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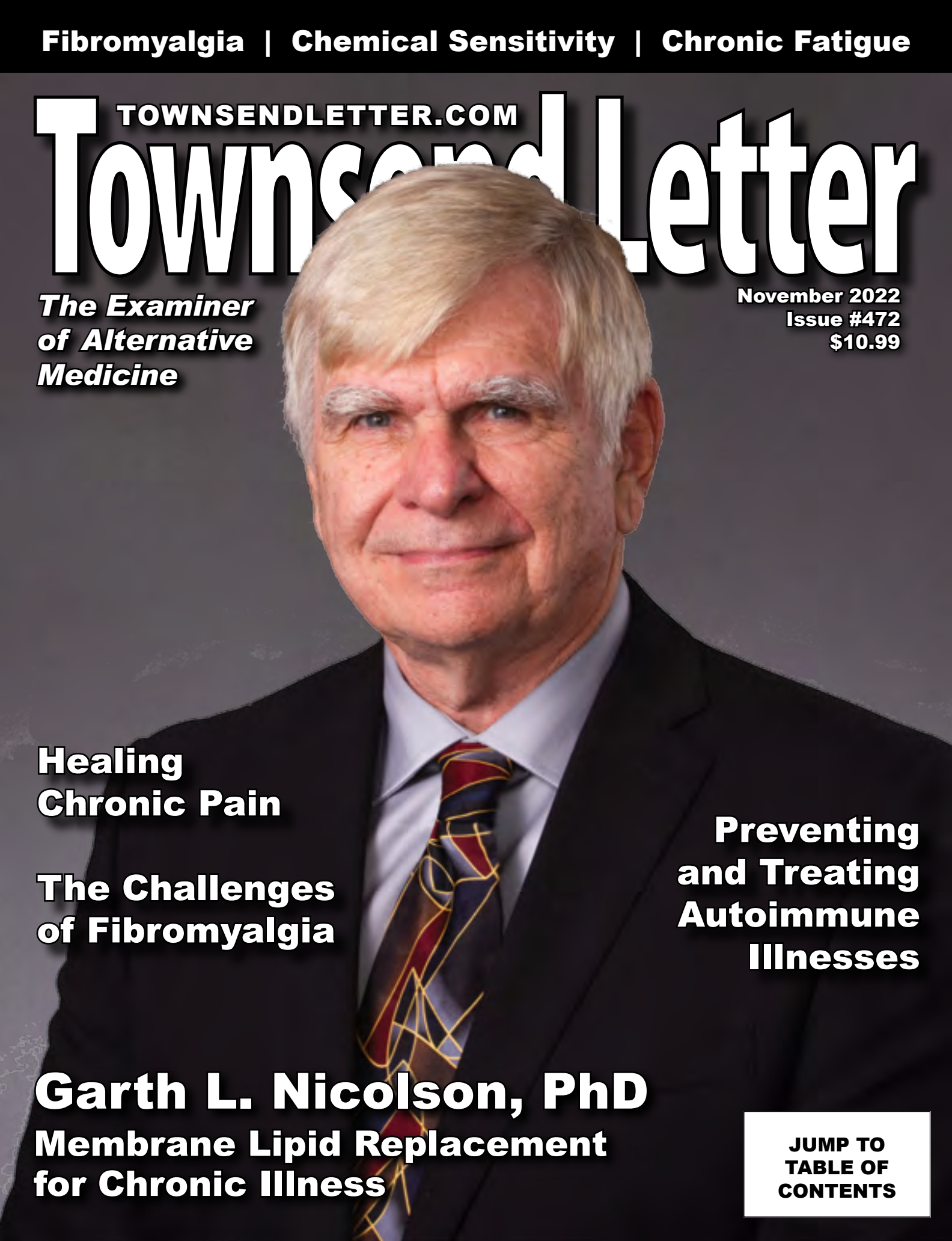

Healing Chronic Pain

The Challenges of Fibromyalgia

Preventing and Treating Autoimmune Illnesses

Garth L. Nicolson, PhD
Membrane Lipid Replacement for Chronic Illness

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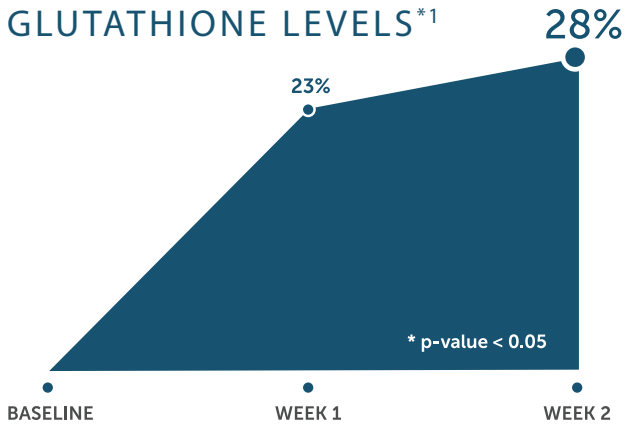

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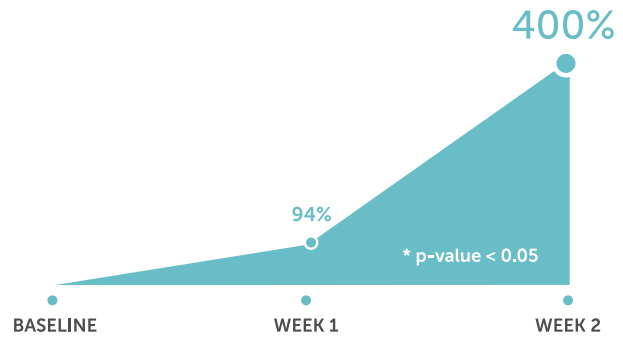

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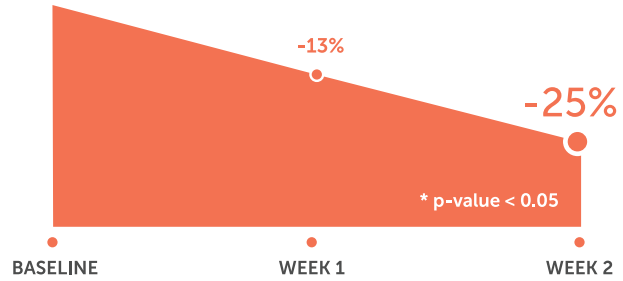

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[1]Sinha R, Sinha I, Calcagnotto A, et al. Oral supplementation with liposomal glutathione elevates body stores of glutathione and markers of immune function. Eur J Clin Nutr. 2018;72(1):105-111. doi:10.1038/ejcn.2017.132

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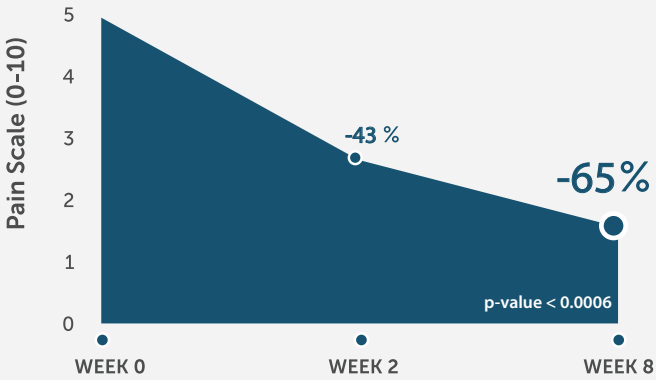

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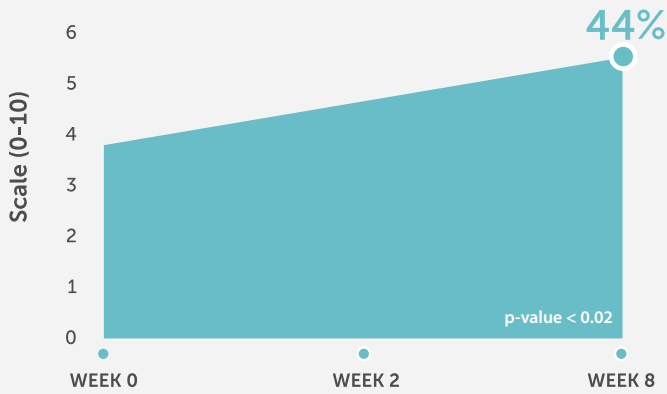

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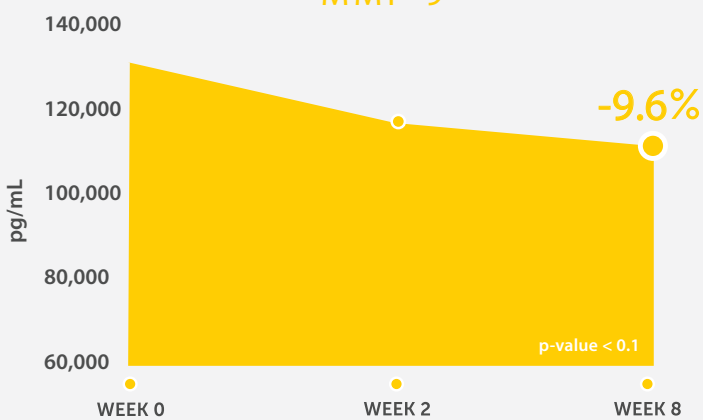

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[1] Journal of Pain Research (D Hamilton, G Jensen). Pain reduction and improved vascular health associated with daily consumption of an anti-inflammatory dietary supplement blend. J Pain Res. 2019; 12: 1497–1508.

