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**Ozone therapy and inflammation: an *in vivo* study to evaluate the possible involvement of the GSH, TXN based system and NF- $\kappa$ B-dependent genes. Preliminary Results.**

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# The Pharmacology of Ozone Therapy

New Concepts and Definitions

Ozone as a Hormetic Stress

# RECENT LITERATURES

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In the last years we observed a striking increase in the scientific production related to the ozone uses.

Of the **18,661** Pub Med citations of the word ozone, we can find nowadays **2,836** references regarding ozone therapy in indexed peer reviewed journals.

Among these **140** dealing in dentistry and **49** in veterinary.

This fact demonstrates that, despite its initial anecdotal use, the ozone therapy is now firmly supported by the scientific evidence of its clinical usefulness.



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One of the most important point regarding the opposition to the Ozone Therapy is the a lack of an adequate pharmacological definition as Therapeutic Agent.

To our opinion it is time that a new terminology is finally introduced.

As most of our colleagues know, ozone therapy can't be considered a simple interaction between the molecule (drug) and the receptor (membrane protein) — according to classical schemes of pharmacology currently spread in the medical faculties — but rather as a

***"Hormetic Stress".***

As it is known, ozone is a molecule with strong oxidizing properties, and then it could be able to evoke from the cell and from the entire organism, a powerful anti-oxidant response.

Our scientific belief that a molecule such as ozone, namely a strong oxidant, could induce benefits in many diseases if used at low doses, is now supported even at the highest scientific levels.

**Hormesis** is the term to define some favorable biological responses to low exposures of toxins and other stressors

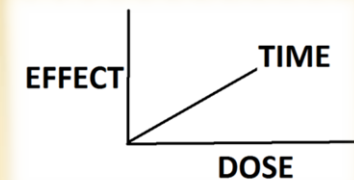
Physiological or biological **stress** is an organism's response to a stressor such as an environmental condition

For all these reasons new definitions will better describe the biological action activated by multiple chemical reactions, helping scientists to better evaluate the clinical efficacy of the ozone effects.

Indeed, on the contrary to what happens for a simple receptor interaction, reactions induced by stress require the introduction of a third parameter vector in addition to the DOSE and the EFFECT:



That is the TIME!



In fact, differently from what happens for a conventional drug that acts on a specific target with an immediate action, stressing agents promote several biological effects through a myriad of interactions that involve many cellular processes and metabolic pathways which in turn produce a stable clinical effect only after a certain time.

## Clinical Variability and Time Relationship of Ozone Effect

	Start	Session 1-5	Session 6-10	Session 11-15	6 Months
Vas Score	% Patients	% Patients	% Patients	% Patients	% Patients
10	100	56	37	32	17
8	0	21	18	5	9
6	0				
4	0				
2	0	23	45	53	74
0	0				

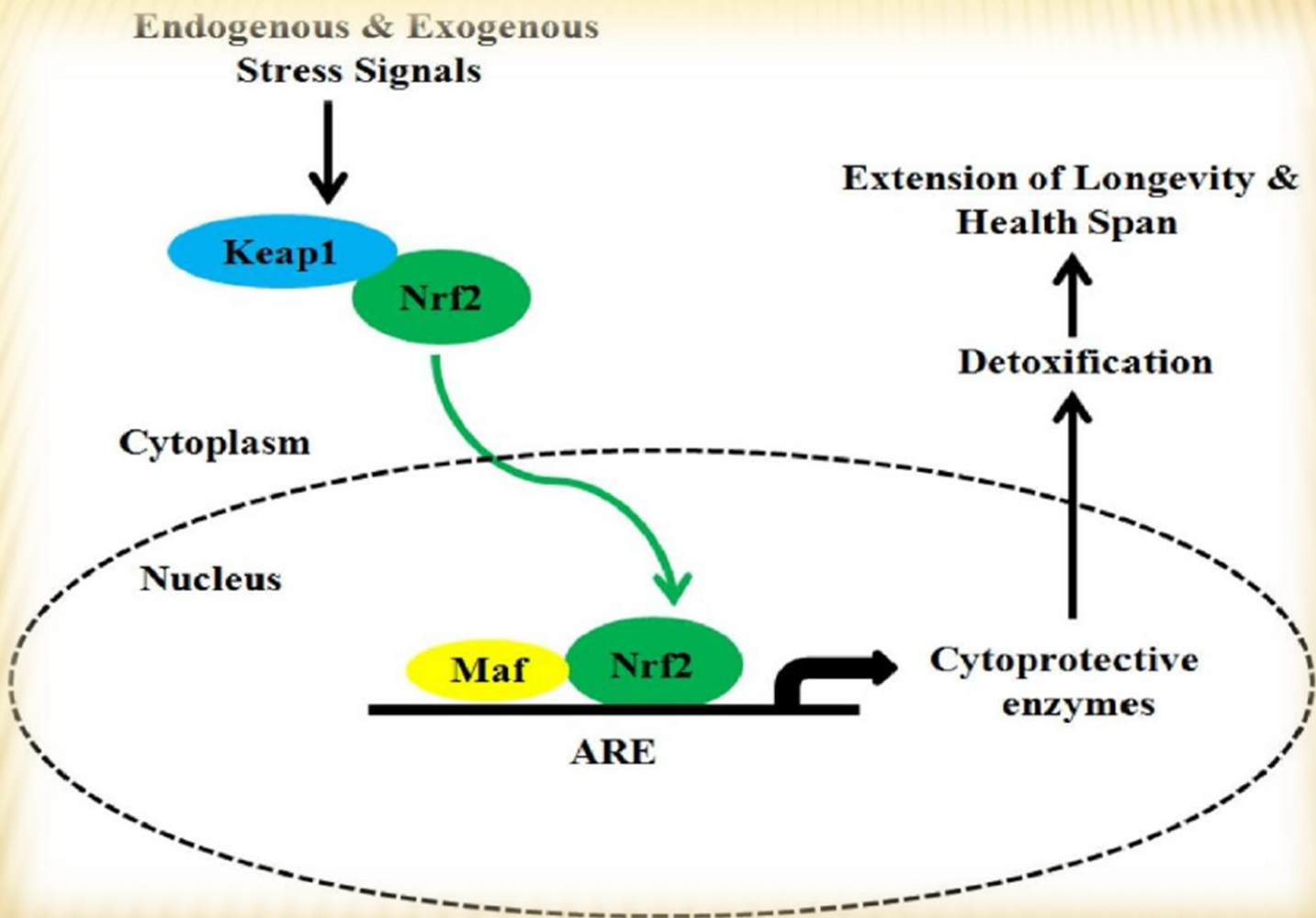
**Statistics on Pain Relief on 1079 Patients treated with Ozone Injections for Arthritic and Traumatic Pain during the years 2009-2010. VAS Score 0=No Pain 10=Very Severe Pain.**



