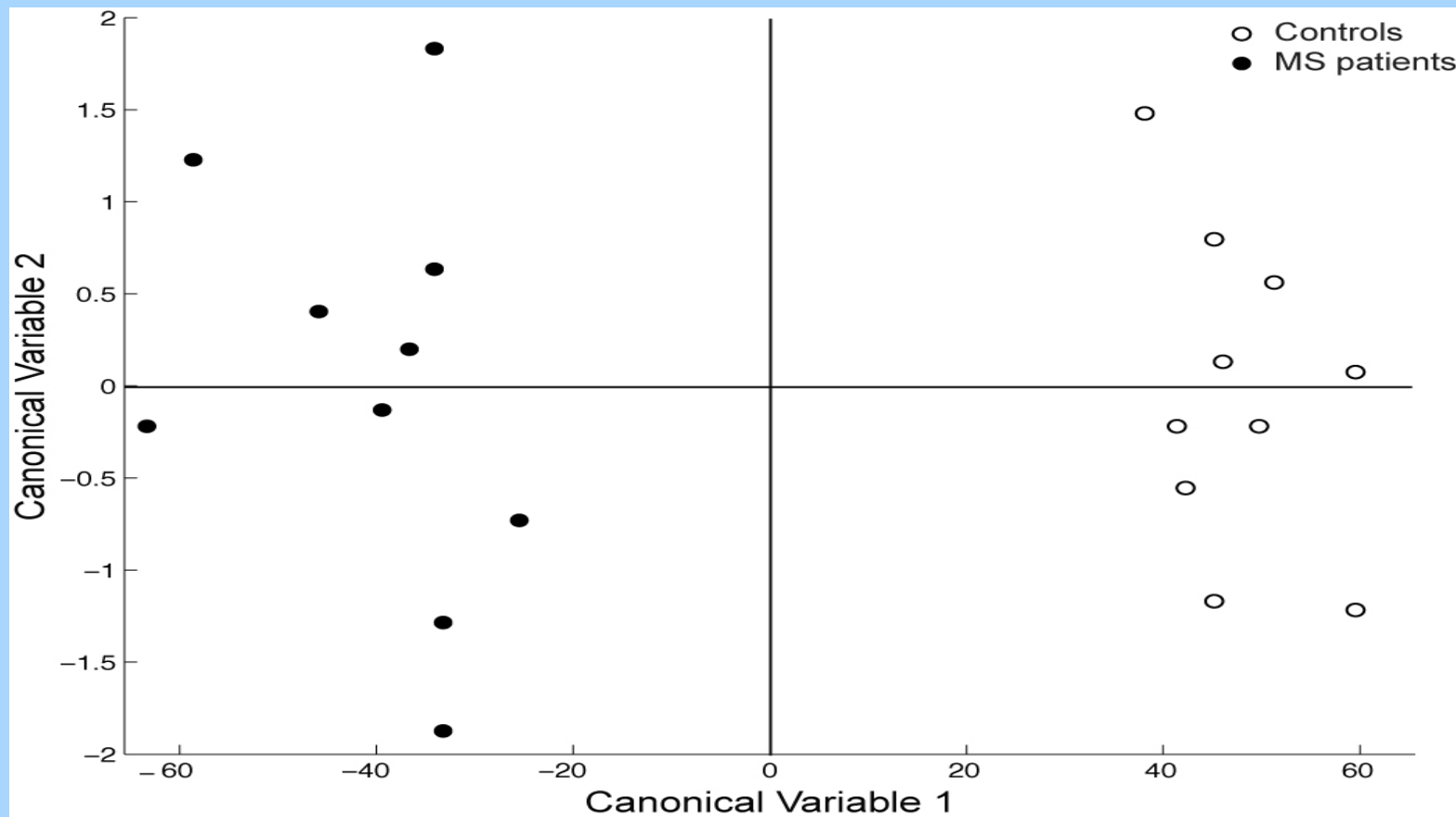


Small variation of blood flow at level of the middle cerebral artery

SPECIFIC STUDY OF MS

Complete analysis in time frequency of NIRS signals among 10 MS RR and 10 healthy patients. Variation quantifier in time and frequency of cytochrome-c-oxidase concentration.

F.Molinari,W.Liboni,M.Franzini,V.Simonetti: 12,oct,2016:Cerebrovascular pattern improved by ozone autohemotherapy : Oct.2016; Medical Biological Engineering & Computing



CHANGES OF CYT-C- OXIDASE

Bibliography

- ✓ Less concentration of CYT-c among MS patients, caused by damages of mytocondrions
- ✓ MS patients have chronic oxidative stress
- ✓ Ozonotherapy has anti-oxidant effect with antioxidant enzymes activity increasing
- ✓ Ozonotherapy may reduce oxidative stress in MS

OUR experiment results

- ✓ Low CYT-c in MS is confirmed
- ✓ CYT-c increases after 20' to 40' of reinfusion
- ✓ Higher level of CYT-c is a diagnostic value between MS patients and those without this disease

MS > CEREBRAL ATROPHY

All patients who are treated with ozonotherapy improve their cognitive capacity.

MS patients lose cerebral volume from 3 to 5 times more than healthy patients: does ozonotherapy reduce cerebral atrophy?

Until the last century, no one believed in brain stem cells

In 2005 Bocci speculated presence of neural stem cells in nigra substance

In 2013 G. Ponti et L.Bonfanti found stem cells in hippocampus and in ventricular-subventricular zone of adult mice. PNAS Published online february 21, 2013

In 2014 Stef.Farioli Vecchioni: Running rescues defective adult neurogenesis by shortening the length of cell cycle of neural stem and progenitor cells in adult mice. Wiley online library Febr 15, 2014

Are they also in human brain ?

