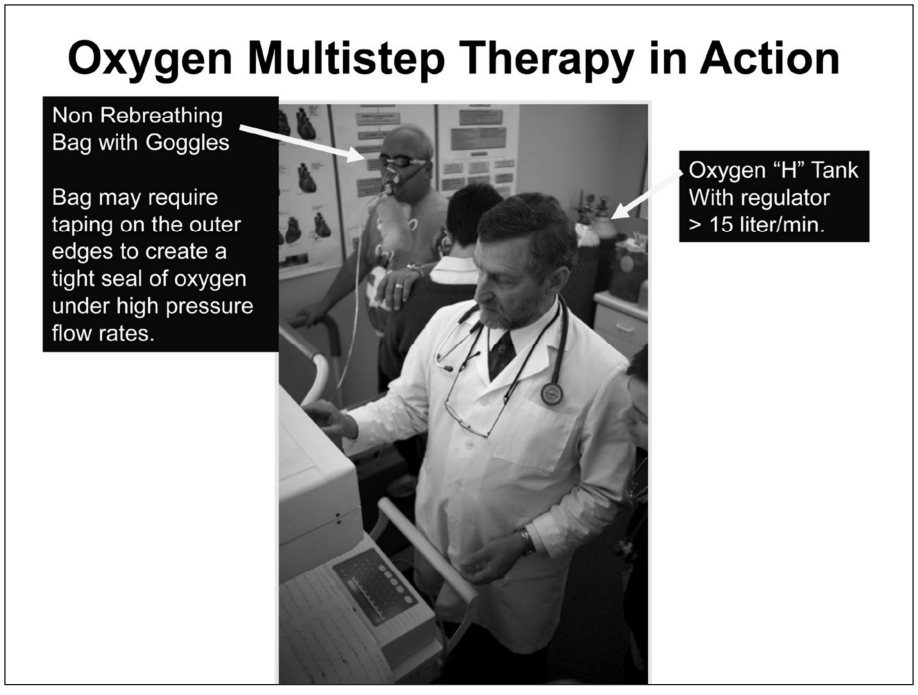
Oxygen Multistep Therapy Enhancing Intracellular Oxygen: A Case Study

by Martin Milner, ND, and Janna Redding, ND

Cellular health determines the health of the organism, and oxygen plays a crucial role in optimum cellular development, maintenance, and repair. The extent of diseased tissue is in part determined by how long it has been deprived of optimal intracellular oxygen.[1] Clinical treatments focused on enhancing delivery and cellular uptake of oxygen may prove useful in the treatment of diseases associated with vascular compromise and/or chronic hypoxia. Below we present a technique called oxygen multistep therapy (OMST). OMST was developed by German physician and researcher Dr. Manfred von Ardenne et al. in the 1970s to facilitate the utilization of oxygen while improving endothelial cell dysfunction and reducing endothelial cell adhesion.[2]

What is Oxygen Multistep Therapy?

OMST has been implemented in various clinical settings to promote healing and regeneration of tissues. Dr. Martin Milner, medical director at the Center for Natural Medicine (CNM) in Portland, Oregon, was introduced to OMST in 1983 by Dr. Marvin Schweitzer. Schweitzer, speaking fluent German, had the opportunity to train directly with von Ardenne in Eastern Europe, where he learned different OMST techniques.



In his publication *Oxygen Multistep Therapy: Physiological and Technical Foundations,* von Ardenne explained how OMST produces its remarkable effects. By the patient's exercising while breathing high flow rates of oxygen, an arterial pressure and cellular oxygen regulating mechanism occurs that von Ardenne refers to as a "switching mechanism" at the microcirculation level and greatly increases the amount of oxygen delivered to cells.[3]

In an ideal situation, the pressure of oxygen in the arteries will be almost the same as the pressure in the alveoli. This is the case in younger individuals. However, with age, the arterial pressure of oxygen declines and the amount of oxygen that is able to enter the cell is diminished.[4] OMST helps raise the arterial pressure of oxygen back to youthful levels. Furthermore, von Ardenne proved that after OMST, the pressure of oxygen (pO2) in the arterioles increased while venous pO2 is reduced, confirming increased uptake of cellular oxygen.[5] Research starting in 1977 demonstrates the effectiveness of this therapy in a variety of clinical settings, and OMST techniques are now employed worldwide.