# Basic Components of Major Stress Response Pathways

Pathway	TF	Sensor	Major transducers
→ Oxidative stress	Nrf2	Keap1	MAPK, ERK, p38, PKC
Heat shock response	HSF-1	Hsp90	CaMK2, CK2
DNA damage	p53	MDM2	ATM, JNK, Chk1, Chk2
Hypoxia	HIF-1	VHL	p38, PI3K
ER stress	XBP-1, ATF6, ATF4	BiP	IRE1 $\alpha$ , S2P
Metal stress	MTF-1	None	PKC, CKII, TKs
Inflammation	NF- $\kappa$ B	I $\kappa$ B	IKK
Osmotic stress	NFAT5	None	p38, ATM, PKA





# IN VIVO STUDY ON GENE EXPRESSION DURING SYSTEMIC OZONE THERAPY

After our previous research, in which we demonstrated the activation of Nrf2 after Systemic Ozone Therapy, our last work will complete the picture of the possible effects of ozone in vivo in humans mainly looking at different biochemical pathways, mostly related to inflammation.

I'll show here the preliminary results of our last study, still under data evaluation. We measured some genes activity regarding the **TXN** systems and subset of **NFkB**-dependent genes, including pro-inflammatory genes in patients suffering from any disease with some degree of associated inflammation.

Ozone treatment  **Nrf2** activation  Increasing of transcripts levels of **Nrf2**-dependent genes  diminished **NFkB** activation due to reduced oxidant stress  lowering transcripts levels of **NFkB** -dependent genes.

# PROTOCOL OF THE STUDY

Our study is resumed as follow:

- 1- Evaluation of the TXN-based gene(TRX<sub>1</sub>).
- 2- Evaluation of the NF-kB genes together with IL-8, MCP-1.
- 3 – Nrf2 was again evaluated in all the patients.

We admitted to the study 12 patients, both sexes, never treated before with ozone and actually suffering from some associated inflammation.

The recruitment was done in cooperation with the Internal Medicine Department of Civitanova Hospital.

The patients were submitted to three treatments of Systemic Ozone Therapy , Hematic route (SOT-H) in agreement with the protocol and sequence of the previous NRF2 study with the method of Real Time PCR (See Next Slide).

We performed the following measures:

- First** in the bottle on untreated blood,
- Second** in the bottle after bubbling oxygen in the blood,
- Third** in the bottle after bubbling oxygen/ozone mixtures in the blood,
- Fourth** from the circulating blood 1 hour after the first SOT-H,
- Fifth** from the circulating blood 5 hours after the first SOT-H,
- Sixth** 2 days after the last SOT-H.



# GENE EXPRESSION PRIMERS UTILIZED IN OUR STUDY

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## **Nrf2**

Forward: AGTGGATCTGCCAACTACTC;  
Reverse: CATCTACAAACGGGAATGTCTG

Nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (**NFkB1**)

Forward: AACAGAGAGGATTTTCGTTTCCG  
Reverse: TTTGACCTGAGGGTAAGACTTCT

## **IL8**

Forward: ATGACTTCCAAGCTGGCCGTGGCT  
Reverse: TCTCAGCCCTCTTCAAAAATTCTC

## **MCP-1**

Forward: TCTGTGCCTGCTGCTCATAG  
Reverse: GTGACTGGGGCATTGATTG

## **Human Trx1**

Forward: CTGCTTTTCAGGAAGCCTTG  
Reverse: TGTTGGCATGCATTTGACTT

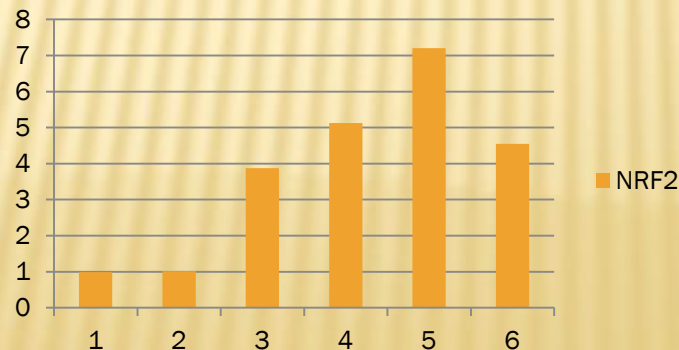
# PRELIMINARY RESULTS

## Nrf2

Nuclear factor (erythroid-derived 2)-like 2, also known as NFE2L2 or Nrf2, is a transcription factor that in humans is encoded by the NFE2L2 gene [Moi P et al, Proceedings of the National Academy of Sciences of the United States of America 91 (21): 9926–30].