Prolonged stress

- > TNF α > insulin resistance
- > Cortisol < Linfociti < Defenses

Motor-cognitive stress: > brain atrophy MS

Martin Weygandt PNAS 2016

Insulin facilitates inflammation

Insulin: among the main triggers inflammation.

it changes membrane potential

it increases K intracellular

it decreases Na intracellular

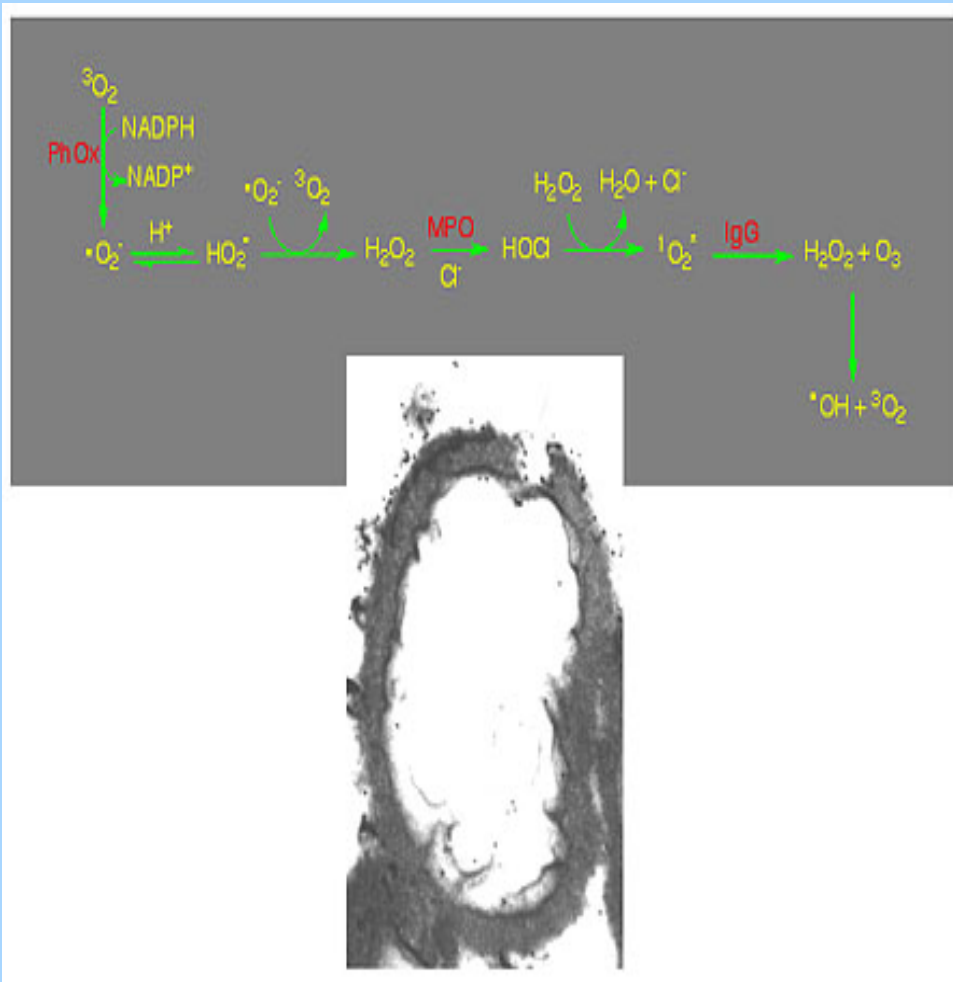
Facilitates cardiac arrhythmia

Ozone reduces insulin resistance and glycemia

restores membrane potentials

reduces arrhythmia

MORE CHEMICAL EVIDENCE FOR AN ANTIBODY KILLING MECHANISM in ALL BEINGS



Way of ABOx in human neutrophils: antibodies create, while oxidation way of water, (H_2O_2 and O_3) both with bactericide effect, for action of phagocyte oxidase (Phox), myeloperoxidase (MPO) and IgG.

Picture with E.M. of bacterium E. Coli killed by antibody with way of the water oxidation: it's an important morphology of breaking of cell wall and membrane after

OZONE

- Immunosuppressive action

Plopper CG et al. *Toxicol Appl Pharmacol* 1994; 127(1):124-31

- Inhibits system of NF-kB and production of TNF- α on oral mucosae

Huth KC et al. *J Dent Res* 2007; 86(5):451-6

- Reduces production of TNF- α , IL-1 β , IL-6 in synovia fibroblast of patients with rheumatoid arthritis

Chang JD et al. *Rheumatol Int* 2005; 26(2):142-51

OZONE

- Reduces production of proinflammatory cytokines: IL-2, IL-4, IFN- γ , TNF- α
- Activates Th2 and suppresses Th1

Larini A, Bocci V. *Toxicol In Vitro*. 2005;19(1):55-61

Terasaki N et al. *J Vet Med Sci* 2001; 63(12):1327-30

- Reduces the relationship between CD4+/CD8+ (p<0,05) and CD3+ HLADR, constant in MS, if you do Oz. > 40 γ /ml

Simonetti V et al. *Manusia F Tip Aurelia* 2001

OZONE: INHIBITS THE RELEASE OF TNF- α

TABLE 1. Effects of ozone oxidative preconditioning on serum TNF- α levels in mice treated with LPS.

Treatment (mg/kg)	TNF- α (pg/mL)	
	Mean \pm SEM	Inhibition (%)
Saline	0	0
Ozone /oxygen (1.2), IP	0	0
LPS (0.1 mg/kg)	2200 \pm 780	—
Ozone /oxygen IP (0.2) + LPS	485 \pm 120*	78
Ozone /oxygen IP (0.4) + LPS	33 \pm 17**	98.5
Ozone /oxygen IP (1.2) + LPS	30.6 \pm 5**	99
Dexamethasone (30 mg/kg) + LPS	29 \pm 10**	98.7

* $P < .05$.

** $P < .01$ versus respective control (LPS) by Student t test ($n = 5$). The animals were pretreated with five IP applications of ozone (one daily) at 0.2, 0.4, and 1.2 mg/kg twenty four hours after the last ozone administration LPS was given (0.1 mg/kg) and 1 hour later blood samples were taken to measure TNF- α levels in serum. Dexamethasone (30 mg/kg IP, 30 minutes before LPS) was used as a control drug.

OZONE

- Reduces Immunoglobulins and intermediaries of the inflammation in asthmatic patients with increase of efficacy of antioxidant system

Hernandez Rosales FA et al. *Arch Med Res* 2005; 36(5):549-54

- Reduces circular immune complex

Maslennikov OV. *Klin Med*, 1997; Bocci V, 2000

OZONE

1) Activates antioxidant enzymes:

- Catalase
- Superoxide-dismutase
- Glutathione

Bocci V et al. *J Biol Regul Homeost Agents* 1998; 12:67-75

2) Reduces the proteins of acute phase and increases endogenous antioxidant answer

Jakuboswsk K et al. *Pol J Vet Sci* 2004; 7(4):283-7

3) Reduces C- reactive protein

Tylicki L, *Mediators Inflamm*, 2005

OZONE

- Reduces: total Cholesterol, LDL and Triglycerides (Hernandez, 1995)
- Homocysteine (Simonetti V, 2006)
- Increases: HDL (Bisetti, 1988)

MS: POST-TRANSLATION MODIFICATION

- Glycation(reaction between sugars and fats or proteins): it activates protein CD59 with cell lysis, caused by MAC (Complex of Cell Membrane Attac)

Acosta J et al. *Proc Natl Acad Sci USA* 2000; 97:5450-5

- MAC induces the release of inflammatory agents and the demyelination in MS. Its inhibition is protective.

