



HOLTORF MEDICAL GROUP, INC.

CENTER FOR HORMONE IMBALANCE, HYPOTHYROIDISM AND FATIGUE

23456 Hawthorne Blvd. Suite160, Torrance, CA 90505 Tel: 310-375-2705 Fax: 310-375-2701

NUMEROUS STUDIES HAVE demonstrated that chronic infections of viruses, intracellular bacterial and parasites are associated with and may cause or contribute to the symptoms of chronic fatigue syndrome (CFS) and fibromyalgia (FM) (see infections in CFS/FM). In addition, many patients have a number of markers associated with chronic infections including low natural killer cell activity and high RNase-L-activity. While standard testing for the presence of chronic infections is rather specific (infection is present if the test is positive), the tests suffer from very low sensitivity, as there is often an infection present despite negative tests. Thus, identification of the existing chronic infection(s) can be problematic, but there is a considerable likelihood of a contributing infectious etiology in the majority of CFS and FM patients. Thus, utilizing natural broad spectrum anti-infectious agents that have been shown to have activity against a wide range of infections, included viruses, bacteria and yeast and have a considerable safety record are logical choices. These include intravenous very dilute hydrogen peroxide, high dose intravenous vitamin C and intravenous oligodynamic silver.

Hydrogen peroxide (H₂O₂) is naturally produced in the body and is the body's main defense against infections. There is evidence that a common cause of immune deficiency may be a diminished ability to produce hydrogen peroxide (1). CFS and FM patients often have a mix of chronic infections including viruses such as Epstein Bar (EBV), Cytomegalovirus (CMV), HHV6, bacteria such as Mycoplasma, and Chlamydia pneumonia and yeast such as Candida. One would have to take specific antibiotics for the bacteria, specific antivirals for the viruses and antifungals for the yeast. Alternatively, one can simply use very dilute IV H₂O₂ to help eradicate all the infections without the toxicity of commonly prescribed antimicrobial medications. Additionally, the hydrogen peroxide activates the body's white cells for a lasting boost in immunity and boosts mitochondrial function.

A recent study by the National Institutes of Health (NIH) published in the September

2005 Proceeds of National Academy of Science entitled Pharmacologic Ascorbic Acid Concentrations Selectively Kill Cancer Cells, demonstrated that very large doses of intravenous vitamin C were harmless to normal cells and that the action of the vitamin C is

“Intravenous administration of dilute hydrogen peroxide significantly improves tissue oxygenation and protection against cardiac ischemia.”

as a pro-drug to deliver hydrogen peroxide to tissues (2). The authors conclude, “Taken together, these data indicate that ascorbate at concentrations achieved only by i.v. administration may be a pro-drug for formation of H₂O₂, and that blood can be a delivery system of the pro-drug to tissues. These findings give plausibility to i.v. ascorbic acid in cancer treatment, and have unexpected implications for treatment of infections where H₂O₂ may be beneficial (2).”

Hydrogen peroxide and large doses of vitamin C, and thus hydrogen peroxide, have been shown to improve natural killer cell activity, which is a consistent abnormality in CFS patients and severely low in many CFS and FM patients, making them unable to eradicate chronic viral infections (3,4).

Chronic stimulation of opioid receptors as occurs in chronic pain states are shown to decrease hydrogen peroxide production in macropahages, resulting in immune deficiency (5).

Mitochondrial dysfunction has been shown to be a common denominator in the pathophysiology of CFS (6,7). Hydrogen peroxide has been shown to boost mitochondrial function and metabolic rate (8,9). A 1988 study published in the Journal of Advancement in Medicine entitled Physiological and Biochemical Responses to Intravenous Hydrogen Peroxide in Man measured the

Review: Intravenous Very-dilute Hydrogen Peroxide

metabolic effects of intravenous hydrogen peroxide in normal individuals. The authors conclude, “We have demonstrated H₂O₂, when administered intravenously, has a pronounced effect to stimulate metabolic respiration... Intravenous and intra-arterial infusions of hydrogen peroxide (H₂O₂), reported since H₂O₂ kills bacteria, parasites, yeast, protozoa, inhibits virus and oxidizes immuunocomplexes (8).”