Nrf2 is a basic leucine zipper (bZIP) protein that regulates the expression of antioxidant proteins that protect against oxidative damage triggered by injury and inflammation [Gold R et al, The New England Journal of Medicine 367 (12): 1098–107]. Several drugs that stimulate the NFE2L2 pathway are being studied for treatment of diseases that are caused by oxidative stress

## NRF2

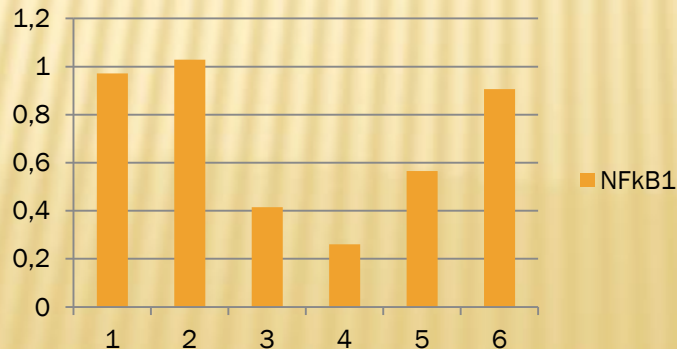


# PRELIMINARY RESULTS

## NFkB1

NF- $\kappa$ B (nuclear factor kappa-light-chain-enhancer of activated B cells) is a protein complex that controls transcription of DNA, cytokine production and cell survival. NF- $\kappa$ B is found in almost all animal cell types and is involved in cellular responses to stimuli such as stress, cytokines, free radicals, ultraviolet irradiation, oxidized LDL, and bacterial or viral antigens. NF- $\kappa$ B plays a key role in regulating the immune response to infection ( $\kappa$  light chains are critical components of immunoglobulins). Incorrect regulation of NF- $\kappa$ B has been linked to cancer, inflammatory and autoimmune diseases, septic shock, viral infection, and improper immune development. NF- $\kappa$ B has also been implicated in processes of synaptic plasticity and memory.

## NFkB1





# PRELIMINARY RESULTS

## IL8

Interleukin 8 (IL-8) or CXCL8 is a chemokine produced by macrophages and other cell types such as epithelial cells, airway smooth muscle cells and endothelial cells. In humans, the interleukin-8 protein is encoded by the IL8 gene. IL-8 is initially produced as a precursor peptide of 99 amino acids long which then undergoes cleavage to create several active IL-8 isoforms. In culture, a 72 amino acid peptide is the major form secreted by macrophages.

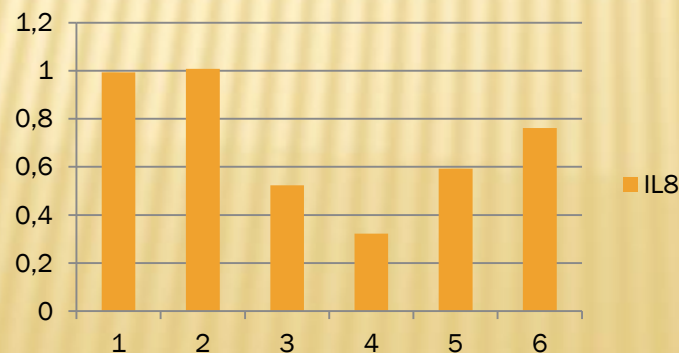
Through a chain of biochemical reactions, IL-8 is secreted and is an important mediator of the immune reaction in the innate immune system response.

Interleukin-8 is a key mediator associated with inflammation where it plays a key role in neutrophil recruitment and neutrophil degranulation. As an example, it has been cited as a proinflammatory mediator in gingivitis and psoriasis.

Interleukin-8 secretion is increased by oxidant stress, which thereby cause the recruitment of inflammatory cells and induces a further increase in oxidant stress mediators, making it a key parameter in localized inflammation.

IL-8 was shown to be associated with obesity.

## IL8



# PRELIMINARY RESULTS

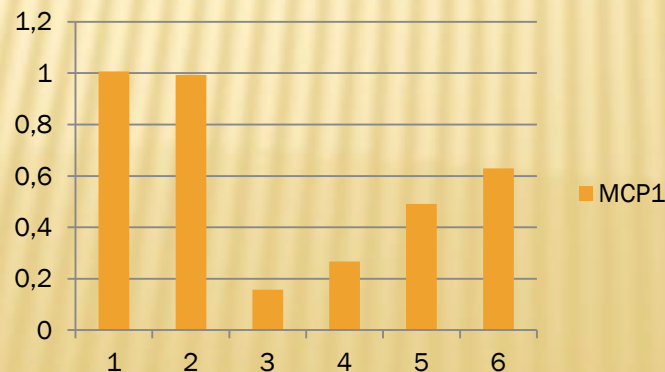
## MCP<sub>1</sub>

MCP<sub>1</sub>: Monocyte chemotactic protein-1, a member of the small inducible gene (SIG) family, plays a role in the recruitment of monocytes to sites of injury and infection. The gene for MCP<sub>1</sub> is on chromosome 17 in region 17q11.2-q12.

MCP<sub>1</sub> has been found in the joints of people with rheumatoid arthritis where may serve to recruit macrophages and perpetuate the inflammation in the joints. MCP<sub>1</sub> has also been found elevated in the urine of people with lupus as a sign warning of inflammation of the kidney.