Barnum SR et al. *Immunol Res* 2002; 26:7-13

MAC

- Is expressed in kidneys and nerves of diabetics, but not in laudable person.

Qin X et al. *Diabetes* 2004; 53:2653-61

- Causes lysis of endothelial cells and the release of growth factors, pro-inflammatory cytokines and pro-thrombosis liable for inflammation and thrombosis: complicating disease of diabetes.

Acosta J et al. *Proc Natl Acad Sci USA* 2000; 97:5450-5

OZONE

- Reduces glycemic levels and it facilitates recovery of diabetic ulcer

Martinez-Sanchez G et al. *Eur J Pharmacol* 2005; 523(1-3):151-61

- Anti-thrombosis effect with a decrease of platelet aggregation

Maslennikov OV. *Klin Med*, 1997

- Then: ozone decreases the MAC, among the main activators of inflammation

MS: INFECTIVE HYPOTHESIS

- Herpes virus 6 A type was found in MS relapsing-remitting

Alvarez-Lafuente R et al. *Mult Scler* 2007; 13:578-583

- High levels of antibodies anti-Epstein Barr virus was found(anti-EBNA-1 and 2) in MS

Cannoni S. *XVI Congresso AINI* 2006

- Causal relationship between the presence of Epstein Barr virus and inflammatory answer in cerebral lesion, typical for MS

Aloisi F et al. *J Exp Med* 2007

OZONE

- Antibacterial action:
 - phagocytosis increasing
 - ROS: lysis of bacterial wall
- Virustatic action
 - Peroxidase of proteines of the capsid and of the viral anti-receptor
 - Lipoperoxidase of envelope
- Improves local perfusion \diamond increases transport and distribution of substances and drugs

Madej P et al. *Inflammation*, 2007

Sunnen GV. *Ozone in medicine*, 1994

Kekez MM et al. *Phys Med Biol* 1997; 42:2027-39

Bassi P et al. *Riv Neurobiol* 1982; 28(3-4): 328-333

OZONE: HERPES SIMPLEX-1

Morphological alteration of capsid icosaedric nucleus

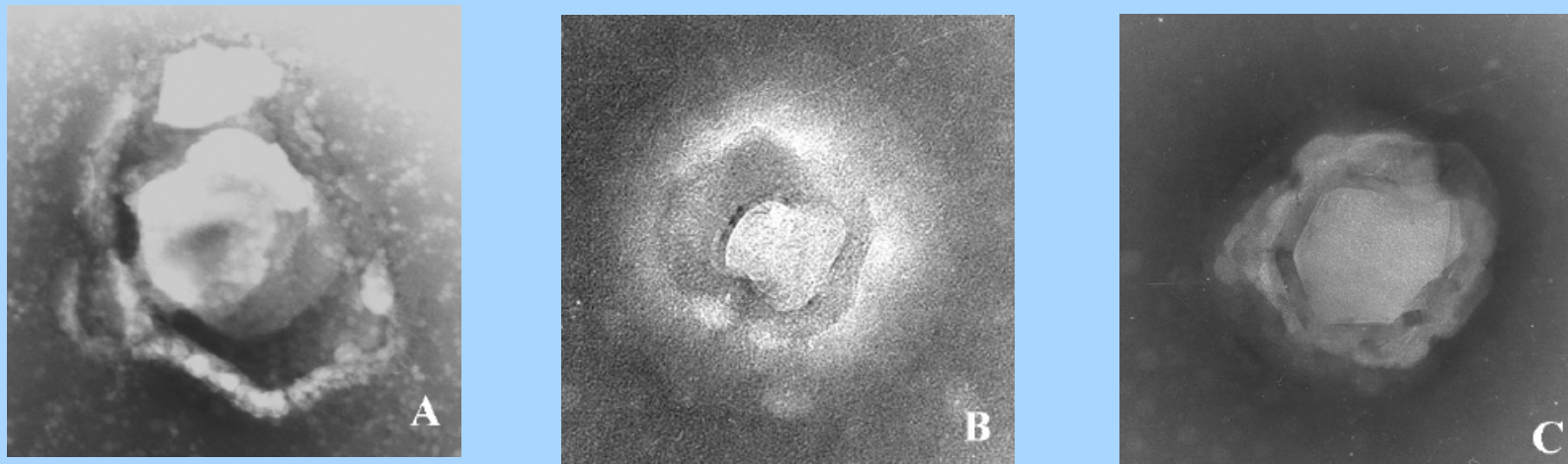
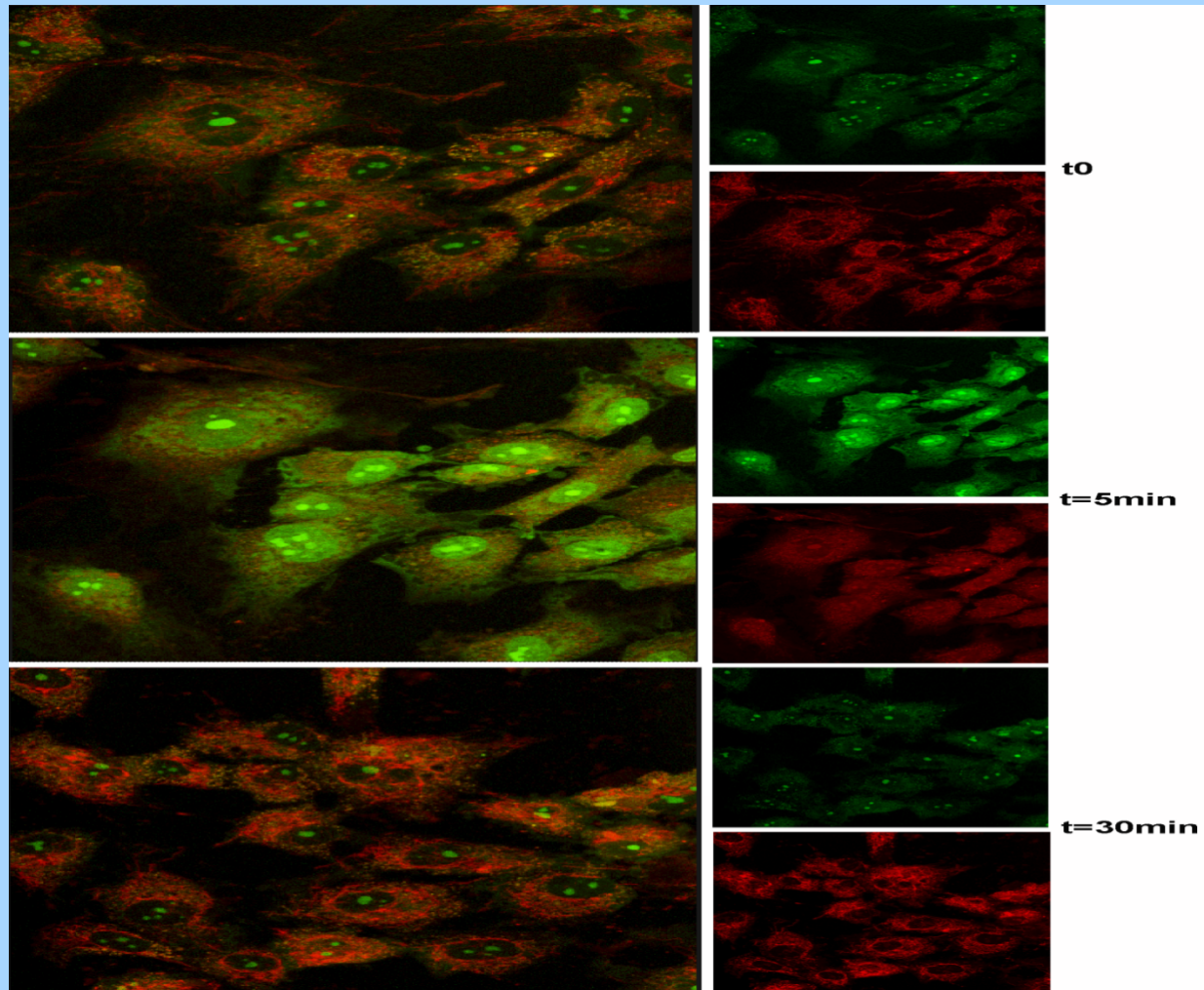