A study published in Circulation entitled Hydrogen Peroxide, an Endogenous Endothelium-Derived Hyperpolarizing Factor, Plays an important role in Coronary autoregulation in Vivo, demonstrates that hydrogen peroxide is essential for the vasodilatation and autoregulation of arteries (10). This autoregulation has been demonstrated to be abnormal in CFS and very dilute intravenous hydrogen peroxide is a potential means of normalizing this abnormality (10,11,12).

There is evidence that there is poor oxygen offloading to tissues in CFS and FM that can result in relative tissue hypoxia and subsequent fatigue and pain, and there is evidence that abnormally low 2,3-diphosphoglycerate (2,3-DPG) in CFS patients causes or contributes to this tissue hypoxia. Oxidative therapies result in an increase in the red blood cell glycolysis rate. This leads to the stimulation of 2,3-DPG which leads to an increase in the amount of oxygen released to the tissues. There is a stimulation of the production of the enzymes which act as free radical scavengers and cell wall protectors: glutathione peroxidase, superoxide dismutase and catalase. They activate the Krebs cycle by enhancing oxidative carboxylation of pyruvate, improving mitochondrial function and stimulating the production of ATP (8,13,14,15,16,17).

In a study published in the Annals New York Academy of Sciences entitled Protection of the Ischemic Heart with DMSO Alone or DMSO with Hydrogen Peroxide demonstrated that intravenous administration of dilute hydrogen peroxide significantly improves tissue oxygenation and protection against cardiac ischemia. It was also demonstrated that by adding DMSO to the dilute

(over)

hydrogen peroxide, an additional beneficial effect was seen (18). A study published in Circulation entitled Cardiac Resuscitation with Hydrogen Peroxide demonstrate that successful resuscitation of a patient in V-fib, who was unresponsive to conventional resuscitation methods, was achieved with the use of intravenous dilute hydrogen peroxide. This study also commented that DMSO added further benefit (19). Other studies have also confirmed this improved tissue oxygenation, which is a significant benefit in patients with CFS (20,21).

New research has shown that hydrogen peroxide protects neuronal tissue. This was analyzed in a study published in the 2005 Journal of Neuroscience Research entitled Generation of Hydrogen Peroxide During Brief Oxygen-Glucose Deprivation Induces Preconditioning Neuronal Protection in Primary Cultured Neurons. The authors state that "...hydrogen peroxide is likely the main trigger involve in the mechanism of IPC-induced neuronal protection (22)."

The mechanism of many natural supplements that are shown to have antimicrobial actions is through the production of hydrogen peroxide. In a study published in the 2005 Journal of Food Protection entitled Inhibition of Staphylococcus aureus by Oleuropein Is Mediated by Hydrogen Peroxide demonstrates that the effectiveness of the antimicrobial effect of olive leaf extract is via the production of hydrogen peroxide (23).

Giving very dilute hydrogen peroxide (H₂O₂) intravenously is a very safe and effective treatment for CFS and FM. The safety and efficacy of dilute intravenous H₂O₂ has been published in numerous journals including The Lancet (24), Nature (25), Southern Medical Journal (26), Circulation(27), Annals of NY Academy of Sciences (28), American Journal of Cardiology (29) and American Journal of Surgery (30) and others (5,16,24,31,32,33,34). Intravenous very dilute hydrogen peroxide is a form of oxidative treatment, which includes ultraviolet blood irradiation, ozone and hydrogen peroxide. The oxidative treatments kill bacteria, viruses and yeast and have been shown to be extremely safe and effective for decades. Studies have shown these treatments are, in many ways, superior to antibiotics as well as being safer and without the problematic side effects of antibiotic

treatment (5,8,16,24,31,32,33,34). The Study in the American Journal of Cardiology infused 0.2% hydrogen peroxide (over 5 times the concentration typically utilized to over 150 individuals without any ill effects. They conclude that ... "H₂O₂ appears

This treatment had a cure rate of 98 to 100% in early and moderately advanced infections, and approximately 50% in terminally moribund patients.

to be a safe, reliable and very effective agent (29)." A study published in the American Journal of Surgery entitled Use of Intra-arterial Hydrogen Peroxide to Promote Wound Healing demonstrated that dilute hydrogen peroxide given intra-arterially could dramatically improve tissue healing (30).