MCP<sub>1</sub> has also been called small inducible cytokine A<sub>2</sub> (SCYA<sub>2</sub>) and monocyte chemotactic and activating factor (MCAF)

## MCP<sub>1</sub>



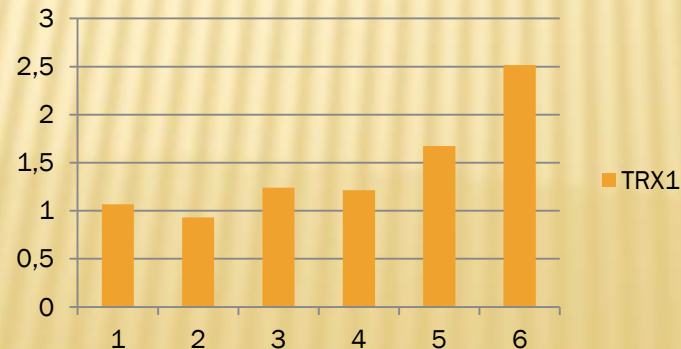
# PRELIMINARY RESULTS

## TRX<sub>1</sub>

Thioredoxin (TRX) is an antioxidant protein that control cellular signalling and redox balance, although their response to exercise is unknown. The encoded protein is active in the reversible S-nitrosylation of cysteines in certain proteins, which is part of the response to intracellular nitric oxide. This protein is found in the cytoplasm. Two transcript variants encoding different isoforms have been found for this gene.

TRX<sub>1</sub> is a class of small redox proteins known to be present in all organisms. It plays a role in many important biological processes, including redox signaling. In humans, it is encoded by the TXN gene. Loss-of-function mutation of either of the two human TXN genes is lethal at the four-cell stage of the developing embryo. Although not entirely understood, TRX<sub>1</sub> plays a central role in humans and is increasingly linked to medicine through their response to reactive oxygen species (ROS). In plants, TRXs regulate a spectrum of critical functions, ranging from photosynthesis to growth, flowering and the development and germination of seeds. It has also recently been found to play a role in cell-to-cell communication.

## TRX<sub>1</sub>





# OXIDATIVE STATUS

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## REDOX

A portable, free radicals (FRs) determination system (D-Roms test, Diacron, Grosseto, Italy) was used.

This test is based on the ability of transition metals to catalyse in the presence of peroxides with formation of FRs which are trapped by an alchilamine.

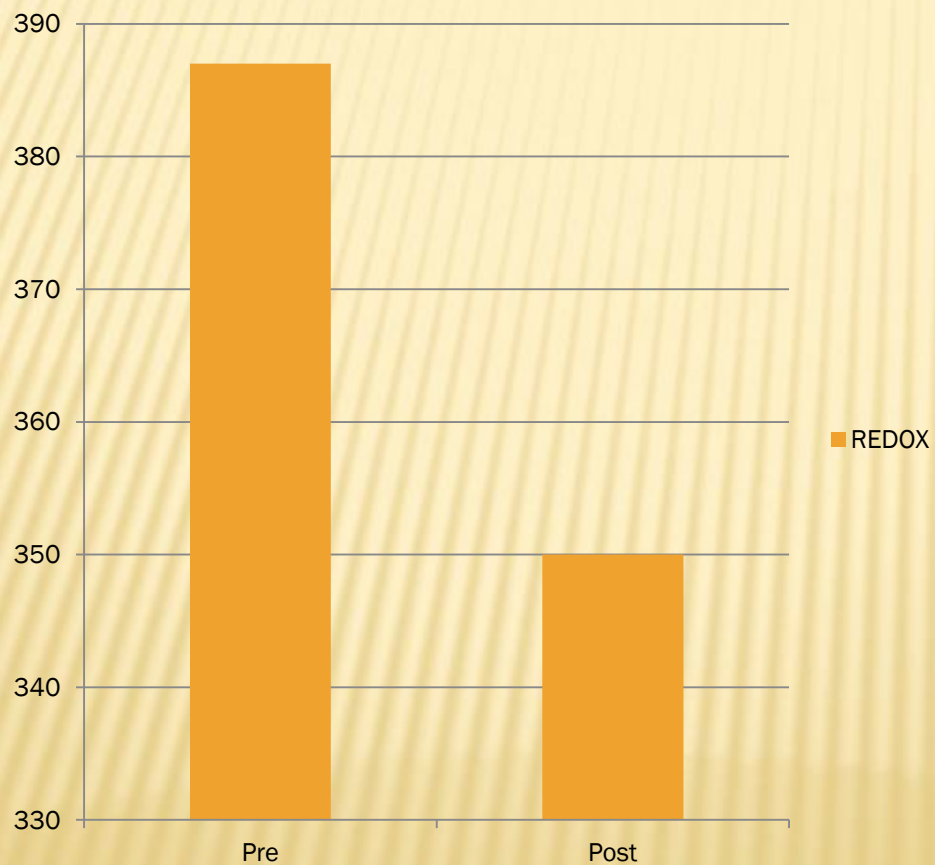
The alchilamine reacts forming a coloured radical detectable at 505 nm.

Int Angiol. 1999 Jun;18(2):127-30.

### **A simple test to monitor oxidative stress.**

Cesarone MR<sup>1</sup>, Belcaro G, Carratelli M, Cornelli U, De Sanctis MT, Incandela L, Barsotti A, Terranova R, Nicolaidis A.

## REDOX



Patients	REDOX	
	Start	End
1	412.00	400.00
2	394.00	324.00
3	385.00	311.00
4	364.00	315.00
5	598.00	454.00
6	389.00	371.00
7	347.00	320.00
8	425.00	415.00
9	303.00	302.00
10	371.00	341.00
11	341.00	353.00
12	316.00	304.00
Mean	387.08	350.83
St Err	21.89	14.25

# INFLAMMATION PARAMETERS

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## ESR

The erythrocyte sedimentation rate (ESR) determination is a simple and inexpensive laboratory test that is frequently ordered in clinical medicine.

The test measures the distance that erythrocytes have fallen after one hour in a vertical column of anticoagulated blood under the influence of gravity.