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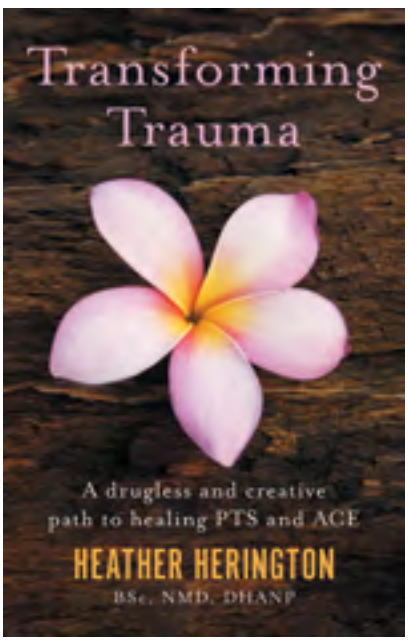
From the Publisher

Book Review: *Transforming Trauma*
by Heather Herington, NMD

Post-Traumatic Stress Disorder (PTSD) is a condition we associate with war veterans who have been physically and mentally traumatized in the course of their military operations.



For not a few veterans the traumatic event(s) they experienced triggered an overwhelming state of fear and anxiety that their brains would not and could not process adequately. Subsequently these individuals face a state of hypervigilance, hyperreactivity, avoidance of triggers reminding them of the trauma, and continuous re-experiencing of the event(s) mentally. The overbearing fear and anxiety cause nightmares, temper tantrums, anti-social behavior, and inability to live life purposefully. PTSD is not, of course, limited to military personnel; all first responders and emergency workers are subject to similar events of violence and endangerment, setting up a triggering trauma. Non-professionals, especially refugees fleeing war zones, as well as victims of terrorism are also at high risk from encountering one or more experiences subjecting them to PTSD. Serious accidents and natural catastrophes pose long-term mental risks for survivors.

Of course, one of the largest cohorts of PTSD victims have never faced a war zone or car accident. Instead they were assaulted sexually, frequently raped, and were largely powerless to fight back. Sexual trauma to the child is particularly egregious given the perpetrator's familiarity to the child. The parents who sell off their children to traffickers are probably intergenerational victims of sexual child abuse themselves. It is of note that those trafficked and forced into prostitution may not be suffering as much PTSD as the victim of a single rape, but each person experiences PTSD differently. Statistically we experience more PTSD in the US than anywhere else in the world with the exception of countries in Asia. Women experience PTSD nearly twice as often as men; it is likely that 10% of us will face post-traumatic stress before we die. For a condition that affects us so broadly, one would expect the medical profession would be able to offer effective diagnosis and treatment. Unfortunately, while a diagnosis may be forthcoming, treatment is not necessarily effective and is difficult.

Dr. Heather Herington's soon to be released book, *Transforming Trauma*, offers a "manual" for integrative and naturopathic physicians (as well as clients) to understand PTSD thoroughly with a comprehensive approach to treating the condition without drugs. Herington has experienced PTSD herself; she refers to the condition as PTS dropping the "D," calling it post-traumatic stress. Dr. Herington developed autoimmune thyroiditis as an adult, which was treated conventionally but without good results. When she inferred that PTS may be an underlying factor to her development of thyroid disease, she embarked on a journey to transform her trauma, which as she discovered was sexual abuse and assault. As a naturopathic physician she also employed the naturopathic and biochemical supports needed to restore her thyroid gland. However, it was the work she had done in understanding her trauma that reversed her thyroid disease. Based on the very effective results she experienced for herself, she devoted much of her professional work to helping others who have experienced PTS. Not surprisingly, she found herself

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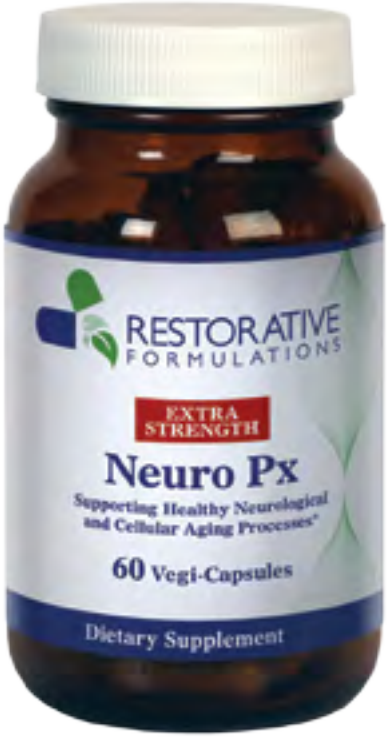

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From the Publisher

➤ *continued from page 2*

treating many women who also encountered sexual assault and who had not addressed their trauma. Herington's work with women PTS victims was greatly empowering; women survivors not only were able to work out their PTS but also restore vitality in their health as well as resilience and happiness in their work, family life, and overall well-being. *Transforming Trauma* is not only a "how-to-do-it" book, but an articulate and enjoyable testimony to Herington's experiences on her teaching path.

For those who are looking for something more than handing a patient a referral to a psychiatrist or counselor, for those who want more than a prescription of an SSRI, this book is also a primer for the PTS individual to consider what is needed to break the pattern of hypervigilance, nightmare, and shutdown. Herington examines the neuroanatomy involved in PTS – the prefrontal cortex, the hippocampus, and the amygdala are all involved. Many individuals are depleted nutritionally and toxic biochemically; of course, lab evaluation is helpful in assessing one's deficiencies and imbalances. Herington advises vitamin supplements and herbal extracts rather than pharmaceuticals. Additionally, she embraces the power of homeopathy in helping to calm the terrors that PTS engenders.

What does one do to get the PTS individual to face the trauma and the triggers? Of course, there is therapy, but Herington prefers active engagement by the individual to actively face the demons. Instead of talk she prescribes journaling or writing verse. Rather than always verbalizing, why not sing about the emotion experienced or even paint it? Indeed, for some the best means to face the trauma is to engage it through self-acting, even as an improvised theatrical play. All of these arts require that the anxious, fearful individual participate mindfully, learning how to center oneself though meditative contemplation. Breathing is a very powerful tool to Heather; almost any moment of crisis can be brought to calmness through breathing.

For those docs who are experiencing burnout, or something similar, *Transforming Trauma*, may be the perfect guidebook to getting one's life back and restoring wholeness as a healer. I would strongly recommend it for those docs who need to revitalize their lives!

Are Anti-Hypertensives Better to Take in the Morning or Evening?

The elderly (and middle-aged) are becoming increasingly medicated to manage and prevent cardiovascular health. Hypertension, coronary artery disease, atrial fibrillation, hypercholesterolemia, and atherosclerosis necessitate intervention generally of the pharmaceutical variety. Of course, functional medicine and naturopathic support lessen such drug dependency. Nevertheless, many patients use one or more medications to control their circulation. The question is does the anti-hypertensive work better in the morning or at night.

The answer according to Dr. Russell Foster, director of the Sleep and Circadian Neuroscience Institute of Oxford University, is before bed – definitely. An excerpt of his book, *Life Time: Your Body Clock and Its Essential Roles in Good Health and Sleep*, just published by Yale University Press, was published in the August 13, *Wall Street Journal.*

The reasoning is that it takes time for the drug to assimilate and be metabolized. Taking the blood pressure medication before sleep allows four-to-six hours to reach peak levels and break down into active metabolites by early morning, the time period when heart

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From the Publisher

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attack and stroke risk is highest (from 6 am to noon). Most patients are informed to take their cardiovascular meds in the morning; unfortunately, this leaves them vulnerable to the most dangerous time for cardiovascular events, what the Germans call Todesstreifen or "death zone," the term used in the 1960s-80s if a person were to amble into the no-man land between East and West Berlin.