A study published in the Journal of Integrative Medicine found that an integrative treatment protocol that includes very dilute intravenous hydrogen peroxide resulted in significant improvement in 150 fibromyalgia patients. Excellent or good outcome was achieved in 84.7% of the patients without ill effects (5). The authors state that they have safely administered thousands of doses of intravenous hydrogen peroxide (5).

A study entitled Influenzal Pneumonia: The intravenous Injection of Hydrogen Peroxide published in The Lancet, demonstrated that intravenous hydrogen peroxide in 24 patients with severe influenza infection produced rapid improvement in a significant percentage of patients without any ill effects (24).

A review of intravenous oxidative therapies was published in the 1996 International Journal of Biosocial Medicine Research. The author concludes, "This treatment had a cure rate of 98 to 100% in early and moderately advanced infections, and approximately 50% in terminally moribund patients. Healing was not limited to just bacterial infections, but also viral (acute polio), wounds, asthma, and arthritis. Recent German literature has demonstrated

profound improvements in a number of biochemical and hematologic markers. There has never been reported any toxicity, side effects or injury except for occasional Herxheimer type reactions. As infections are failing to improve with the use of chemical treatment, this safe and effective treatment should be revisited (16)."

A study published in the 1983 Infection and Immunity entitled Killing of Blood-Stage Murine Malaria Parasites by Hydrogen Peroxide demonstrated the effectiveness of hydrogen peroxide in killing malaria. The authors state, "We now present evidence that hydrogen peroxide, which can also be released by macrophages, is effective against murine blood-stage malaria at concentrations which might occur naturally (32).

Interferon treatment has been shown to result in significant improvement in CFS patients, but its cost and high incidence of side effects precludes its use as an effective treatment (35,36). Intravenous hydrogen peroxide is a safe and natural way to improve natural interferon production (8,33).

Intravenous immunoglobulin therapy has been shown to have a significant beneficial affect on patients with CFS (37,38). The effect of intravenous immunoglobulin has been shown to be mediated via the production of hydrogen peroxide (39), and the killing of bacteria by antibodies has been demonstrated to be due to hydrogen peroxide and ozone formation (40).

Use of very dilute intravenous hydrogen peroxide is taught at workshops and seminars sponsored by the International Association of Oxidative Medicine (a member of the American Board of Specialties of Alternative Medicine). Literally millions of intravenous doses of dilute hydrogen peroxide have been given by doctors to patients over the last 80 years with approximately 6000 doses given a month in California alone and there has never been a serious side effects from its use. The worst that has happened is inflammation of the vein, which can happen with any IV, even saline.

Unfortunately, there was wide media coverage of a patient with multiple sclerosis that underwent treatment with intravenous hydrogen peroxide by a physician in South Carolina. The patient died several days after



her latest intravenous H₂O₂ treatment and the pathologist erroneously stated the cause of death was a result of her treatment with hydrogen peroxide. This case was investigated by the South Carolina Medical Board and charges related to the use of intravenous hydrogen peroxide were dropped when it was determined that it did not cause or contribute to the patient's death. Rather, the death was a known side effect of the medications, Copaxone (glatiramer acetate) and Tegretol (carbamazepine), which she was using to treat her multiple sclerosis.

There have been clear warnings by the FDA that long term use of Tegretol and Copaxone, can result in the exact mechanism of death described in this case. The coroner presumed the death was not a result of the use of these medications because she had been on them for a number of months, but this was the scenario specifically warned against by the FDA based on post marketing surveillance. He failed to read the package inserts and published warnings by the FDA about the risks of long term use of Copaxone and Tegretol which clearly state that they can cause the complications in the exact same manner and circumstances leading to her death (41,42). On the other hand, there is no potential for intravenous hydrogen peroxide to cause any of the effects that resulted in her death. Consequentially, the case against the use of intravenous hydrogen peroxide was dropped.

Intravenous very dilute hydrogen peroxide is a safe and effective part of an integrative treatment approach to CFS and FM. Its unique broad-spectrum activity against viruses, bacteria and yeast, make it ideally suited to the treatment of these conditions.