Indications

OMST may be helpful for the following conditions: coronary artery disease (with or without angina), post-stent deployment or CABG (coronary artery bypass graft)

procedure, intermittent claudication, and peripheral artery disease. It promotes accelerated wound healing after operation or infection and may prevent the necessity of amputation. It may also improve cancer outcomes, mental acuity, macular degeneration, hepatic failure, and migraines.[2]

Hypothetically OMST could be considered a third-line treatment after high flow rates of oral oxygen or hyperbaric oxygen therapy for carbon monoxide poisoning. Additionally, improvements may also be seen in small vessel coronary artery and peripheral vascular disease, stroke rehabilitation, and in exercise performance reserve that has been impaired by lack of activity after a serious illness. At CNM we also use OMST as an adjunctive therapy in certain cancer patients and to enhance athletic performance in elite athletes.

Potential Contraindications

Precaution should be taken with those who have underlying lung compromise such as chronic obstructive pulmonary disease (COPD). Recent studies have shown that when COPD patients who have chronically compensated elevated CO2 levels (known as "CO2 retainers") are in respiratory compromise and are put on high flow supplemental oxygen, the CO2 in their blood may increase.[6,7] This can further inhibit their hypercarbic drive and either put them into respiratory failure or worsen their current level of respiratory distress. We therefore recommend that all individuals with risk factors for lung disease perform pulmonary function testing before engaging in OMST. At CNM we have developed low flow oxygen delivery modifications, allowing us to safely use OMST with many COPD patients while carefully monitoring for changes in oxygen saturation during and after exercise.

OMST Procedure in the Clinical Setting

After the patient's lung function has been confirmed to be within normal limits with spirometric testing, the patient is exercise tolerance tested (ETT). Depending upon the patient's activity limitations, a treadmill, a recumbent bicycle, or an arm bicycle machine is used as exercise equipment. ETT is then performed at a target aerobic heart rate of 50% to 80% of maximum heart rate prior to participation in OMST or any other exercise-based cardiac rehabilitation program. After OMST or cardiac rehabilitation is completed, intermittent and ongoing ETT is strongly recommended and may be repeated as changes in the patient's clinical condition warrant.

One of the many OMST exercise protocols involves the patient's being primed with oral and sublingual nutrients before the procedure. These agents help the uptake and utilization of oxygen, and are customized for each individual based on his/her presentation and problem list (see Table 1). In our standard protocol, the patient's target aerobic heart rate is then calculated at 50% to 80% of maximum heart rate. Oxygen is delivered through a non-rebreathing bag at high flow rate of 15 to 25 liters per minute. The edges of the oxygen mask are sealed with tape and the patient's eyes are protected with goggles. Eye goggles are worn to eliminate the risk of high flow oxygen leaking through the sides of the non-rebreathing bag from damaging the oxygen-sensitive surface of the cornea of the eye. The patient is exercised until the target aerobic heart rate is achieved and maintained for 15 minutes followed by a 3- to 5-minute cool down period. At our facility, continuous treadmill electrocardiogram (ECG) monitoring is performed to assess changes in cardiac rhythm and ischemic status.

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Table 1

√	Pill#	Supplement
❑	___	Arginine 500 mg, vasodilator via nitric oxide
❑	___	Coenzyme Q10 100 mg, antioxidant
❑	___	Dimethylglycine, 125 mg, oxygenator, glutathione precursor
❑	___	Grapeseed extract, slow release, platelet aggregation inhibitor, improves small vessel circulation
❑	___	G-strophanthin, alkalinizing to myocardium, 6 mg
❑	___	L-glutamine, 500 mg, glutathione precursor
❑	___	Magnesium glycinate, 120 mg, vasodilator
❑	___	Magnesium orotate, 100 mg
❑	___	NAC (N-acetylcysteine), 600 mg, quenches nitric oxide as glutathione precursor
❑	___	Niacin 250 mg, immediate release, vasodilator
❑	___	Niacin 500 mg, slow release, vasodilator
❑	___	Oxy Quench (antioxidant), 1–2
❑	___	*Panax ginseng*, 50 mg
❑	___	Resveratrol, 100 mg, slow release
❑	___	Rx, dipyridamol 25, 50, 75 mg Rx 50 mg/70 kg BW, platelet aggregation inhibitor, dilates coronary arteries
❑	___	Rx, Hydralazine, peripheral vasodilator, 10 mg (contraindicated in CAD)
❑	___	Vitamin B complex, active form, sublingual, 1–2, cellular energy
❑	___	Vitamin B 1 (thiamin), 30 mg, swallow, cellular energy
❑	___	Vitamin B 15, pangamic acid, 30 mg
❑	___	Vitamin C, 1000 mg, 1-2-3, swallow, antioxidant
❑	___	Vitamin E 1:1, high gamma-tocopherol, antioxidant vasodilation protection