It would make sense for those advising herbals as anti-hypertensive medication to instruct their patients to take the extract at night using the same reasoning. Although research has not confirmed taking anti-coagulation therapy in similar fashion, it would probably be logical to take aspirin or anti-coagulant therapy at night to achieve protection against increased blood clotting in the morning when heart attacks and strokes are more common.

In this issue Raul Ibarra, MD, writes about biological rhythms not just over 24 hours but also over the month, season, and year. We certainly acknowledge this during pre-menopause, noting different estrogen and progesterone levels as the month proceeds. For this reason, practitioners may advise supplementation of estrogen earlier in the month and progesterone later in the month. It has been my personal experience that women occasionally need higher dosing of their thyroid treatment during the winter compared to the summer, but I have not read confirming research. There have been reports that the timing of breast cancer surgery, mid-cycle versus at menses, impacts survival; most recent reports fail to establish that there are significant survival benefits based on timing of such surgery.

NEJM Randomized Trial Fails to Show Benefit of Ivermectin for Covid-19

We have published a number of reports over the past three years stating that ivermectin has an effective role in the treatment of Covid-19. The August 19th *NEJM* randomized trial using three drugs, metformin, ivermectin, and fluvoxamine failed to show any benefit in prevention of hypoxemia, emergency room visits, hospitalizations, or death for Covid-19 infection.[1] Only metformin demonstrated slight benefit for Covid-19 treatment, not ivermectin, nor fluvoxamine. Unfortunately, the investigators skewed the study by intentionally limiting the administration of ivermectin to three days while the metformin and fluvoxamine were both given for 14 days. The FLCCC protocol recommends ivermectin to be used for five days or until symptoms resolve. In other words, there is a reasonable likelihood that ivermectin may have had benefit if patients received a full treatment course for the two weeks.

Meanwhile, the *NEJM*'s faulty study adds to the growing collection of reports failing to show ivermectin's benefit for Covid-19.

Cover Article: Membrane Lipid Replacement with NTFactor Lipids® by Prof. Garth Nicolson, PhD

Long-time readers of the *Townsend Letter* are familiar with Dr. Garth Nicolson's work with the proprietary supplement, NTFactor Lipids®, on chronic fatigue, chemical sensitivity, brain fog, and pain. He has co-authored numerous articles about membrane lipid replacement (MLR) in this publication as well as numerous other journals. What I did not realize is Prof. Nicolson's major contribution to medicine and science together with Dr. Seymour Singer with the publication, in 1972, of their "fluid mosaic model" to describe functioning of cell membranes.[2] Nicolson and Singer's work demonstrated that previous descriptions of the cell membrane structure were incorrect from a thermodynamic vantage point. Nicolson and Singer established that the membrane was composed of a lipid bilayer with embedded proteins enabling elasticity and fluidity. The liquid characteristic of the bilayer restricts diffusion of lipid and protein components. So important is the functioning of the bilayer membrane that numerous cell activities depend on its integrity, including cell division, apoptosis, and cell signaling.

Nicolson has been a professor at numerous universities and medical centers, including the University of California at Irvine, University of Texas, Texas A & M, the Salk Institute for Biological Studies, and the University of New Castle in Australia. His work in biochemistry and cell biology focused on cancer biology at the MD Anderson Cancer Center in the 1980s and on internal medicine at the University of Texas in the 1990s. Nicolson founded the Institute for Molecular Medicine in 1996 where he continues to conduct his research. He is recognized as a major authority on the cause and treatment of Gulf War syndrome. Based on his research the condition is thought to not only have a chemical causation but also a biologic one that appears to have had a possible biologic warfare origin by a bacterium named *Mycobacteria fermantens*.

Nicolson et al.'s article in this issue discusses the *in vitro* research of NTFactor Lipids' effect on intestinal absorption of CoQ10, curcumin, and quercetin. Additionally, the authors studied the role membrane lipid replacement treatment plays in treating Gulf War veterans. Nicolson posits that with the aging process disrupting optimal membrane functioning, MLR should be considered as an anti-aging support.

Jonathan Collin, MD

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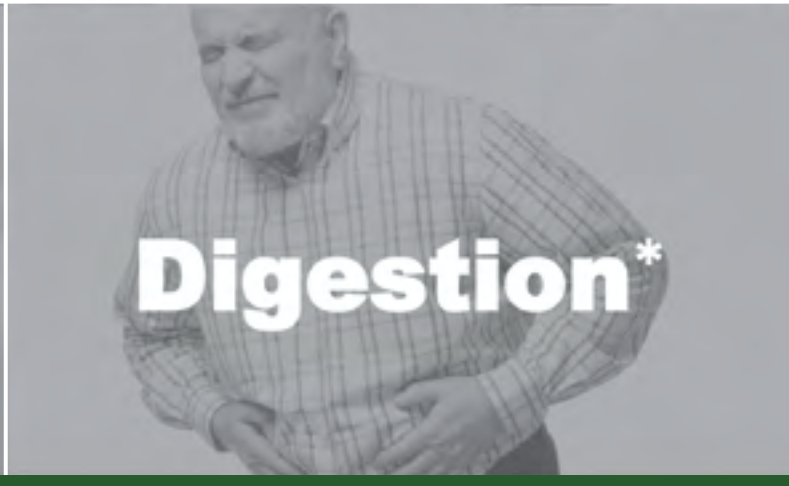

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Shorts

briefed by Jule Klotter
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Low-Dose Naltrexone for Fibromyalgia

Two European randomized, placebo-controlled, double-blind studies are testing the effects of low-dose naltrexone (LDN) in women with fibromyalgia. Naltrexone, used to prevent relapse in people with opioid or alcohol addictions, has an analgesic effect when given at low doses. For several years, it has been used off-label to treat pain and inflammation in people with fibromyalgia (FM) as well as multiple sclerosis and Crohn's disease. Although the US FDA has approved three drugs for treatment of FM (pregabalin, duloxetine, and milnacipran), the European regulators have not; they rejected the drugs because of the small effect size in trials and the drugs' adverse effects. These LDN trials may provide the evidence needed to gain European approval for FM treatment.

The first trial (NCT04270877) at a single center in Denmark aims to enroll 100 women (age 18-64 years) who fulfill the American College of Rheumatology 1990 criteria for FM and have a minimum pain score – averaged over 7 days – of 4 on a 0-10 scale. Exclusion criteria include pregnancy or breastfeeding, use of opioids or NSAIDs up to 4 weeks before the trial, substance abuse, known inflammatory or demyelinating disease, liver or kidney dysfunction, active cancer, suicide ideation, or known allergy to naltrexone hydrochloride. The participants will be randomly assigned to receive a placebo or LDN for 12 weeks.

During the first four weeks, the LDN cohort will follow a dose-escalation plan, beginning with a daily dose of 1.5 mg (taken between 7 pm and 11 pm) for one week that will be increased by 1.5 mg each week until a dose of 6 mg (or highest tolerated dose level) is achieved in week four. The Danish researchers had previously tested a range of doses and found that 3.88 mg reduced pain in 50% of tested FM patients and 5.40 mg reduced pain in 95% of the patients. They decided to aim for 6.0 mg in this study since patients were able to tolerate doses that ranged from 4.5 mg (the dose commonly used in studies) and 6.0 mg.

The primary measure is average pain intensity (over the last 7 days of the trial), using the first item in the symptom part of the Fibromyalgia Impact Questionnaire Revised. In addition, secondary outcomes, including pain distribution, fatigue, sleep disturbance, depression, anxiety, cognition, stiffness, physical function, and quality of life measures will be accessed. Blood collected at baseline and after 12 weeks will be analyzed for pro- and anti-inflammatory cytokines. Also, exploratory outcomes regarding muscle exhaustion, pain sensitivity, and variations in pain will be investigated. According to the ClinicalTrials.gov site, the estimated completion date for this study is June 2023.

The second LDN randomized study is a phase III trial being conducted at a single center in Spain (NCT04739995). The INNOVA study is testing the effect of 4.5 mg of LDN/day for 12 months against a placebo in 120 women with FM (60 patients in each group). All patients will also receive usual care for FM from the Spanish National Health System. The participants must fulfill the American College of Rheumatology 2016 criteria for FM and have a pain intensity of ≥4 out of 10 on a 10-point scale in the previous week. The exclusions are similar to the Danish trial.