FIGURE 12. Transmission electron micrograph analysis of herpes simplex virus type-1 in 100% DPBS, treated with 1200 ppmv ozone for 15 min. HSV-1 was treated with 1200 ppmv ozone, oxygen flow rate of 2000 ml/min and fluid pump rate of 252 ml/min. Samples were negatively stained with PTA and micrographs were taken at 52,000X, 120 kV and enlarged with Adobe Photoshop. The disrupted morphology of the icosaedral nucleocapsid is seen in (A, B, and C).

OZONE:ACTIVES MITOCHONDRIONS AND INCREASES ATP



Ferrero M.E. *III International Symposium of Ozone-therapy*, Bergamo 2007

OZONE: MUSCULAR STEM CELLS

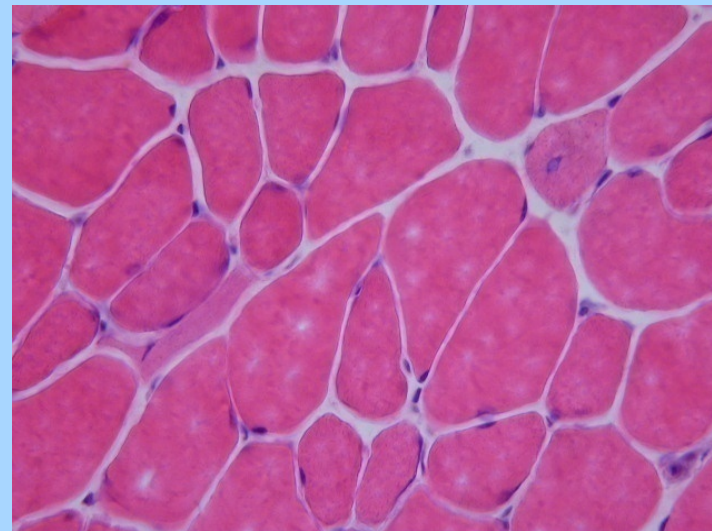
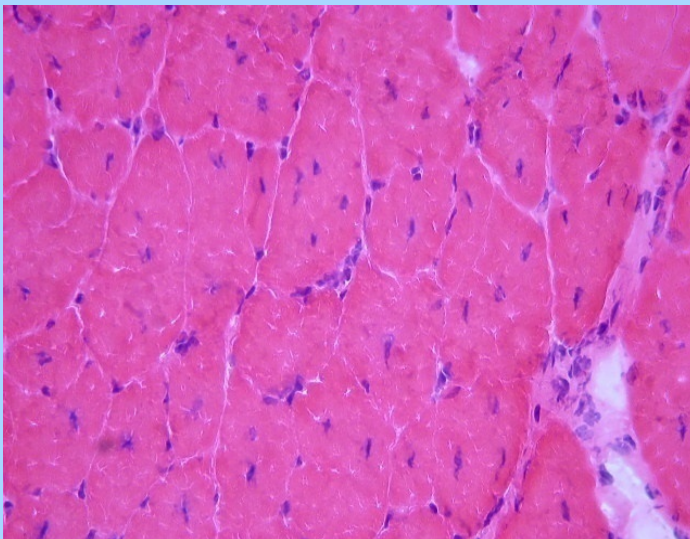
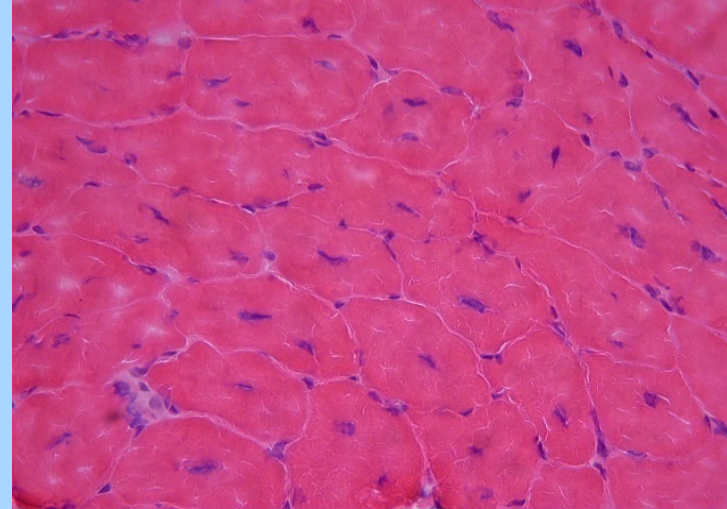
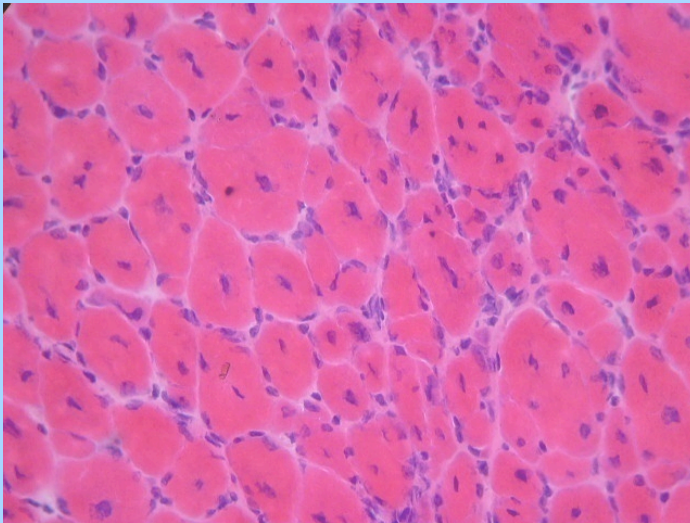
- Increases the contribution of trophic factors
- Mitogen effect and more recruitment on satellite stem cells
- Increases number of nucleous and dimension of regenerate fibers