References

- Walrand S et al. Specific and nonspecific immune response to fasting and refeeding differ in healthy young adult and elderly persons. *Am J Clin Nutr* 2001;74:670-8.
- Chen Q, Espey MG, Krishna MC, Mitchell JB, Corpe CP, Buettner GR, Shacter E, Levine M. Pharmacologic ascorbic acid concentrations selectively kill cancer cells: action as a pro-drug to deliver hydrogen peroxide to tissues. *Proc Natl Acad Sci U S A*. 2005 Sep 20;102(38):13604-9. Epub 2005 Sep 12.
- Heuser et al. Enhancement of Natural Killer Cell Activity and T and B Cell Function by Buffered Vitamin C in Patients Exposed to Toxic Chemical: The role of Protein Kinase-C Immunopharmacology and Immunotoxicology 19(3), 291-312 (1997)
- Vojdani A et al. Enhancement of Human Natural Killer Cytotoxic Activity by Vitamin C in Pure and Augmented Formulation. *Journal of Nutritional & Environmental Medicine* (1997) 7, 187-195.
- Vesna Vujic' a Stanislava Stanojevic' b Mirjana Dimitrijevic' b Methionine-Enkephalin Stimulates Hydrogen Peroxide and Nitric Oxide Production in Rat Peritoneal Macrophages: Interaction of \bar{I} , % and Opioid Receptors. *Neuroimmunomodulation* 2004;11:392-403
- Russell J M Lane, Michael C Barrett, David Woodrow, Jill Moss, Robert Fletcher, Leonard C Archard. Muscle fibre characteristics and lactate responses to exercise in chronic fatigue syndrome *J Neurol Neurosurg Psychiatry* 1998;64:362-367
- Behan W. et al. Mitochondrial abnormalities in post viral fatigue syndrome. *Acta Neuropathology* 1991;83:61-5.
- Farr C. Physiological and Biochemical Responses to Intravenous Hydrogen peroxide in man. *Journal of Advancement in Medicine* 1988;1:113-129.
- Munns SE; Lui JK; Arthur PG. Mitochondrial hydrogen peroxide production alters oxygen consumption in an oxygen-concentration-dependent manner. *Free Radic Biol Med* 2005 Jun 15;38(12):1594-603
- Yada et al. Hydrogen Peroxide, an Endogenous Endothelium Derived Hyperpolarizing Factor, Plays and important role in Coronary autoregulation in Vivo. *Circulation* 2003;107:1040-1045.
- Ichise M, Salit IE, Abbey SE, Chung DG, Gray B, Kirsh JC, Freedman M. Assessment of regional cerebral perfusion by 99Tcm-HMPAO SPECT in chronic fatigue syndrome. *Nucl Med Commun*. 1992 Oct;13(10):767-72.
- Machale S et al. Cerebral perfusion in chronic fatigue syndrome and depression. *The British Journal of Psychiatry* (2000) 176: 550-556
- Graham J. Chronic Fatigue syndromes-A review. *Journal of Australian College of Nutritional & Environmental Medicine* Vol. 20 No. 2; August 2001: pages 19-28
- Lindman R, Hagberg M, Bengtsson A, et al. Capillary structure and mitochondrial volume density in the trapezius muscle of Chronic Trapezius Myalgia, Fibromyalgia and healthy subjects. *J Musculoskeletal Pain* 3(3) 1995, 5-22.
- Jeschonneck M, Grohmann G, Hein G, Sprott H. Abnormal microcirculation and temperature in skin above tender points in patients with fibromyalgia. *Rheumatology (Oxford)* 39(8), Aug, 2000, 917-21.
- Rowen RJ. Ultraviolet Blood Irradiation Therapy (Photo-Oxidation) The Cure That Time Forgot. *Int J. Biosocial Med Research* Vol. 14(2) 115-32, 1996.
- Frick, G., A Linke: Die Ultraviolet bestrahlung des Blutes, ihre Entwicklung und derzeitiger Stand., *Zschr.arztl., Forth.* 80, 1986
- Finney JW et al. Protection of the Ischemic Heart with DMSO Alone or DMSO with Hydrogen Peroxide. *Annals New York Academy of Sciences*
- Urshel HC et al. Cardiac Resuscitation with hydrogen peroxide. *Circulation*
- Rowen RJ. Ultraviolet Blood Irradiation Therapy (Photo-Oxidation) The Cure That Time Forgot. *Int J. Biosocial Med Research* Vol. 14(2) 115-32, 1996.
- Frick, G., A Linke: Die Ultraviolet bestrahlung des Blutes, ihre Entwicklung und derzeitiger Stand., *Zschr.arztl., Forth.* 80, 1986
- Furuichi T et al. Generation of hydrogen Peroxid During brief Oxygen-Glucose deprivation Induces Preconditioning Neuronal Protection in Primary Cultured Neurons. *Journal of Neuroscience research* 2005;79:816-24.
- Zanichelli D et al. Inhibition of Staphylococcus aureus by Oleuropein Is Mediated by Hydrogen Peroxide. *Journal of Food Protection*, Vol. 68, No. 7, 2005, Pages 1492-1496
- Oliver, T. H., et al., Influenzal pneumo-