Like the Danish trial, this trial's primary endpoint is pain intensity, and numerous secondary outcomes will be assessed using several questionnaires. The participants will undergo clinical assessment at baseline, 3 months, 6 months, and 12 months. They will also use a smartphone app (Monitor de Dolor) to track daily pain intensity, fatigue, perceived control over pain, depression, anxiety, stress, sleep disturbance, activity level, interference with leisure activities and work-related activities, adverse effects, and rescue medications. Inflammatory biomarkers in blood samples will be measured at baseline and at three months, and half of the participants in each group will undergo MRI scans at the same timepoints "to explore the neurobiological underpinnings of LDN." The estimated completion date is December 31, 2024.

The Spanish researchers hope that their INNOVA study and the Danish FINAL study can "facilitate the approval of the first drug indicated for the treatment of FMS in Europe." They add, "If our respective findings strongly differ in efficacy or safety, we might analyze which factors can account for the divergence and plan a multicountry confirmation trial with an agreed design and methodology."

Bruun KD, et al. Low-dose naltrexone for the treatment of fibromyalgia: protocol for a double-blind, randomized, placebo-controlled trial. *Trials.* 2021; 22.804.

Colomer-Carbonell A, et al. Study protocol for a randomized, double-blinded, placebo-controlled phase III trial examining the add-on efficacy, cost-utility and neurobiological effects of low-dose naltrexone (LDN) in patients with fibromyalgia (INNOVA study). *BMJ Open.* 2022;12:e055351.

Gene-Environment Interaction in Gulf War Illness

Since the 1991 Persian Gulf War, thousands of military personnel have suffered from Gulf War illness (GWI), consisting of a variety of often debilitating symptoms that include fatigue, memory and concentration impairment, insomnia, vertigo, severe pain, tingling and numbness, and GI disturbance. Although environmental exposures are the likely cause, pinpointing the exact etiological factors has been hampered by lack of objective data. In a 2022 study, Robert W. Haley and colleagues investigated a relationship between polymorphisms in the *PON1* gene that directs the PON1 enzyme (which breaks down organophosphate cholinesterase-inhibiting chemicals, including nerve agents) and GWI. The researchers explain, "QQ homozygous individuals produce only the Q isoenzyme, which efficiently hydrolyzes nerve agents like sarin; RR homozygotes produce only the R isoenzyme, which is relatively ineffective against nerve agents; and QR heterozygotes produce variable proportions of both; moreover, within genotype the level of Q isoenzyme activity varies >10-fold."

The researchers obtained blood samples from 508 veterans who met GWI Research case definition criteria and from 508 veterans who did not have any of the defined GWI symptoms. All participants had been deployed to Kuwait during the war. The researchers also drew on previous research regarding alarms from chemical warfare detection devices that sounded – sometimes more than 10 times a day – after US and Coalition forces bombed Iraqi chemical weapons facilities.

Haley et al found significantly more R polymorphisms in the GWI group compared to the control: (GWI) QQ 24.2%, QR 57.7%, and RR 18.1% vs. (control) QQ 47.7%, QR 39.3%, RR 13.0% ($p<0.001$). In addition, logistic regression analysis showed that GWI increased as the number of nerve agent alarms increased. While this study provides strong evidence that nerve agent exposure is a causal factor in GWI, the authors say it does not exclude other factors that have been implicated by epidemiological studies, including pesticides, pyridostigmine bromide, antibiotics, immunizations, insect repellants, and psychological effects of deployment.

Haley, RW, et al. Evaluation of a Gene-Environment Interaction of *PON1* and Low-Level Nerve Agent Exposure with Gulf War Illness: A Prevalence Case-Control Study Drawn from the US Military Health Survey's National Population Sample. *Environmental Health Perspectives.* May 2022

mRNA Vaccines and Safety

In an April 2022 article for *Food and Chemical Toxicology,* Stephanie Seneff and co-authors present evidence from the scientific literature that shows the SARS-CoV-2 mRNA vaccinations, unlike natural infections, impair innate immune function. Researchers have found that these injections suppress Type I interferon – especially IFN-α, an immune-modulating protein that has a major role in protecting against viral infections and cancers. The injections can also disrupt intracellular communication conducted by exosomes, resulting in significant inflammation. These biological effects, according to the authors, could lead to reactivation of viral infections (including herpes zoster), immune thrombocytopenia, Guillain Barré and neurologic injury, Bell's palsy and other inflammatory conditions, liver damage, and myocarditis.

Unlike traditional vaccines that use an actual live or killed pathogen (antigen) to confer immunity, the mRNA technology instructs the body's cells to create the antigen, to which the immune system responds. In order to keep the body from

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immediately attacking and neutralizing the injected mRNA, "… mRNA vaccines are formulated as lipid nanoparticles containing cholesterol and phospholipids, with the modified mRNA complexed with a highly modified polyethylene glycol (PEG) lipid backbone…." As a result, the mRNA persists in lymph nodes, synthesizing the SARS-CoV-2 spike glycoprotein for up to eight weeks after vaccination (Röltgen K, et al. *Cell.* March 17, 2022; 185(6): 1025-1040).

In addition to a literature review, Seneff and co-authors retrieved data from the Vaccine Adverse Event Reporting System (VAERS), co-managed by the US Food and Drug Administration and the Centers for Disease Control. VAERS was set up in 1990, to act as the nation's "early warning system to detect possible safety problems in US-licensed vaccines." Using the online site http://wonder.cdc.gov/vaers.html, Seneff et al determined the following: "In total, there were 737,689 events reported in VAERS for COVID-19 vaccines in 2021, representing a shocking 93% of the total cases reported for any vaccine that same year." About 60% of the AEs occurred within 48 hours of an mRNA covid injection.

VAERS captures only a 'fraction' of the actual number of AEs, as CDC admits. The high number of covid doses given in 2021 cannot account for the 93% adverse event (AE) rate, as the authors explain in their article. (Agencies recommended two doses and a booster to be fully protected. Only one dose of the flu vaccine is recommended in a year. More doses give more opportunity for adverse events.) Seneff et al broke the numbers down into inflammatory conditions, heart disorders, liver disease, thrombosis, and neurodegenerative disease.

They state: "…we acknowledge that no report to VAERS establishes a causal link with the vaccination. That said, the possibility of a causal relationship is strengthened through both the causal pathways we have described in this paper, and the strong temporal association between injections and reported AEs."

Seneff et al are not the only researchers looking at VAERS. In September 2021, Josh Guetzkow, PhD, used the method that CDC had publicly stated it would use to monitor the safety of these experimental injections – proportional reporting ratio (PRR) using VAERS data. CDC's "Vaccine Adverse Event Reporting System (VAERS) Standard Operating Procedures for COVID-19 (as of 29 January 2021)" states: "CDC will perform PRR data mining on a weekly basis or as needed. PRRs compare the proportion of a specific AE following a specific vaccine versus the proportion of the same AE following receipt of another vaccine…." Guetzkow, a senior lecturer in the Department of Sociology & Anthropology and the Institute of Criminology at the Hebrew University of Jerusalem, used the same comparator vaccines that CDC listed in its guidelines (adjuvanted vaccines like Shingrix and/or Fluad for adjuvanted COVID-19 vaccines).

Puzzled that CDC was not acknowledging any safety concerns when he found safety signals were "loud and clear," Guetzkow asked Children's Health Defense (CHD) legal team to make a Freedom of Information Act (FOIA) request to the CDC. After rejecting CHD's first request as too broad, CHD finally received an email from CDC on June 16, 2022, that stated" "…program staff within the Immunization and Safety Office inform me that no PRRs were conducted by CDC. Furthermore, data mining is outside of the agency's purview; staff suggest you inquire with FDA." The news that CDC said it had not followed its VAERS standard operating procedures for covid quickly spread through alternative news sources.

On July 23, 2022, Zachary Stieber of *The Epoch Times* reported that Dr. John Su, head of the VAERS team at the CDC's Immunization Safety Office, stated in an email to him that CDC had, indeed, been doing PRRs since February 2021. A few weeks later (August 11), Stieber reported that CDC had again emailed him and admitted that the agency had only performed PRRs from March 25, 2022 (over a year after the mRNA vaccines were in use) to July 31, 2022.

The Epoch Times made its own FOIA request, in July 2022, for all CDC reports from the team that was supposed to study VAERS post-vaccination heart inflammation data. CDC informed Stieber that it had not made any reports on myocarditis through October 2021 – even though doctors in the US military were voicing concerns about post-vaccination heart inflammation by April 2021, and CDC itself admitted a link in June 2021.