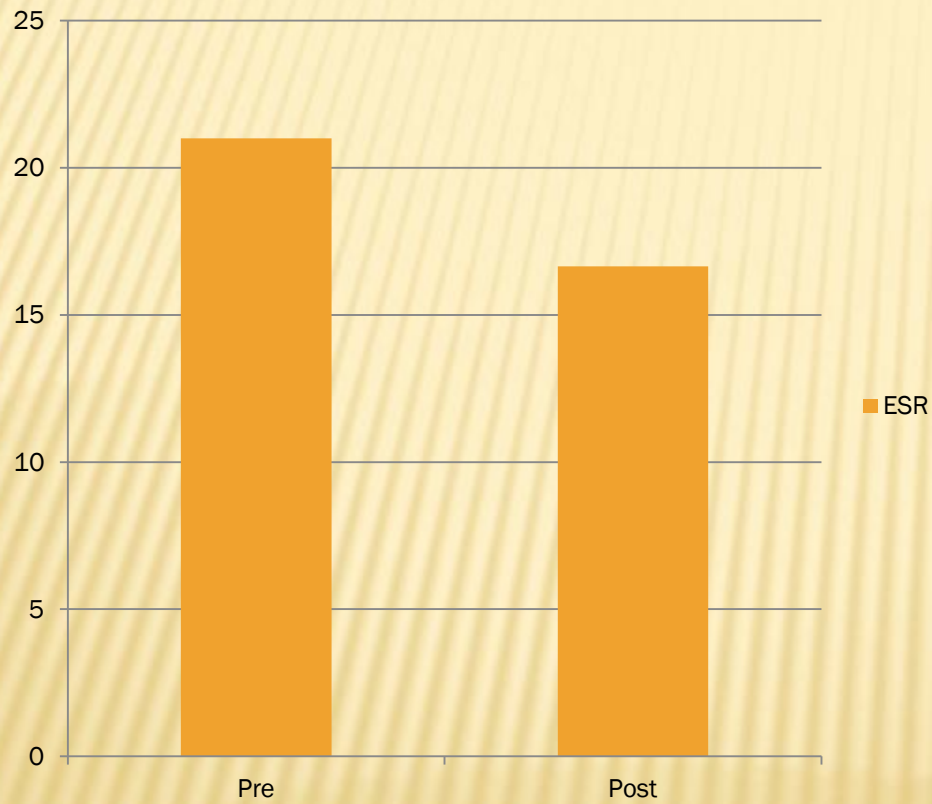
The basic factors influencing the ESR have been understood since the early part of this century; the amount of fibrinogen in the blood directly correlates with the ESR.

The most satisfactory method of performing the test was introduced by Westergren in 1921.

1. Saadeh C. The erythrocyte sedimentation rate: old and new clinical applications. *South Med J.* 1998;3:220-5.
2. Brigden M. The erythrocyte sedimentation rate: still a helpful test when used judiciously. *Postgrad Med.* 1998;103:257-74.
3. Sox HC Jr, Liang MH. The erythrocyte sedimentation rate: guidelines for rational use. *Ann Intern Med.* 1986;104:515-23.



## ESR



Patients	ESR	
	Start	End
1	41.00	40.00
2	30.00	22.00
3	17.00	10.00
4	16.00	8.00
5	23.00	23.00
6	18.00	18.00
7	26.00	25.00
8	34.00	20.00
9	4.00	3.80
10	5.00	3.00
11	8.00	7.00
12	25.00	20.00
Mean	20.58	16.65
St Err	3.32	3.10

# INFLAMMATION PARAMETERS

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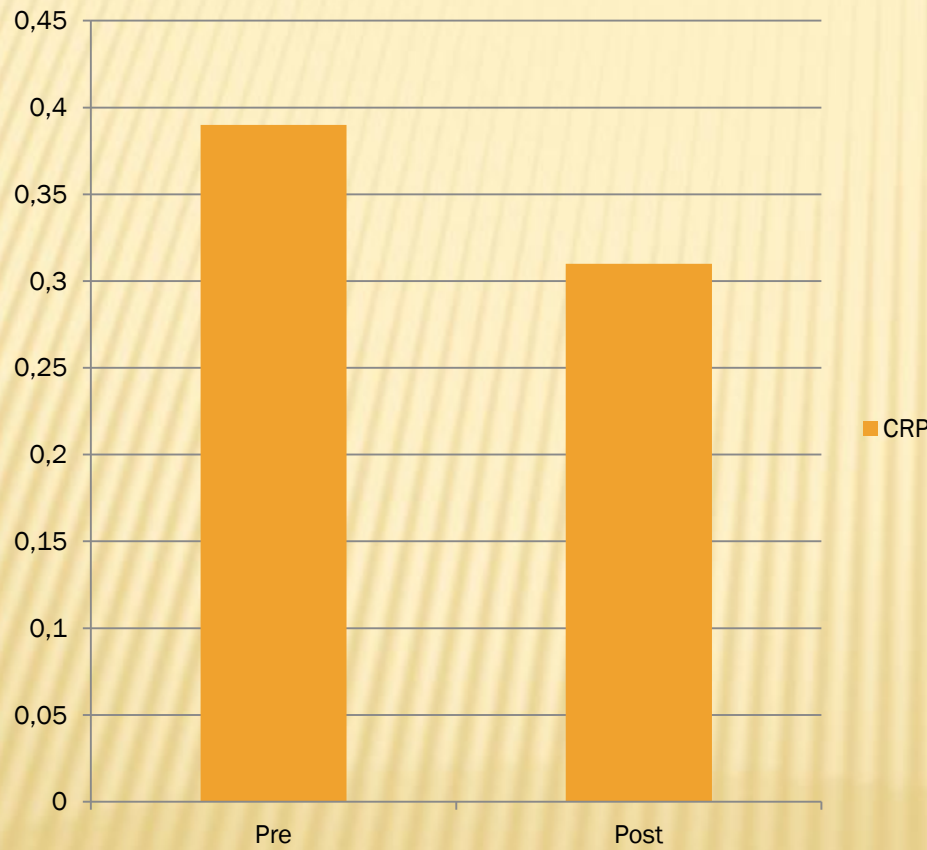
## CRP