O3 ACTIVATES STEM CELLS

Cobra venom destroyed quadriceps muscle femoris of rats

After 40 days rats which weren't treated with Ozone had only scar tissue; rats treated with Ozone before cobra venom had myocytes bigger than average

PICTURES OF REGENERATION: (during 4 weeks)



OZONE EFFECTS

- Myorelaxant
- Anti-edema action

Clavo B et al. *J Altern Complement Med* 2003; 9:251-6

SOMMARRY OF OZONE EFFECTS

Anti-inflammatory

Anti-Oxidant

Immunity regulating

Antibiotic and Virustatic

Improves capillary perfusion

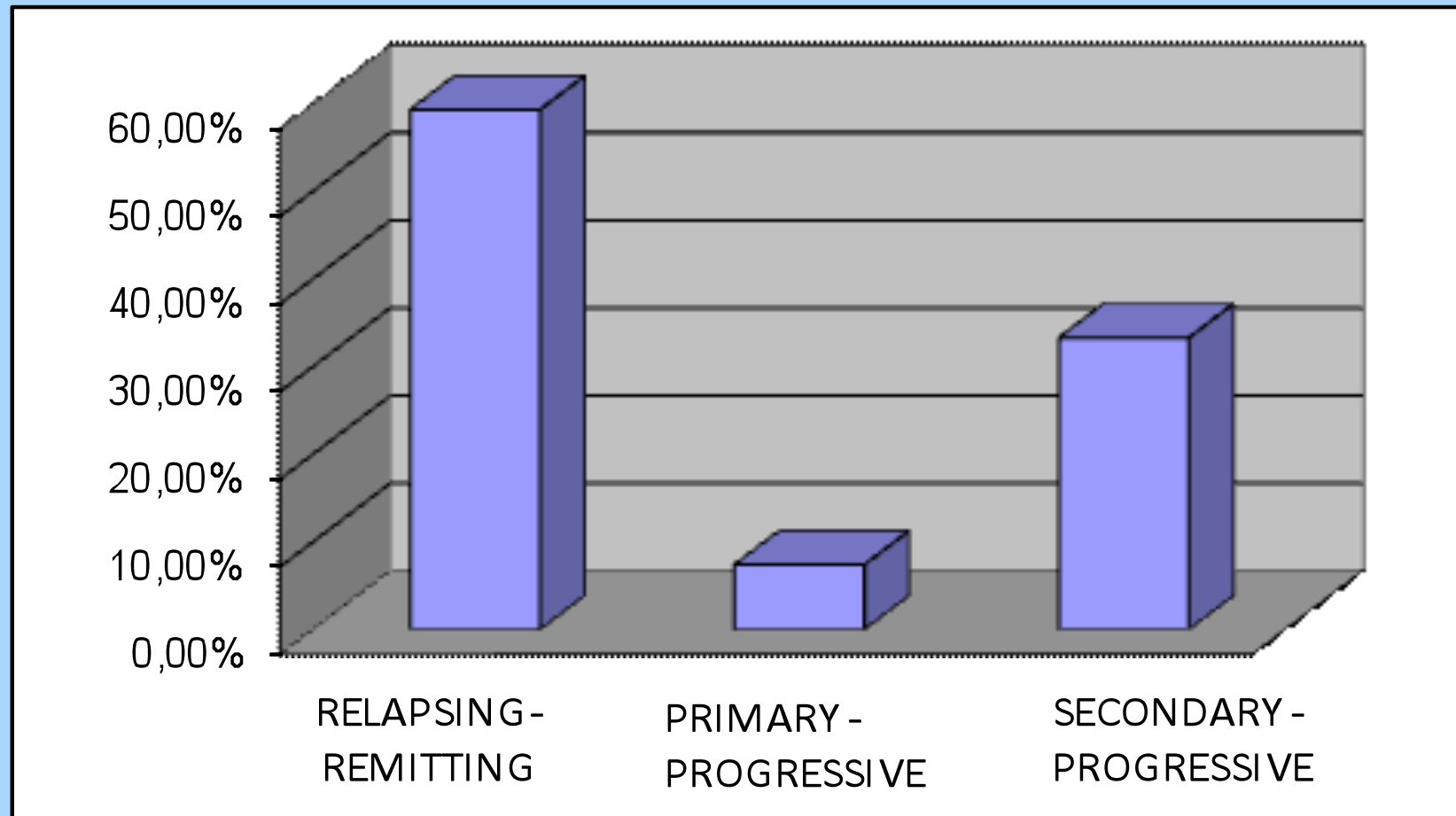
Safe therapy

Significant reduction of costs

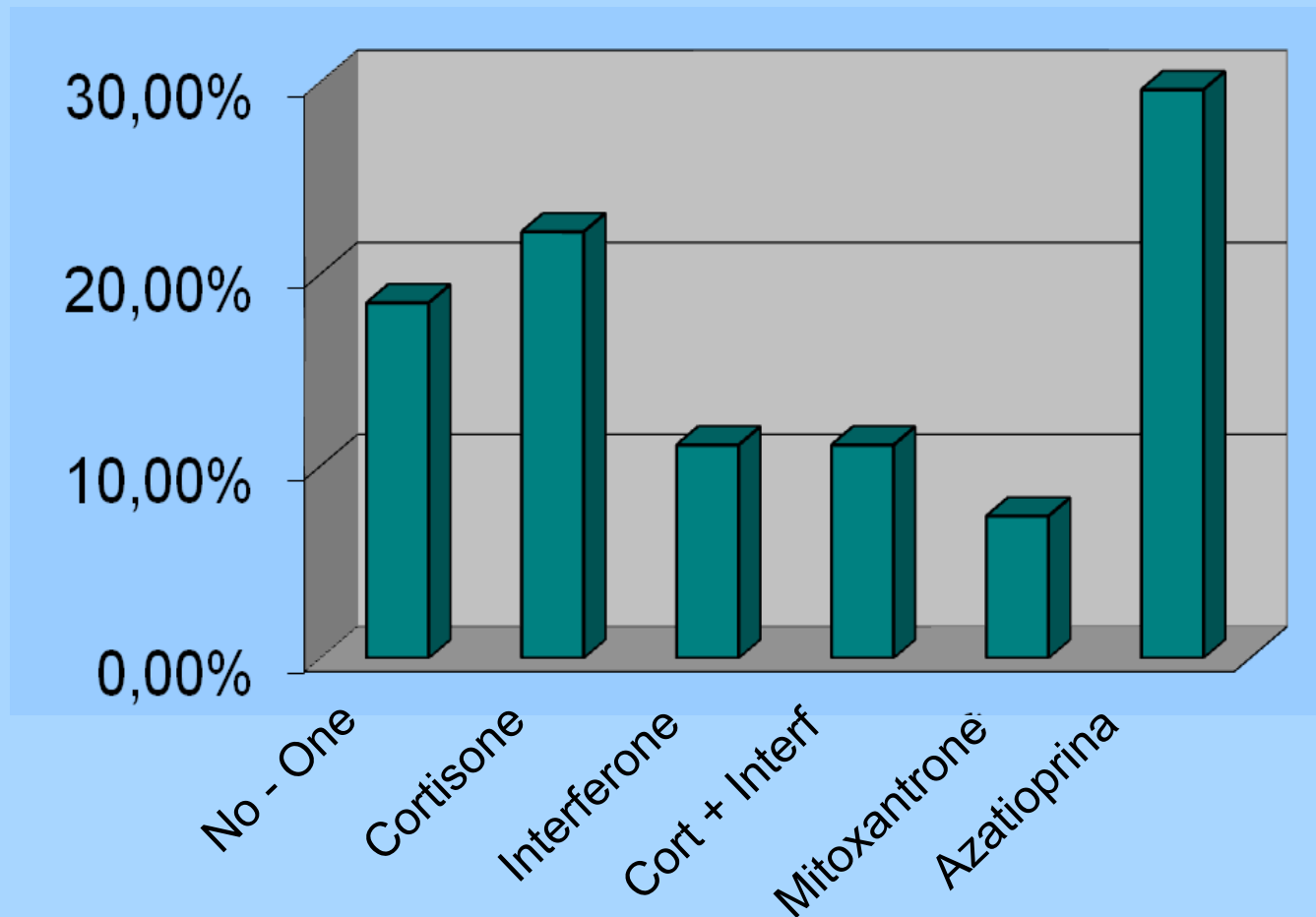
MS:CLINICAL RECORDS

- MS Patients: 49
- Average age: $44,67 \pm 13,339$
- M:F = 1:1,45
- Diagnosis and monitoring in care of regional reference for MS
- Years of observation: $6,5 \pm 2,9$
- Treatment: Major AHT, Ozone 45-55 γ / ml