The CDC spokesperson who contacted Stieber said that CDC had 'misinterpreted' the requests from CHD and *Epoch Times* and referred Stieber to FDA, who said it would conduct empirical Bayesian data mining on VAERS data. As of August 11, 2022, FDA had refused to share its results with *The Epoch Times.*

Guetzkow J. CDC Admits It Never Monitored VAERS for COVID Vaccine Safety Signals. *The Defender.* June 21, 2022.
Guetzkow J. The CDC Gave Me Whiplash. September 3, 2022. https://jackanapes.substack.com.
Seneff S, et al. Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs. *Food and Chemical Toxicology.* 2022;164:113008.
Stieber Z. CDC Admits It Gave False Information About COVID-19 Vaccine Surveillance. *The Epoch Times.* August 11, 2022.

Chronic Fatigue Syndrome and Long Covid

A retrospective descriptive study from Japan sought to differentiate between long covid (aka post-acute sequelae of SARS-CoV-2 infection) and chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). The study involved 279 patients who visited a Japanese Covid-19 aftercare clinic from February 2021 to April 2022. Symptoms of long covid include general malaise, dysosmia (disordered smell perception), dysgeusia (distorted taste sensation), low-grade fever, headache, and hair loss. Fatigue and post-exertional malaise are the most common symptoms of CFS/ME.

The researchers used three internationally standardized sets of CFS/ME criteria to assess the participants: the Fukuda criteria, the Canadian Consensus Criteria (CCC), and the Institute of Medicine (IOM) criteria. "The percentages of patients meeting the three sets of criteria were 17.2% for Fukuda Criteria, 17.9% for the CCC, and 17.9% for IOM criteria. Forty-seven patients (16.8%) met all of the three sets of criteria." Of those 47 patients, 48.9% (n=23) were male and 51.1% (n=24) were female. Usually, the prevalence of CFS/ME is higher in women (about 70-80%) than in men (20-30%).

The authors advise practitioners to be aware that, in some cases, long covid may actually be CFS/ME – particularly if fatigue and post-exertional malaise are prolonged symptoms.

Tokumasu K, et al. Clinical Characteristics of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (M/CFS) Diagnosed in Patients with Long COVID. *Medicina.* 2022;58:850.

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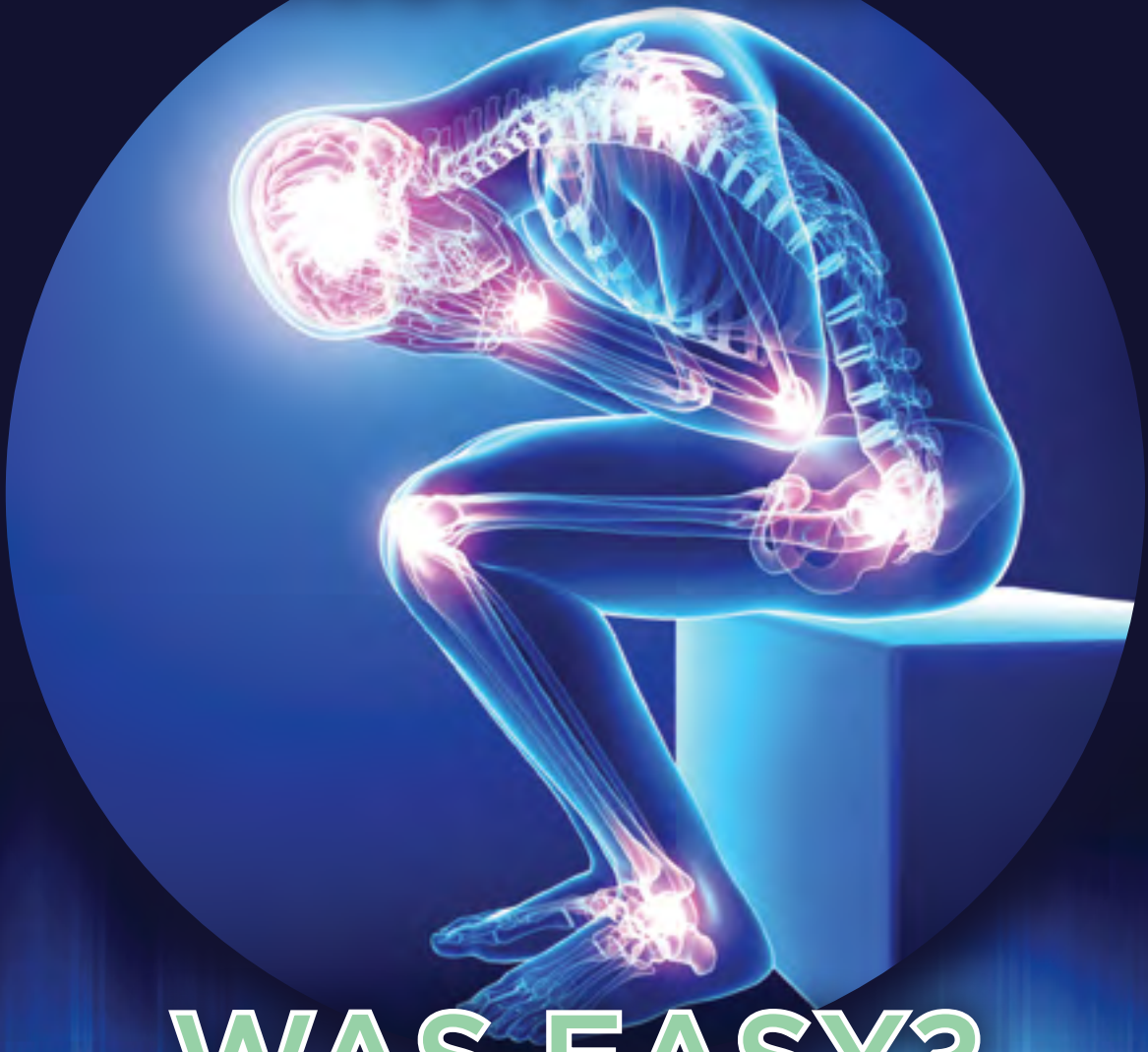
WHAT IF TREATING FIBROMYALGIA



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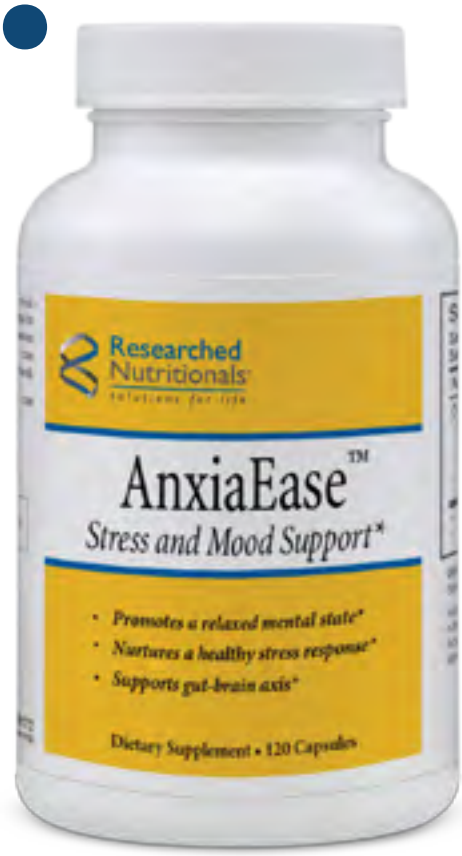

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Literature Review & Commentary

by Alan R. Gaby, MD
drgaby@earthlink.net

Niacinamide and Pyruvate for Glaucoma

Forty-two patients (mean age, 65 years) being treated with intraocular pressure-lowering medication for open-angle glaucoma, who had moderate visual field loss in at least one eye, were randomly assigned to receive, in double-blind fashion, in a 2:1 ratio, the combination of niacinamide and pyruvate or placebo. Niacinamide was used because it increases nicotinamide adenine dinucleotide (NAD) levels and pyruvate was used because it can overcome deficits in glycolysis. The dose of niacinamide was 1,000 mg per day for one week, then 2,000 mg per day for one week, then 3,000 mg per day for one week. The dosage of pyruvate was 1,500 mg per day for one week, then 3,000 mg per day for two weeks. Thirty-two patients completed the study (21 in the treatment group and 11 in the placebo group). The primary outcome measure was the number of visual field test locations that improved beyond normal variability in the study eye. The number of test locations that improved was higher in the treatment group than in the placebo group (median, 15 vs. 7; p = 0.005).