The clinician chooses one of the three between L-arginine, dipyridamol, or Hydrazine as best vasodilator at the safest dose given the patient's resting blood pressure. Vasodilators may be contraindicated in cancer patients. Beware of the agonistic effects of adding magnesium and niacin with other vasodilators. When giving L-arginine or nitroglycerin directly, add vitamin E 1:1 high gamma-tocopherol and/or CoQ10 and consider adding the glutathione precursors of dimethylglycine, glutamine, and cysteine or NAC. Glutathione, gamma-tocopherol, and CoQ10 quench the adverse effects of nitric oxide.

Oxygen Multistep Therapy

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Case Study: Postsurgical Bicuspid Aortic Valve Replacement

This therapy is particularly useful as a replacement for, or an addition to, postsurgical cardiac rehabilitation therapy. As with conventional cardiac rehabilitation, OMST further maximizes chances of collateral small vessel formation with increasing load to safe maximum tolerance. Below we discuss the case of a 68-year-old female who performed a total of six OMST treatments at CNM with favorable results.

M. T. is a delightful person who first presented to our clinic 4 months after surgery for bicuspid aortic valve replacement. Her main postoperative complaints were of fatigue, insomnia, and digestive distress. She had no history of concomitant hypertension, congestive heart failure, chest pain, or stroke. Her medications included metoprolol, a selective beta-1 receptor blocker, which appeared to be contributing to her fatigue and lethargy. We explained the necessity of continuing this medication for at least 9 months after surgery to minimize the load on the heart during the cardiac remodeling phase. It was at this time that we scheduled her initial ETT.

The patient's resting electrocardiogram revealed a right bundle branch block, but was otherwise normal. She had taken metoprolol 2 hours before the procedure. Her target aerobic heart rate was calculated to range from 103 to 122 bpm at 50% to 70% of her maximum heart rate. The patient was exercised for 5 minutes until the target aerobic heart rate of 103 bpm was achieved; 120 bpm was achieved at 10 minutes. Although M. T. appeared fatigued, she completed a satisfactory pretreatment ETT, and we subsequently prescribed a once weekly series of three OMST treatments. She was instructed to hold her morning dose of Metoprolol before exercise sessions in order to achieve an increased target heart rate of 115 to 126 bpm at 60% to 70% of her maximum.

Table 2

	Dysrhythmia During Exercise	Dysrhythmia During Recovery
Pre-Tx ETT	None*	None*
OMST #1	None	3 isolated PVCs 5 bigeminal paired PVCs
OMST #2	4 isolated PVCs during stage II 1 isolated PVC at stage III 4 isolated PVCs at stage IV	2 isolated PVCs
OMST #3	7 isolated PVCs during stage III 1 isolated PVC at stage IV	7 isolated PVCs

* beta blocker was likely controlling heart rate and rhythm

Table 3

	Dysrhythmia During Exercise	Dysrhythmia During Recovery
OMST #4	None	None
OMST #5	1 isolated PVC during stage II	2 isolated PVC 1 bigeminal paired PVC
OMST #6	None	3 isolated PVC
Post-Tx ETT	None	1 isolated PVC

After the first three treatments, the patient reported an increase in energy and improved exercise tolerance. Frequent and intermittent isolated premature ventricular contractions (PVCs) and occasional bigeminal PVCs were observed during exercise and recovery (see Table 2). These beats were not associated with symptoms and resolved after 10 minutes of rest. Our impression was that she might benefit from further oxygen therapy, and we recommended a series of three additional OMST treatments. We also increased her exercise intensity in order to achieve a heart rate of 125 to 134 bpm, 70% to 80% of her maximum heart rate.

M. T. noted a significant increase in energy and well-being after completion of the second three treatments, and premature beats were reduced (see Table 3). She denied any symptoms of palpitations or shortness of breath with exertion. Her sleep had significantly improved and most of her initial presenting complaints had resolved. Overall, her outward demeanor and vigor were noticeably enhanced. She made an appointment with her MD cardiologist, who, after reviewing an echocardiogram that showed good left ventricular function, agreed to let her wean off metoprolol with close monitoring of blood pressure.