- nia: the intravenous injection of hydrogen peroxide, *Lancet* 1:432-433 (1920)).
25. Green HN, Westrop JW. Hydrogen peroxide and tumor therapy. *Nature* 1958;181:128-9
 26. Mallams JT, Finney JW, Balla GA. The use of hydrogen peroxide as a source of oxygen in a regional intra-arterial infusion system. *South Med J* 1962;55:230-2.
 27. Urschel HC, Finney JW, Morale AR, et al: Cardiac Resuscitation with Hydrogen Peroxide. *Circ* 1965; 31(suppl 11): 11 - 21.
 28. Finney JW, Urschel HC, Balla GA, et al: Protection of the Ischemic Heart with DMSO alone or DMSO with Hydrogen Peroxide. *Ann NY Acad Sci* 1967; 151: 231 - 241
 29. Gaffney F et al. Hydrogen Peroxide contrast Echocardiography. *American Journal Cardiology* 1983;52:607-9
 30. Balla GA, Finney JW, Aronof BL, et al: Use of Intravenous Hydrogen Peroxide to Promote Wound Healing. *Am J Surg* 1964: 108: 621 - 629.
 31. Takeshita S et al. Intravenous immunoglobulin preparations promote apoptosis in lipopolysaccharide-stimulated neutrophils via an oxygen-dependent pathway in vitro. *APMIS* 2005;113:269-77.
 32. Dockrell H et al. Killing of Blood-Stage Murine Malaria Parasites by Hydrogen Peroxide. *Infection and Immunity* 1983;39:456-459.
 33. Tetsuo M et al. Induction of Interferon-gamma production by Human Natural Killer Cells Stimulated by Hydrogen Peroxide. *Journal of Immunology* 1985;134:2449-32.
 34. Finney JW, Jay BE, Race GJ, et al: Removal of Cholesterol and Other Lipids from Experimental Animal and Human Atheromatous Arteries by Dilute Hydrogen Peroxide. *Angiology* 1966; 17: 223 - 228
 35. See DM, Tilles JG. Immunol Invest. alpha-Interferon treatment of patients with chronic fatigue syndrome. 1996 Jan-Mar;25(1-2):153-64.
 36. Brook MG, Bannister BA, Weir WR. Interferon-alpha therapy for patients with chronic fatigue syndrome. *J Infect Dis.* 1993 Sep;168(3):791-2.
 37. Lloyd A et al. A Double-blind, Placebo-controlled Trial of Intravenous Immungobulin therapy I Patients wit Chronic Fatigue Syndrome. *The American Journal of amedicine*;89:561-9.
 38. Rowe K et al. Double-blind Randomized controlled Trial to Assess the Efficacy of Intravenous Gammaglobulin of the Management of Chronic Fatigue syndrome. *J psychiat Res* 1997;31:133-45.
 39. Takeshita S et al. Intravenous immunoglobulin preparations promote apoptosis in lipopolysaccharide-stimulated neutrophils via an oxygen-dependent pathway in vitro. *APMIS* 2005;113:269-77.
 40. Wentworth P Jr, McDunn JE, Wentworth AD, Takeuchi C, Nieva J, Jones T, Bautista C, Ruedi JM, Gutierrez A, Janda KD, Babior BM, Eschenmoser A, Lerner RA. Evidence for antibody-catalyzed ozone formation in bacterial killing and inflammation. *Science.* 2002 Dec 13;298(5601):2143-4.
 41. Medwatch: The FDA Medical Products Reporting Program COPAXONE (glatiramer acetate) Injection. July 6, 2000.
 42. Physicians Desk Reference. Medical Economics Thomson Healthcare, 2005