**C-reactive protein (CRP) is an annular (ring-shaped), pentameric protein present in blood plasma, whose levels rise in response to inflammation.**

**It is an acute-phase protein of hepatic origin that increases following interleukin-6 secretion by macrophages and T cells.**

**Its physiological role is to bind to lysophosphatidylcholine expressed on the surface of dead or dying cells (and some types of bacteria) in order to activate the complement system via the C1Q complex.**

# CRP



Patients	CRP	
	Start	End
1	0.84	0.80
2	0.98	0.95
3	1.22	0.60
4	0.08	0.05
5	0.20	0.20
6	0.09	0.08
7	0.06	0.05
8	0.69	0.60
9	0.47	0.44
10	0.03	0.02
11	0.18	0.17
12	0.06	0.06
Mean	0.39	0.32
St Err	0.13	0.10



# COMMENTS

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The results of our study show for the first time in vivo that ozone can increase the level of Nrf2 protein, which in turn promotes the antioxidant and detoxifying enzymes of phase II.

Last results show further modulation of genes expression related to inflammation and protection against oxidative damage induced by Ozone when used following standard and *well consolidated* procedures.

The effect can be dissociated from the oxygen, since the values of the control samples (T1) were obtained after treatment of blood with only oxygen (ozone vehicle).

Furthermore, a significant increase of SOD and CAT enzymes has been observed at the end of the treatment.

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Taking into account all data presented herein, we can conclude that ozone could be very helpful as integrative and complementary support for pharmacological therapy modulating the oxidative stress component in many illnesses.

Furthermore it could be emphasized its use in the elderly, where side effects and therapeutic costs are going to be even often a serious problems for the health authorities and for the medical care personnel:

***[Laroche et al. Is inappropriate medication use a major cause of adverse drug reactions in the elderly? Br J Clin Pharmacol. Feb; 63(2): 177–186 (2007)].***

# CONCLUSIONS

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Considering the data discussed above, we can firmly propose *Ozone Therapy* as a useful resource to complement and integrate the pharmacological approach actually utilized both for the most common symptoms and for rare diseases, still orphan of proper medical treatment.

*(Re et al., Journal of Experimental and Integrative Medicine, 2012)*



THE SURGICAL USES OF OZONE.

BY GEORGE STOKER, M.R.C.P. IREL., M.R.C.S. ENG., MAJOR, ROYAL ARMY MEDICAL CORPS.

The accompanying tabulated statement of the results of the first 21 cases treated by ozone at the Queen Alexandra Military Hospital cannot be regarded as anything but satisfactory from every standpoint, be it humanitarian, scientific, or economic. The cases were, for the most part, those of cavities and sinuses in the femur and tibia. It is the experience of those who have seen a great deal of war surgery that such cases obstinately resist treatment and are apt to remain unhealed for months and years.

The treatment consists of the application of ozone to the affected parts; it is, therefore, necessary to have an apparatus for generating ozone which shall be portable and easily worked. The one I am accustomed to use is known as Andrioli's ozoniser. It is called into operation by a four-volt battery animating a 4-inch sparking Rhumkorff coil. The oxygen passes from a cylinder through the ozoniser, and in doing so comes in contact with a metal armature, the effect of this being to transform the oxygen into ozone.

Table of Wounds, Sinuses Treated by Oxygen and Ozone.

No.	Name	Nature of disability.	Pre-vious duration.	Dura-tion of treat-ment.	Result.
1	J. B., Lincoln.	Compound comd. fracture of femur resulting in cavity 1 x 1 1/2 inches and sinus 1 1/2 inches deep.	20 mos.	2 mos.	Cure.
2	W., Lincoln.	2 large surface wounds on forearm 5 x 4.	5 wks.	2 "	"
3	H. H. B., H. Surreys.	3 sinuses opening from back of scapula, each 6 inches long.	9 mos.	2 "	"
4	G. G. T., M., K.O.R.L.	Ulcer on end of stump. Wound on shoulder.	3 "	3 wks.	"
5	M., H. D., Scots Guards.	Sinus in tibia 1 1/2 inches deep. Ulcer on instep.	12 "	4 "	"
6	H. D., Scots Guards.	Ulcer on instep.	25 "	7 "	"
7	A. A. A., Canadians.	Cavity and sinus in femur, 2 1/2 inches deep.	14 "	2 mos.	"
8	F. G. B., Grenadier Guards.	Two sinuses in leg, one 3 and one 5 inches long.	8 "	1 mth.	"
9	J. W., Grenadier Guards.	Cavity in finger after whitlow.	3 wks.	8 days.	"
10	P. V., Suffolk.	Cavity and sinus, 2 inches deep, in left humerus.	14 mos.	5 wks. & 3 days.	"
11	G. C., R. Fusiliers.	Sinus in stump after amputation.	6 "	5 days.	"
12	T. C., D.L.I.	Wound in shoulder below clavicle, leaving sinus 2 1/2 inches deep.	4 "	16 "	"
13	Major M., R. Inniskilling Fusiliers.	Sinus in lower end of outside of R. humerus 1 1/2 inches deep.	10 "	5 "	"
14	J. G., Seaford Highlanders.	Ulcer in centre of amputation flap.	9 "	3 wks.	"
15	Sister N., Q.A.M.N.S.	Large opening at back of right ear following 2 operations for mastoiditis.	7 "	3 "	"
16	W. B., Lifeguards.	Suppuration of eye sockets at or enucleation of eyeball.	6 "	3 "	"
17	Lieut. H., R. Warwick.	Sinus leading down to right femur, 2 inches deep.	7 "	3 "	"
18	Lieut. H., Canadian Inf.	Trench gingivitis with ulceration of gums.	3 wks.	3 "	"
19	W. M., Hants.	Sinus and abscess cavity in amputation stump.	6 mos.	5 "	"
Total ... ..			157 mos. 2 wks.	18 mos. 2 wks.	