Comment: In this study, the combination of niacinamide and pyruvate produced short-term improvement in visual function in patients receiving medical treatment for open-angle glaucoma. Previous research has suggested that an age-related impairment of mitochondrial energy production by retinal ganglion cells plays a role in the pathogenesis of glaucoma by rendering these cells more susceptible to degeneration and more vulnerable to the adverse effects of increased intraocular pressure. This impairment of mitochondrial function appears to be due at least in part to a decline in NAD levels, which may be reversible by supplementing with niacinamide. The importance of pyruvate is less clear. The results of the present study are consistent with a previous 12-week study in which niacinamide supplementation improved visual fields in glaucoma patients.[1] If these findings can be confirmed in studies of longer duration, it would represent a major advance in the treatment of glaucoma.

De Moraes CG, et al. Nicotinamide and pyruvate for neuroenhancement in open-angle glaucoma: a phase 2 randomized clinical trial. *JAMA Ophthalmol*. 2022;140:11-18.

Interpreting 25-Hydroxyvitamin D Levels in Selected Situations

The median serum 25-hydroxyvitamin D (25[OH]D) level was 4.6 ng/ml in children with steroid-responsive nephrotic syndrome in relapse, 10.6 ng/ml in children with steroid-responsive nephrotic syndrome in remission, and 17.6 ng/ml in healthy controls ($p < 0.001$ for each group of patients vs. controls). However, values for free 25(OH)D did not differ between groups. The levels of parathyroid hormone (which increase in response to vitamin D deficiency) also did not differ between patients and controls. Total 25(OH)D but not free 25(OH)D correlated significantly and inversely with the degree of proteinuria.

In a second study, the mean 25(OH)D concentration was significantly lower in 38 patients with critical illness than in 68 healthy controls (14.8 vs. 22.8 ng/ml). However, the mean estimated concentration of free 25(OH)D was higher in patients with critical illness than in controls (10.4 vs. 7.6 pg/ml; statistical significance not stated).

Comment: I have argued previously that serum 25(OH)D is often an unreliable indicator of vitamin D status. The two studies discussed above illustrate situations in which 25(OH)D is particularly unreliable. Around 99.9% of 25(OH)D in plasma is bound to protein: 85-90% is bound to vitamin D-binding protein and 10-15% is bound to albumin. It is thought that only free 25(OH)D is biologically active. Patients with nephrotic syndrome lose both vitamin D-binding protein and albumin in their urine, and therefore have less of these proteins available to bind vitamin D. In these patients, it appears that a higher-than-normal proportion of circulating vitamin D is in the free form, as opposed to being protein-bound. While the levels of total 25(OH)D were lower in these patients than in healthy controls, levels of biologically active free vitamin D were similar to those of controls. The fact that parathyroid hormone levels did not differ between groups supports the concept that the vitamin D status of children with nephrotic syndrome was

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not any worse than that of control children, even though the former had much lower 25(OH)D levels than the latter.

The second study found that total 25(OH)D levels, but not estimated free 25(OH)D levels, were decreased in patients with critical illness. That is because vitamin D-binding protein and albumin are negative acute-phrase reactants (i.e., their levels fall in response to inflammation). Measuring total 25(OH)D in patients with critical illness potentially underestimates vitamin D status and overestimates the number of patients who are deficient in vitamin D.

In patients with nephrotic syndrome or critical illness, free 25(OH)D is probably more reliable than total 25(OH)D as an indicator of vitamin D status. Direct measurement of free 25(OH)D by liquid chromatography-tandem mass spectrometry is not readily available, and immunoassay methods have been reported to be unreliable. However, the concentration of free 25(OH)D can be estimated by measuring total 25(OH)D, vitamin D-binding protein, and albumin levels, and using an equation that includes all of these variables.

Banerjee S, et al. Free vitamin D levels in steroid-sensitive nephrotic syndrome and healthy controls. *Pediatr Nephrol*. 2020;35:447-454.

Palmer D, et al. Unbound vitamin D concentrations are not decreased in critically ill patients. *Intern Med J*. 2022;52:89-94.

Kidney Stones Are Becoming More Common

The incidence of kidney stones was assessed using data from the National Health and Nutrition Examination Survey (NHANES) from 2015 to 2018. Participants were asked, "In the past 12 months, have you passed a kidney stone?" Data were available on 10,521 participants older than 20 years. The 12-month incidence of stones was 2.1%, which was substantially higher than in previous reports. There was a significant positive relation between hypertension and incidence of stones. Being Hispanic, Black, or Asian, as compared with being White, was associated with a significant decrease in incidence.

Comment: Previous studies found that the 12-month incidence of kidney stones was 0.6% in 2005 and 0.9% in 2015. The present study found that the incidence of stones has increased even further. It is not clear why the incidence is rising. Previous studies found that supplementation with 300 to 500 mg per day of magnesium can decrease the recurrence rate of stones by as much as 90%. If calcium supplements are being used, they should be taken with meals, since taking them between meals may promote the development of calcium oxalate kidney stones.

Hill AJ, et al. Incidence of kidney stones in the United States: the continuous National Health and Nutrition Examination Survey. *J Urol*. 2022;207:851-856.

Can Vitamin D Prevent COVID-19?

Three hundred twenty-one frontline healthcare workers from four hospitals in Mexico City who were caring for patients hospitalized for COVID-19 and who themselves tested negative were randomly assigned to receive, in double-blind fashion, 4,000 IU per day of vitamin D or placebo for 30 days and were followed for a total of 45 days. The study was conducted from July 15 to December 20, 2020. PCR testing was performed if subjects developed symptoms consistent with COVID-19. Serum IgG antibodies against COVID-19 were

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The editors of the *Townsend Letter* recommend that all patients (and physicians) review further reports provided in the article's references and investigate the practitioner's techniques before undertaking an alternative diagnosis, examination, or treatment. Please discuss such treatments and examinations with a reputable health practitioner in your community. If you do use an alternative treatment discussed in the *Townsend Letter*, we would appreciate your report of the outcome, any side effects, and costs.

measured at baseline and on day 45. One hundred ninety-two subjects completed the trial. Six participants in the vitamin D group (6.4%) and 24 in the placebo group (24.5%) developed a COVID-19 infection ($p < 0.001$). Of the 30 positive cases, 12 were diagnosed by a positive PCR test and 18 were diagnosed by IgG antibody testing. It was not stated how many in each group were diagnosed by PCR testing vs. antibody testing. The relative risk of COVID-19 infection in those receiving vitamin D was 0.23 (95% confidence interval, 0.09-0.55). The beneficial effect of vitamin D was independent of baseline vitamin D status (as determined by serum 25-hydroxyvitamin D levels).

Comment: In this study, supplementation with 4,000 IU per day of vitamin D prevented COVID-19 infection in highly exposed individuals. Some previous studies found that vitamin D supplementation can decrease the severity of COVID-19 infection, but there had been little prior research on whether vitamin D can prevent people from becoming infected.

A double-blind study conducted in Canada found that long-term use of large doses of vitamin D (i.e., 4,000 IU per day or more for 3 years) accelerated bone loss in men and women between the ages of 55 and 70 years.[2] This effect was greater in women than in men.[3] The risks and benefits of using high-dose vitamin D should be assessed on an individual basis.

Villasis-Keever MA, et al. Efficacy and safety of vitamin D supplementation to prevent COVID-19 in frontline healthcare workers. a randomized clinical trial. *Arch Med Res*. 2022;53:423-430.

Gaby's Literature Review

Does Eating Processed Food Cause Inflammatory Bowel Disease?

The association between consumption of ultra-processed foods and risk of developing Crohn's disease and ulcerative colitis was examined in a prospective study of three cohorts of health professionals in the United States: the Nurses' Health Study (1986-2014), the Nurses' Health Study II (1991-2017), and the Health Professionals Follow-up Study (1986-2012), which included a total of 245,112 participants. During 5,468,444 person-years of follow-up, 369 incident cases of Crohn's disease and 488 incident cases of ulcerative colitis were documented. The median age at diagnosis was 56 years. Compared with participants in the lowest quartile of ultra-processed food consumption, those in the highest quartile had an increased risk of Crohn's disease (hazard ratio [HR] = 1.70; p for trend < 0.001). Among different subgroups of ultra-processed foods, the strongest positive associations with Crohn's disease were seen for ultra-processed breads and breakfast foods; frozen or shelf-stable ready-to-heat and ready-to-eat meals; and sauces, cheeses, spreads, and gravies. There was no consistent association between intake of ultra-processed foods and risk of ulcerative colitis.