The patient was instructed to continue with home exercise at a target heart rate of 130 bpm for 30 minutes every other day. In addition to this we prescribed a customized nutrient packet for her to take before exercise to encourage oxygen utilization that included the following:

- 4 capsules arginine (500 mg each)
- CoQ10 100 mg
- dimethylglycine sublingual 250mg
- magnesium glycinate 120 mg
- active B complex, 1 tab sublingual
- vitamin E 1:1 (gamma-tocopherol), 400 IU

Clinical Application and Implications

The effects of OMST are promising and potentially far reaching in the management of a wide range of conditions associated with impaired oxygen uptake and cellular utilization. It is clear that more clinical research and case studies should be conducted in this regard to further substantiate efficacy. This protocol would also lend itself to a double-blinded prospective study. We are continuing to pursue clinical application of this therapy, and encourage physicians interested in promoting optimal health in their patients to consider doing the same.

Notes

1. Kumar V, Abbas AK, Fausto N. *Robbins & Cotran Pathologic Basis of Disease*. 7the ed. Elsevier Health Sciences; 2004:11–12.
2. Von Ardenne M. *Oxygen Multistep Therapy Physiological and Technical Foundations*. Thieme Medical Publishers; 2000.
3. Ibid.
4. Blom H, Mulder M, Verweij W. Arterial oxygen tension and saturation in hospital patients: effect of age and activity. *BMJ*. September 17, 1988;297(6650):720–721. PMCID: PMC1834124.
5. Von Ardenne. Ibid.
6. Kim V, Benditt JO, Sharafkhaneh A. Oxygen therapy in chronic obstructive pulmonary disease. *Proc Am Thorac Soc*. 5(4):513–518, May 1, 2008.
7. Austin MA, Wills KE, Blizzard L, Walters EH, Wood-Baker R. Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomized controlled trial. *BMJ*. Oct. 19, 2010;341:c5462. http://dx.doi.org/10.1136/bmj.c5462.
8. Nunn JF. *Nunn's Applied Respiratory Physiology*. 2nd ed. Boston: Butterworths 1977:375.
9. TK Hunt, B Zederfeldt, TK Goldstick. Oxygen and healing. Am *J Surg*. 1969;1(18):521–525.

No economic conflicts of interests are associated with this publication. ◆

Martin Milner, ND, has been in private practice since 1983 and is the medical director of the Center for Natural Medicine Inc. CNM functions as an integrated group medical practice, a naturopathic patient-centered primary care home (PCPCH), and as a teaching clinic of National College of Natural Medicine (NCNM). CNM is also active in research with both Helfgott Research Institute and Naturopathic Education and Research Consortium (NERC). Dr. Milner is the professor of cardiovascular and pulmonary medicine at NCNM and has been since 1987. He is the 2013 recipient of the prestigious NCNM-OANP Living Legend Award. He continues to supervise and mentor 48 ND student interns per year in the Heart & Lung Wellness Program, which he has maintained since 1999. He trains two ND residents each year, one who assists him in the Heart & Lung Wellness Program, currently Dr. Nathaniel Bingham, and one in his private practice, currently Dr. Janna Redding. Dr. Milner is actively pursuing the creation of the first board certification program for NDs in naturopathic cardiology with Dr. Jeremy Mikolai (his former chief resident, current coattending physician in the H&L program, and current first Integrated Cardiovascular Medicine Fellow at NERC). In December 2013, NCNM announced the formation of the first in the world Center of Excellence in Naturopathic Cardiovascular Medicine, a collaborative alliance between the Center for Natural Medicine's Heart & Lung Wellness program, NCNM, and the Helfgott Research Institute at NCNM.

Janna Redding, ND, is the Center for Natural Medicine's resident physician under the mentorship of Dr. Martin Milner. She earned her BS degree in general science with an option in physical therapy and graduated magna cum laude from Oregon State University in 2006. Her interest in health care from a holistic perspective led her to the National College of Natural Medicine, where she completed her naturopathic doctorate in 2012. While at NCNM, Dr. Redding completed two specialized rotations with Dr. Milner, focusing on cardiopulmonary (heart and lung) and endocrine (hormone) conditions. During her medical training, she also developed an interest and gained experience in treating neurotransmitter imbalances as related to immune and endocrine function. She is invested in individualized care, and committed to promoting and maintaining overall wellness in her patients.