\* In this case treatment was discontinued for four weeks. N.B.—I have only failed in one case, Major S. H. He was twice placed for fracture of the femur. The "plate" acted as a "foreign body."

The properties of ozone, which have a wonderfully healing effect, are, as far as one can say at present, three:—  
 1. It is a strong stimulant and determines an increased flow of blood to the affected part.  
 2. It is a germicide, which destroys all hostile micro-organic growth.  
 3. As the French chemist Hennoque has shown, it has great powers in the formation of oxyhæmoglobin.  
 The ozone is applied on the wounded surface or to the cavities and sinuses for a maximum time of 15 minutes, or until the surface becomes glazed. Ozone has the particular power of disclosing dead bone, foreign bodies, septic

deposits, &c. This, I believe, it does by destroying the granulations and micro-organic growths (presumably unhealthy) that are found in close contact with septic deposits, foreign bodies, or dead bone.

Cleansing and Dressing.

Wounds and sinuses, &c., are washed twice daily with boiled water and a dressing of dry gauze is applied. It must be observed that at first ozone causes an increase of the discharge of pus; later on the pus is replaced by clear serum, which at a still later stage becomes coloured reddish or pinkish. In open wounds it is necessary to strip off the parchment-like film surrounding the edges, which is composed of oxidised serum. This is easily effected by applying a hot compress for 15 or 20 minutes, after which the film can be easily peeled off with a dissecting forceps.

At present our knowledge of the effects of ozone is but small, but later I hope to bring before the medical public further satisfactory facts with reference to its working and results.

Clinical Notes:

MEDICAL, SURGICAL, OBSTETRICAL, AND THERAPEUTICAL.

PLACENTA PRÆVIA AND CÆSAREAN SECTION.

By A. G. TRESIDDER, M.D. LOND., CAPTAIN, INDIAN MEDICAL SERVICE; STAFF SURGEON, POONA.

ONE meets only a few cases of placenta prævia in which the condition of both mother and child justifies the operation of Cæsaræan section. This is more especially so in hospital practice, where such patients are usually admitted in a more or less advanced stage of labour and only after there has been a considerable loss of blood, a state of affairs which would obviously contra-indicate a major operation when other means of delivery are open to us.

In recent years it has been recognised that the best treatment for certain cases of placenta prævia is Cæsaræan section, and the results obtained among these carefully selected cases have been very satisfactory both as regards the maternal mortality and that of the infants. The maternal mortality of placenta prævia treated on the ordinary lines is 4 to 8 per cent., and the average foetal mortality is 60 per cent. Munro Kerr says: "The best figures give 4 per cent. and 35 per cent. respectively, and they are as low as one can ever expect to reach with the present recognised methods of treatment." But in certain cases of placenta prævia, such as the one described below, Cæsaræan section would, I think, justify us in expecting much better results than a maternal mortality of 4 per cent. and a foetal one of 35 per cent.

As regards the mothers, there seems no special reason why Cæsaræan section performed in suitable cases of placenta prævia should not yield quite as good results as it does in cases of contracted pelvis, when the operation is performed under the best conditions, the maternal mortality then being 2-9 per cent. (Amand Routh). Berkeley and Bonney place this maternal death-rate of Cæsaræan section, when this operation is performed under the best conditions, as "probably under 1 per cent." In well-selected cases of placenta prævia the maternal mortality should not, therefore, be greater than about 2 per cent., i.e., about half as great as we could expect from any other method of treatment. One other great advantage to the mother is a lesser risk of morbidity as compared with that which results from the necessary manipulations, often prolonged, which accompany delivery *per vias naturales*.

The foetal mortality must obviously be very greatly reduced by Cæsaræan section, and the rate of 35 per cent. at the best would be reduced to one of about 5 per cent. Further, in most cases the mother should be as well able to nurse her infant as after normal delivery, a result which, because of some slight sepsis or as the result of hæmorrhage before and during delivery, is often denied to the mother who has been otherwise delivered.

Generally speaking, the operation of Cæsaræan section in a case of placenta prævia is indicated under the following

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BY GEORGE STOKER, M.R.C.P. IREL., M.R.C.S. ENG., MAJOR, ROYAL ARMY MEDICAL CORPS.

At present our knowledge of the effects of ozone is but small, but later I hope to bring before the medical public further satisfactory facts with reference to its working and results.



Dr. Stoker has left us a legacy a century ago .... now is for us to finalize its work with data and clinical results worthy of the highest scientific consideration ...