Comment: Ultra-processed food has been defined as ingredients produced from a series of industrial processes. ➤

Gaby's Literature Review

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Ingredients characteristic of ultra-processed foods include high-fructose corn syrup, hydrogenated oils, flavor enhancers, colors, and emulsifiers. Examples of ultra-processed foods include sweet or savory packaged snacks, sugar-sweetened beverages, candy, industrial bread, industrial breakfast cereal, ready-to-heat-and-eat pasta dishes and pizza, and sausages and other reconstituted meat products.

Consumption of ultra-processed foods has increased in the US in recent years. According to data from National Health and Nutrition Examination Surveys, between 1999 and 2018 the estimated percentage of total energy consumed from ultra-processed foods increased from 61.4% to 67.0%, whereas the percentage of total energy consumed from unprocessed or minimally processed foods decreased from 28.8% to 23.5%.[4] In other regions around the world that have been undergoing Westernization, an increase in consumption of ultra-processed food has coincided with an increase in incidence of inflammatory bowel disease. Further research is needed to determine whether these associations represent causation and, if so, which types of ultra-processed foods are implicated the most.

Lo CH, et al. Ultra-processed foods and risk of Crohn's disease and ulcerative colitis: a prospective cohort study. *Clin Gastroenterol Hepatol*. 2022;20:e1323-e1337.

Examining the Pathophysiology of Non-Celiac Gluten Sensitivity

Duodenal biopsies were performed on 261 patients with celiac disease with milder enteropathy (Marsh score of I-II), 175 patients with non-celiac gluten sensitivity, and 262 control cases with normal gastroscopy and histologic findings. The median villus height was shorter in patients with non-celiac gluten sensitivity than in controls (0.6 vs. 0.9 mm; $p<0.001$). The median villus height to crypt depth ratio was lower in non-celiac gluten sensitivity patients with a Marsh score of 0 (normal histology) than in controls ($p<0.001$). The median number of intraepithelial lymphocytes per 100 enterocytes was higher in non-celiac gluten sensitivity patients with a Marsh score of 0 than in controls ($p<0.001$).

Comment: This study demonstrated that the duodenal mucosa of patients with non-celiac gluten sensitivity showed subtle changes, including reduced villus height, increased crypt depth, and increased lymphocyte infiltration consistent with a mucosal immune response to luminal antigens. Abnormalities were seen even in cases where the mucosa was considered normal by standard criteria (Marsh score of 0). This study confirms that, contrary to the view of skeptics, non-celiac gluten sensitivity is a true clinical entity.

Rostami K, et al. Gluten induces subtle histological changes in duodenal mucosa of patients with non-coeliac gluten sensitivity: a multicentre study. *Nutrients*. 2022;14:2487

Vitamin C for Septic Shock

One hundred twenty-six adults hospitalized at one of five intensive care units in Minnesota who were within 24 hours of vasopressor initiation for septic shock were randomly assigned to receive, in double-blind fashion, intravenous vitamin C (10 mg/ml in normal saline) or placebo (an equivalent volume of normal saline). The dosage of vitamin C was 10,000 mg as a bolus over 30 minutes, followed by a continuous infusion of 250 mg per hour for 96 hours. The primary outcome of 28-day all-cause mortality was nonsignificantly lower by 34% in the vitamin C group than in the placebo group (26.7% vs. 40.6%; $p = 0.10$). Initiation of renal replacement therapy was higher in the vitamin C group than in the placebo group (16.7% vs. 3.3%; $p = 0.015$). In post hoc subgroup analysis, 28-day mortality was lower in the vitamin C group than in the placebo group among patients requiring positive-pressure ventilation at the time of enrollment (36.3% vs. 60.0%; $p = 0.05$).

Comment: In this study of patients with septic shock, intravenous vitamin C decreased 28-day mortality by 34%, but this decrease was not statistically significant. A larger study would be needed to determine whether this 34% decrease in mortality was real or due to chance. Post hoc analysis suggested that vitamin C may be beneficial for patients who were more seriously ill (those that required positive-pressure ventilation). However, post hoc analyses should be interpreted with caution. The increased need for renal replacement therapy among patients given vitamin C is concerning. Compromised kidney function is common among patients with critical illness. In those with severely compromised kidney function, vitamin C may be converted in part to oxalate, which can be deposited in the kidneys and cause further renal damage.

High-dose vitamin C appears to be useful for many different viral and some bacterial infections. However, there is no clear evidence at this time that high-dose vitamin C should be given to patients with septic shock.

Wacker DA, et al. Evaluating vitamin C in septic shock: a randomized controlled trial of vitamin C monotherapy. *Crit Care Med*. 2022;50:e458-e467.

L-Carnitine for Cirrhosis

Eighty-three Japanese patients (mean age, 67 years) with hepatic encephalopathy secondary to cirrhosis who were being treated with 1,200 mg per day of rifaximin (an antibiotic used to treat hepatic encephalopathy) were randomly assigned to receive 1,500 mg per day of L-carnitine for 12 weeks or to a control group that did not receive L-carnitine. The proportion of patients who required hospitalization during the study was 68% lower in the L-carnitine group than in the control group (9.8% vs. 30.9%; $p < 0.03$).

Comment: Patients with cirrhosis appear to have an impaired capacity to synthesize carnitine from lysine and methionine. Since carnitine plays a role in the detoxification of ammonia, carnitine deficiency could exacerbate hyperammonemia in cirrhotic patients, with potentially serious consequences. In the present study, supplementation with L-carnitine markedly decreased the need for hospitalization in patients with cirrhosis and hepatic encephalopathy.

Kubota K, et al. Additional L-carnitine reduced the risk of hospitalization in patients with overt hepatic encephalopathy on rifaximin. *Dig Dis*. 2022;40:313-321.

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3. Burt LA, et al. Adverse effects of high-dose vitamin D supplementation on volumetric bone density are greater in females than males. *J Bone Miner Res*. 2020;35:2404-2414.
4. Wang L, et al. Trends in consumption of ultraprocessed foods among US youths aged 2-19 years, 1999-2018. *JAMA*. 2021;326:519-530.

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Sensitive to Everything?
Addressing "Immune Systems Gone Wild" in Fibromyalgia

by Jacob Teitelbaum, MD
Author of *From Fatigued to Fantastic*

Did you know that your mind directs your immune system?

I was surprised in medical school when I learned this. My dad had died when I was younger, and I was paying my own way through by working as a children's hospital nurse. I asked my psych professor to teach me hypnosis when I was getting ready to work on the burn unit, to make it more comfortable for the children to go through their dressing changes

He taught me that if people go into a quick hypnotic state when they burn themselves and let their deep psyche know "heal quickly no injury" soon after the burn, there will be no blister. There is a good reason I am not a surgeon. I am a major league butter fingers and I tend to burn myself quite a bit. Although after a severe burn the skin turns white and dead from the burn, I no longer blister.

The blister is caused not by the burn but rather by the immune system's response to a perceived injury. And yet my psyche can let my immune system know to stand down. As a side note, this also works very well before surgical procedures to dramatically decrease post-op inflammation. In a deep meditative, centered, or hypnotic state, let the psyche know that what is coming is friendly and here to help us, and to simply welcome it and let it be. You will be pleasantly surprised at how much easier and quicker the healing process is!

The Modern Alternative: Be Very Afraid and Hate Everyone Else

When I was a child, the Madison Avenue advertising mantra was "Sex Sells." If you wanted to sell something, you simply put handsome men and women by the product (e.g. – beer, cars, etc.) in the advertisement.

Then about 20 years ago, the news media seem to have adopted a new mantra: "Fear and Divisiveness Sells." They realized they can sell more ads if they leave people scared to death and hating each other, so that they watch 24/7.

This is very unhealthy for our psyche and immune system. I suspect that this constant feeling of being unsafe for no focused reason, leaving our immune system lashing out wildly at everything, results in both immune system and adrenal exhaustion with our bodies suffering from the collateral damage. So perhaps it's no surprise that our immune systems are overreactive.

Have you noticed in your practice an increase in autoimmune illnesses, food allergies, limbic system dysfunction, chronic sympathetic nervous system activation with decreased vagal nerve function, Mast Cell Activation Syndrome (MCAS), increased activity to mold and mold toxins, and symptoms of chronic activation of Cell Danger Response (CDR)?

These are often different faces of the same process. Although it is critical to treat the underlying physical components, we often find that this alone leaves healing incomplete. Often, without also addressing the psyche, healing can't even begin because of sensitivities!