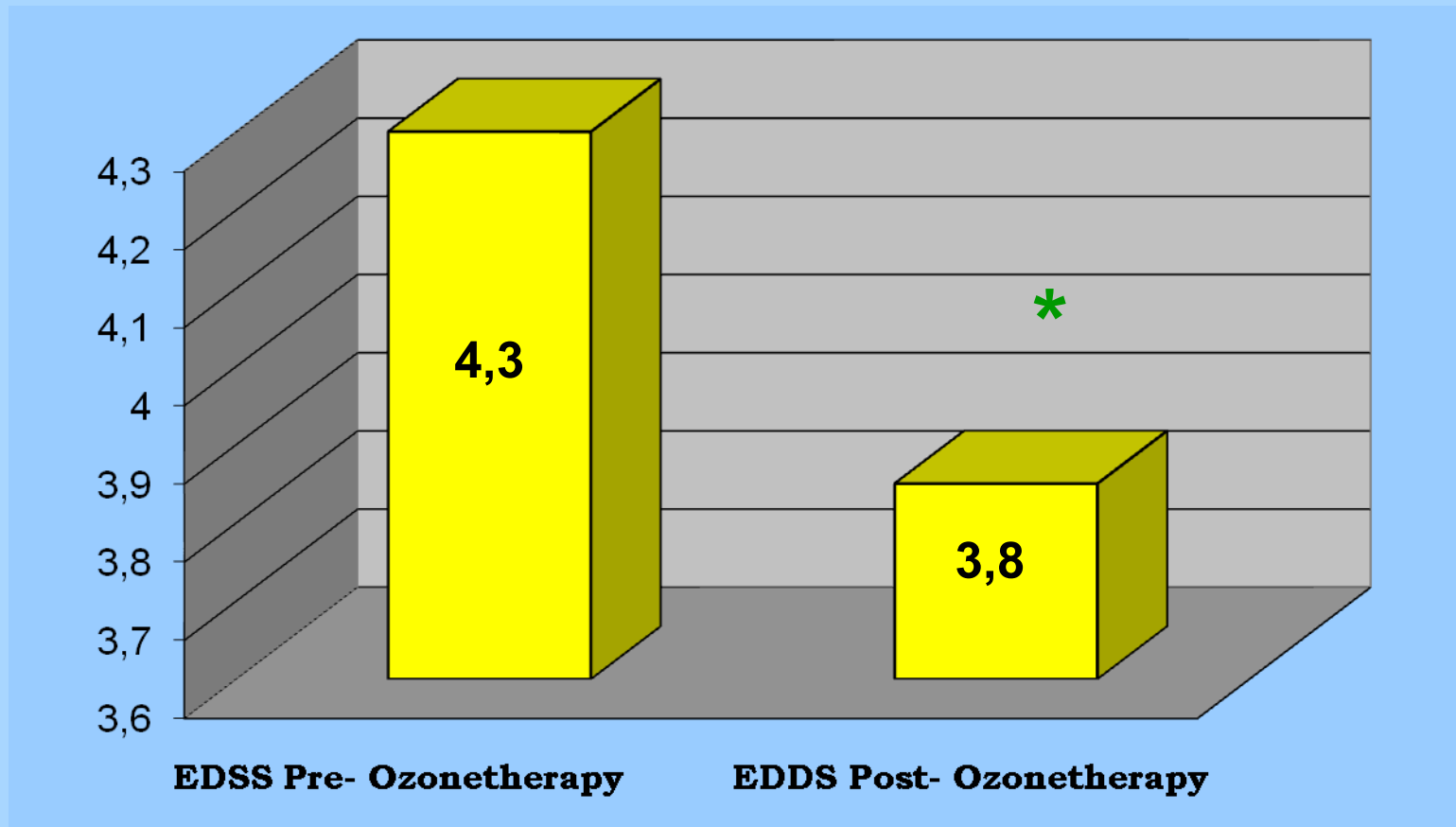
MS: TYPES



MS: CONTEMPORARY THERAPIES

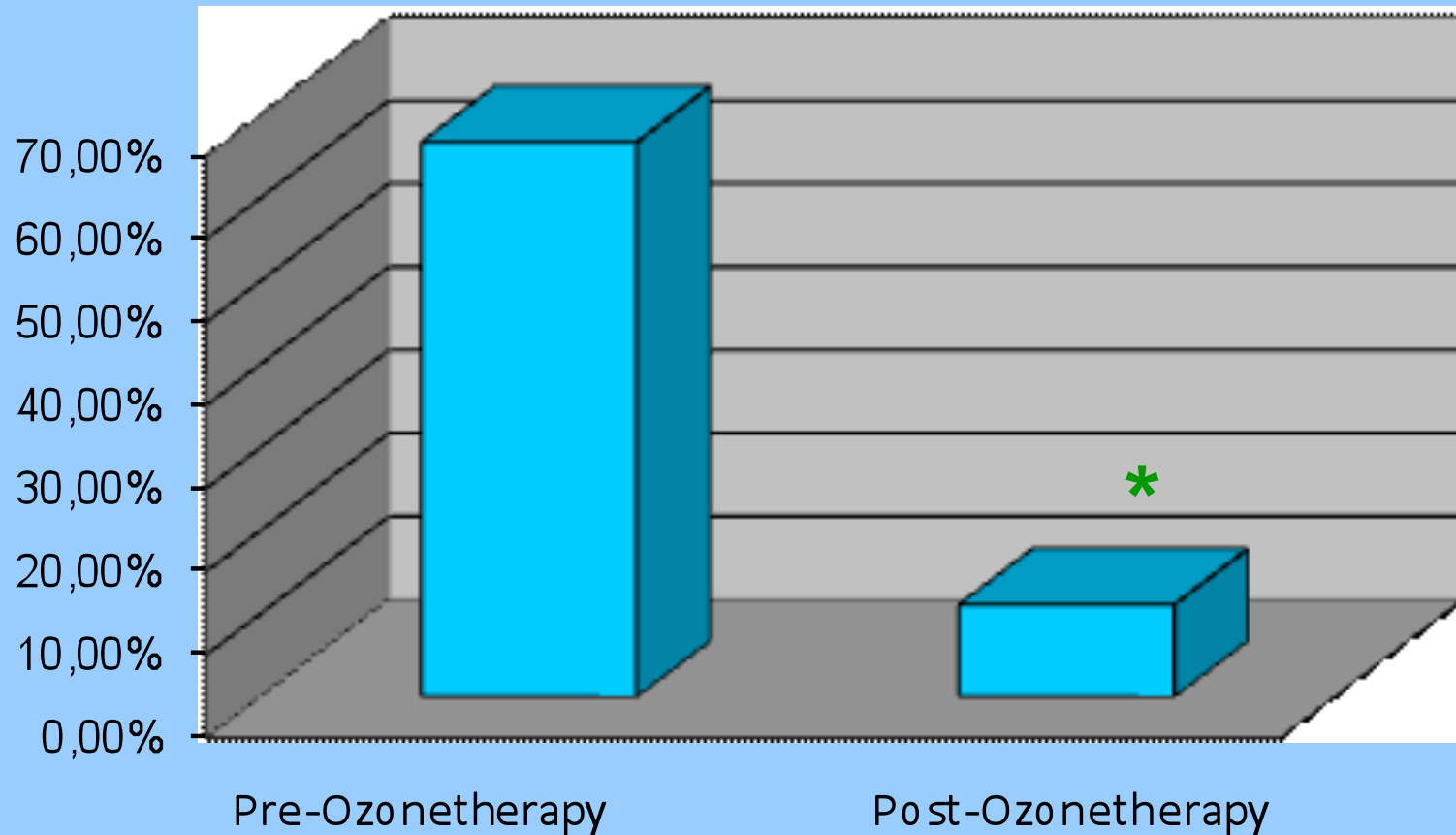


EDSS CHANGE



* $P < 0,05$

FREQUENCY OF RECIDIVATION/YEAR

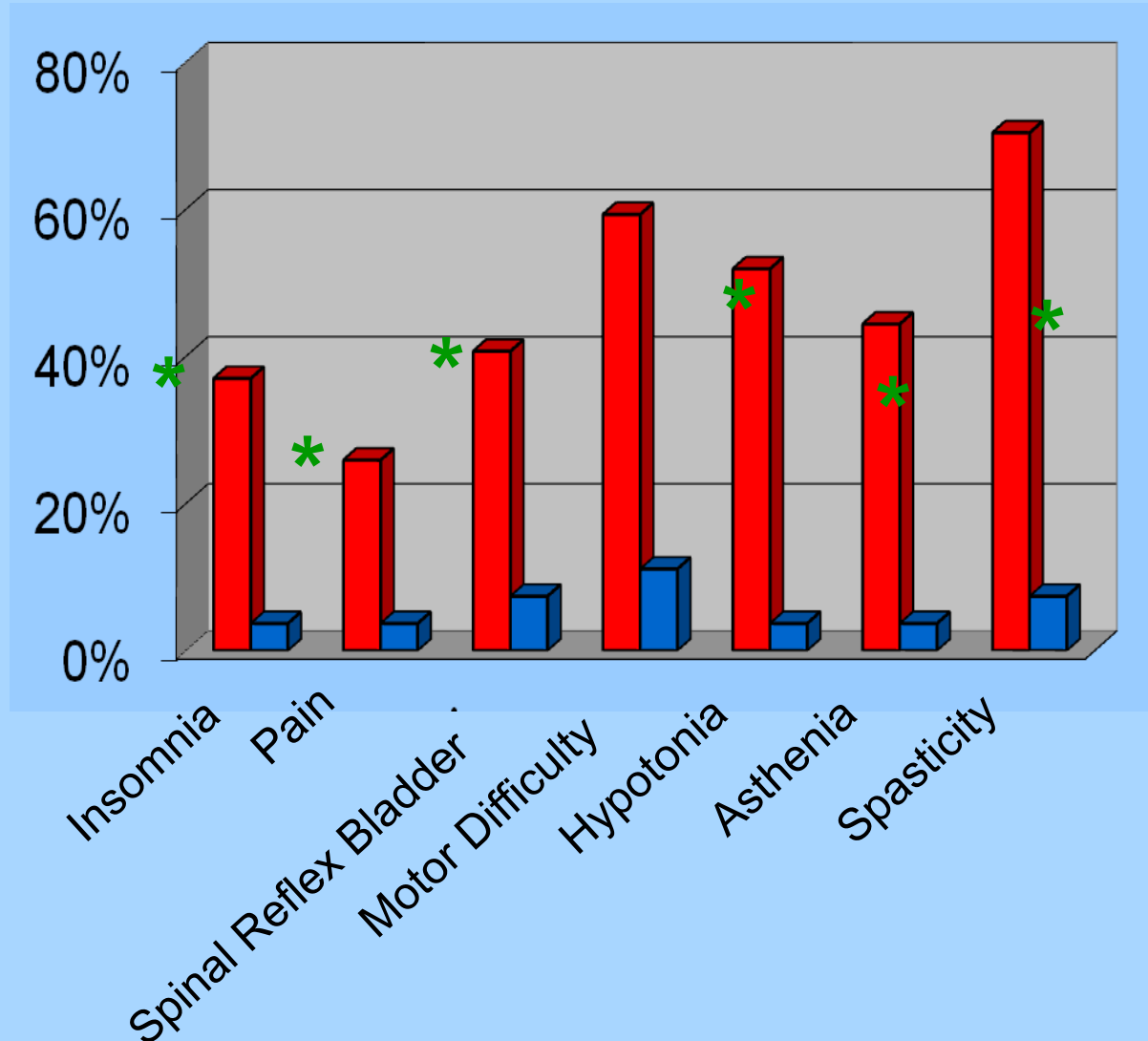


* P < 0,05

POUSSEE TREATMENT

Usually if patient is treated within 72 hours from the beginning of recidivation, all symptoms disappear immediately after one therapy.