FEDERAZIONE ITALIANA DI  
OSSIGENO-OZONOTERAPIA



*World Conference on Ozone Therapy in Medicine, Dentistry and Veterinary  
Ancona (Italy) - September 22<sup>nd</sup> -23<sup>rd</sup> -24<sup>th</sup> , 2017*

*Under the Auspices of WFOT & FIO*

*Official Language : English*

*New Frontiers in Ozone Therapy  
A formidable ally to conventional medical therapy*

*Nuevas fronteras en Ozonoterapia  
Un aliado formidable para la terapia médica convencional*

*Nuove Frontiere in Ozono Terapia  
Un formidabile alleato per la terapia medica convenzionale*

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**Prof. Lamberto Re**

*President of the Italian Federation of Ozone Therapy (FIO)*

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**Honorary Members**

**Prof. Velio Bucci**

**Prof. Marco Leonardi**



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Ramiro Alvarado, Bolivia  
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Ofir Betancourt, Venezuela

In addition to the above Speakers, many prestigious Italian colleagues will be present:

Además de los docentes arriba mencionados, estarán presentes prestigiosos colegas italianos:

Oltre ai docenti di cui sopra, saranno presenti prestigiosi colleghi italiani:

Filippo Albertini, Italy  
Alberto Alexandre, Italy  
Cosma Andreula, Italy  
Dario Apuzzo, Italy  
Federico Berni, Italy  
Matteo Bonetti, Italy  
Emma Borrelli, Italy  
Viviana Covi, Italy  
Nicola Dardes, Italy  
Teodosio De Bonis, Italy  
Angelo Farina, Italy  
Eugenio Luigi Iorio, Italy  
Mauro Martinelli, Italy

Salvatore Loconte, Italy  
Mario Muto, Italy  
Gianni Pellicandò, Italy  
Deborah Puddu, Italy  
Marco Rascardi, Italy  
Raoul Saggini, Italy  
Silvia Santi, Italy  
Paolo Scrollavezza, Italy  
Mario Siritto, Italy  
Gabriele Tabaracci, Italy  
Valter Travagli, Italy  
Gerardo Tricarico, Italy

Full Program coming soon

Pronto el Programa Completo



## REGISTRATION FEE

**SPECIAL DISCOUNT - Register now and save 300 EUR!**

Regular registration:

February 1 <sup>st</sup> - April 30 <sup>th</sup> , 2017	€ 610,00 (500,00 + VAT 22%)
May 1 <sup>st</sup> - August 31 <sup>st</sup> , 2017	€ 732,00 (600,00 + VAT 22%)
On-site	€ 915,00 (750,00 + VAT 22%)
Accompanying person	€ 61,00 (50,00 + VAT 22%)

FIO members:

February 1 <sup>st</sup> - April 30 <sup>th</sup> , 2017	€ 549,00 (450,00 + VAT 22%)
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Special Fee\* for Members of Scientific Societies of Ozone Therapy  
€ 549,00 (450,00 + VAT 22%) - up to April 30<sup>th</sup> 2017

\*if at least 10 members are regularly registered by the end of January 2017  
(the list must be sent directly by the Society while fee payments can be individual)

Fee includes admission to the Conference, coffee break and lunch

**ONLINE REGISTRATION** on [www.congredior.it](http://www.congredior.it)

## ORGANIZING SECRETARIAT



Congress • Meeting • Convention • Event

Corso Amendola n.45 - 60123 Ancona (Italy)  
tel +39 071/2071411; fax +39 071/2075629  
[www.congredior.it](http://www.congredior.it) ; [info@congredior.it](mailto:info@congredior.it)

## CONFERENCE VENUE

Mole Vanvitelliana - Ancona, Italy



Don't hesitate to confirm your participation... Time to move forward all together is finally here.  
Don't miss this opportunity!!

.....

Por favor confirme su participación ... El momento de proceder todos juntos por fin ha llegado.  
No se pierda esta oportunidad !!

.....

Non esitare a confermare la tua partecipazione... Il momento di procedere tutti insieme è finalmente arrivato.  
Non perdere questa occasione!!

**You can't miss this event!**

**The Ancona World Conference will be a unique event to spread the message on Ozone Therapy to the entire World.**

**The conference will host the most excellent speakers from China, Japan, Europe, USA, South Africa, Latin America and many other colleagues from Italy, joined in a sole meeting like a big Family of Scientists, Clinicians and Experts with a huge experience in the field of Ozone Therapy.**

***NO MORE BORDERS!***

**Not only Italy, but all the eyes from all over the world will look to us!**

**Hundreds of participants confirmed their presence already; finalize your inscription as soon as possible to be sure to have a place reserved for you.**

**The last news on ozone in Medicine, in Veterinary and in Dentistry will be discussed at the higher level of excellence.**

**All the most recent evidences and uses of ozone in the different fields of medicine will be discussed by the world's leaders.**

**Round Tables and Workshops will be organized during the meeting and a poster session will be available for the scientific papers on ozone therapy.**

**The Ancona airport (AOI) can be reached from Rome or Munich major Hubs.**

**Alternatively, you can flight to Bologna Airport and reach our city by train.**

**Congredior, the Organizing Secretariat, will help you organize very interesting tours in our Region (Loreto, Recanati, Wineries of Rosso Conero and Verdicchio) and in the most beautiful Italian cities like Florence, Venice or Rome.**

**I look forward to meet you all in Ancona next September 2017.**

**Your friend and colleague,**

**Lamberto**



EUROPEAN COOPERATION  
OF MEDICAL OZONE  
SOCIETIES

EUROPEAN OZONE CONGRESS  
EUROPÄISCHER OZONKONGRESS  
MARCH 24 - 26, 2017  
CHARITÉ BERLIN, GERMANY



Thank  
You



**Ozone therapy and inflammation: an *in vivo* study to evaluate the possible involvement of the GSH, TXN based system and NF- $\kappa$ B-dependent genes. Preliminary Results.**

Lamberto Re, MD, Valentina Langella, MD and Giuseppe Malcangi, MD

*Ancona - Italy*

*President of the Italian Federation of Ozone Therapy  
Chairman of the Scientific Advisory Committee of WFOT*

[www.lambertore.com](http://www.lambertore.com)