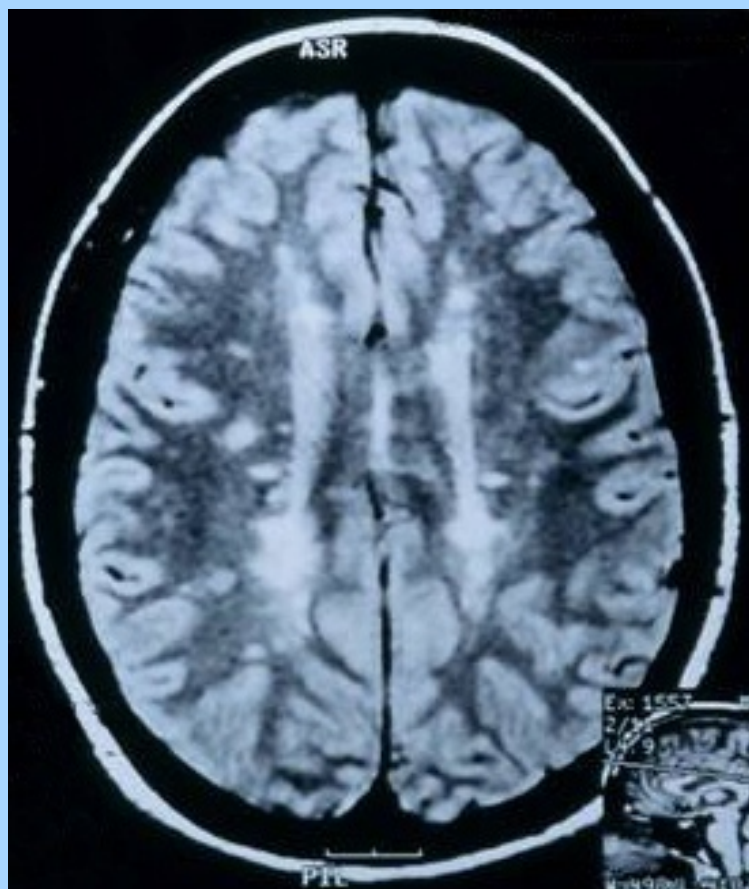
SYMPTOMATOLOGY



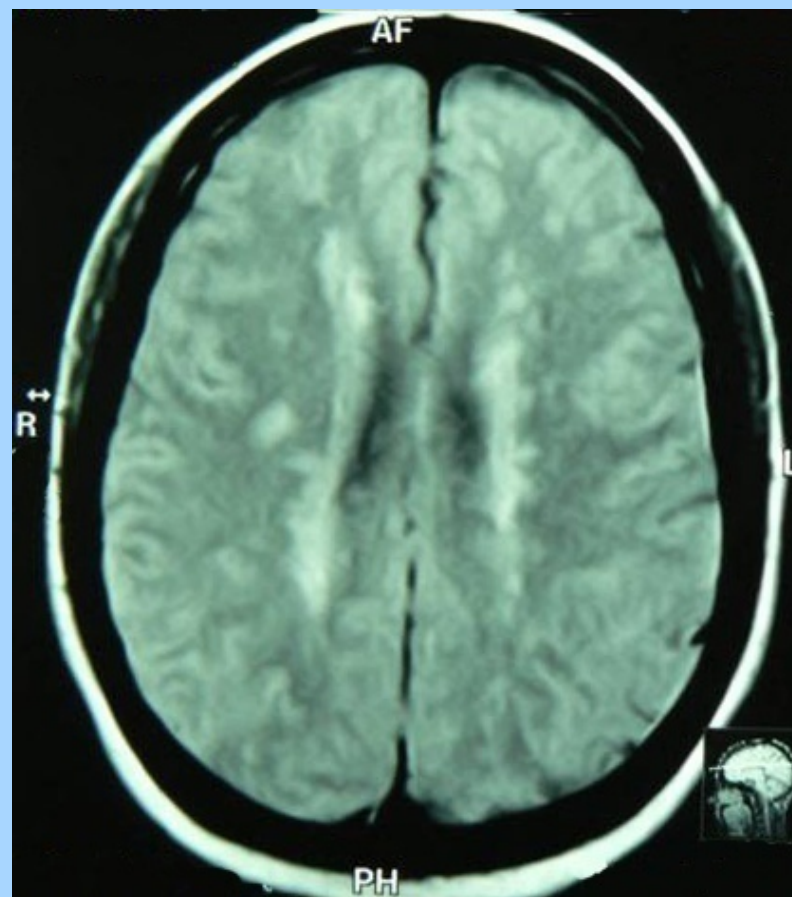
Pre Ozone therapy
Post Ozone therapy

*P < 0005

1997



2006



1997

Hyperintense lesion in
right paraventricular
cerebellar area



2003

Slight hyperintensity
with reduced signal



FOLLOW-UP

- ❖ No patient got worse
- ❖ All urgent urination patients got better or recovered if, apart from Major AHT, were treated with lumbar subcutaneous injections
- ❖ By combining anti-inflammatory diet, stress reduction and ozone therapy you can notice a partial regression of disability even in the secondary progressive form.
- ❖ All have improved cognition

Thank you for your attention

Dr. Vincenzo

Simonetti

simonetti.vinc@gmail.com