Heal the Body with SHINE

In earlier articles, I discussed how to effectively treat fibromyalgia and CFS with SHINE. This optimizes Sleep, Hormones, Immunity, Nutrition, and Exercise as able. My published randomized double-blind placebo-controlled study showed that this resulted in an average 90% increase in quality-of-life ($p<.0001$ vs placebo). For earlier free articles on effective treatment of CFS/fibromyalgia, post-covid, and orthostatic intolerance, feel free to email me at fatiguedoc@gmail.com.

Also feel free to request links to copies of my four new studies on new effective treatments for post-viral CFS and fibromyalgia.

New *Red Ginseng Energy* Study

A unique form of red ginseng (Red Ginseng Energy by EuroMedica) resulted in 60% of post-viral fatigue cases improving, with an average:

1. 67% increase in energy
2. 44% increase in overall well-being
3. 48% improvement in mental clarity
4. 46% improvement in sleep
5. 33% decrease in pain
6. 72% increase in stamina

Again, for any of these, if you would like copies of the articles or free treatment tools simply email me at fatiguedoc@gmail.com. If you live outside of the United States, please also mention that.

The processes below are very treatable physically, but experience shows that in many people the mind body and immune dysfunctions must also be addressed.

Mind-Body Interactions

Mind-body interactions are massive. Here are just a few connections pertinent to sensitivities.

Chronic immune activation results in immune exhaustion. Dr. Mark Sivieri, MD noted to me that he was seeing frequent IgG1 and IgG3 antibody deficiencies in these populations. This has been confirmed in my practice. The research is suggesting that these antibody deficiencies can also be associated with autonomic dysfunction and small fiber neuropathy. Over time, our understanding of the importance of the immune/autonomic connection will grow. Immune exhaustion contributes to numerous persistent and coexisting opportunistic infections, including Lyme and other antibiotic-sensitive coinfections, candida/fungal overgrowth, and viral reactivation.

Candida/fungal overgrowth. Relative to other microorganisms, these bugs are massive in size. They can also contribute to the mycotoxin load, which can be especially problematic in those with severe sensitivities and anxiety. For an excellent discussion on mold toxins, I highly recommend the book *Toxic* by my friend Neil Nathan, MD. In speaking with him recently, he also noted one other important tip.

For those whose sensitivities do not allow them to tolerate antifungal treatments, this is often because lysing the mold cells when you kill them releases large amounts of toxins, which the body cannot handle. In those cases, consider slowly bringing the mold binders on board first, and then killing off the molds while beginning with low doses of the antifungals. This way, the binders are in place to tie up the toxins when the fungal cells are destroyed.

In people who have sensitivities to treatments, begin with the limbic system.

Viral reactivation, especially EBV and HHV-6. Unfortunately, there are no tests that I am comfortable with yet to distinguish viral reactivation from old infection and immunity. So my decision to consider a trial of antivirals is still based on clinical symptoms (e.g. onset with a viral infection and chronic flulike feelings)

Adrenal fatigue. Again, although salivary and other tests can be helpful, simply asking the person if they get irritable when hungry (hypoglycemic) is an excellent way to distinguish if adrenal fatigue is present. Increasing salt and water intake and adrenal support with a mix called Adrenaplex (by EuroMedica) can be very helpful in balancing immunity and improving other symptoms.

"Leaky gut." Absorption of incompletely absorbed proteins puts a major strain on the immune system as well. This is beyond the scope of this article. Be sure to give betaine HCL and a trial of plant-based digestive enzymes (animal-based digestive enzymes are not as effective in my experience) with meals for a few weeks to improve digestion, along with Dr. Jeffrey Bland's "4 R" program for "leaky gut" (Remove, Replace, Re-inoculate, Repair). Gut issues can trigger massive imbalances of neurotransmitters, leaving the person an emotional wreck

Treating Mast Cell Activation Syndrome (MCAS), Food Sensitivities, and Mold Toxins

So many people with fibromyalgia are incredibly sensitive to any treatments. This makes figuring out how to treat them quite the challenge. Here's how to begin. ➤

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Mast Cell Activation. Mast cells are our body's "first responders "when making contact with the outside world. If they meet something in the environment that concerns them, they can pour out over 200 chemicals. But what they react to varies from day-to-day.

Just like our immune system in fibromyalgia can be on overdrive in general, in some people this is also occurring for their mast cells. These guardians then have an itchy trigger finger, seemingly reacting to things at random.

Random is the key word here, and this helps distinguish mast cell activation from regular allergies and sensitivities. One day you may have no reaction to something, but you react excessively to the same trigger on other days. So, no problem eating an ear of corn one day. But the next day, you have may have the sudden onset of flushing, nausea, diarrhea, sweating, or palpitations.

MCAS treatment begins with the following:

1. Quercetin (half hour before meals) 500-1000 mg twice a day. They may gradually increase to four times a day
2. Claritin in the morning and Benadryl at night
3. the medication montelukast (Singulair) 10 mg at bedtime.
4. Pepcid (famotidine – do not use PPIs, which are toxic) 20 to 40 mg twice daily
5. If needed, a low histamine diet.

There are, of course, numerous other treatments, but these are a good beginning. They tend to be well-tolerated and often work within a week or two. Give six weeks to see the full effect.

Food Sensitivities. Many people find that they have a number of food sensitivities. They find themselves limiting their diet and then sometimes find themselves becoming sensitive to the few foods they could eat. They find that they, over time, have 'painted themselves into a corner' where there is nothing left to eat.

As noted above, there are three main things that trigger food sensitivities:

1. Incomplete digestion of proteins because of not enough stomach acid or digestive enzymes
2. Leaky gut from infections, especially candida, and other causes. Anti-inflammatory arthritis medications such as ibuprofen are major triggers.
3. Adrenal fatigue.

An emotional trauma, such as having a parent scream at you, while eating a food may also trigger sensitivities. So what to do?

You know how when your computer goes on the fritz, the first thing tech-support tells you to do is to reboot? Simple techniques can help you hit the reset button on your brain and immune system. My favorite? A simple acupressure technique called NAET

(www.NAET.com) can eliminate food and other sensitivities. Other techniques, such as sublingual neutralization, can also be helpful.

Mold Toxins. When you have severe sensitivities in combination with severe anxiety, think mold toxins. But be aware of the Pandora's box you are opening when you bring this up for those you treat. There is no reliable test for either individuals or their environment, so I suspect a very large percent of people with no mold problem will test positive in both – which may leave them feeling unsafe in their home unless they do tens of thousands of dollars' worth of (possibly unnecessary) home remediation.

So I address other things first, going after mold toxins if the person fails to respond and has a suggestive history. I have clinically simplified how to address mold toxins in the newest edition of my book *From Fatigued to Fantastic*. The book *Toxic* by Dr. Neil Nathan, MD, is – in my humble opinion – the best overall book on mold toxicity.

Addressing The Psychospiritual Aspects

Energetic diagnosis and treatment can of course be very helpful. Like chess, it can take a few hours to learn but a lifetime to master. And like treating biochemistry, addressing biophysics is a massive area.

So it is helpful to have a wonderful new book available by Dr. Neil Nathan, MD, called *Energetic Diagnosis*. In case you can tell, I think very highly of my friend Dr. Nathan.

But where to begin? When addressing sensitivities in people with complex conditions such as fibromyalgia begin with the following.

Reset the limbic system. This includes the hypothalamus, and the effects of doing so can be dramatically healing in general. There are a number of programs that do this. My favorites include ANS Rewire by Dan Neuffer (https://ansrewire.com/) or Dynamic Neural Retraining System by Annie Hopper (https://retrainingthebrain.com/). These are mental exercises that retrain our thought processes and can be found online. It takes several months at one hour a day to really start to see the effects, although the ANS Rewire may work more quickly.

These techniques can sometimes heal fibromyalgia by themselves with no pills. But they take an investment of time. **In people who have sensitivities to treatments, begin with ANS Rewire or DNRS!**

Enhance vagal tone. Does it seem like the person's adrenaline is constantly on overdrive and exhausting? It's often because it is. The vagal system is necessary to balance the adrenaline system. But in people who felt severely unsafe earlier in their life, they may be stuck in adrenal hypervigilance or even in a severe dorsal vagal mode that triggers the "playing possum" state in animals.

Interestingly, recent research showed that about ¼ of people with "Long Covid" had vagal nerve inflammation, with shortness of breath likely due to diaphragmatic flattening. So there may be a number of vagal dysfunction triggers.

Resetting vagal tone requires helping the person you're treating to *feel safe*. A good beginning is by mindfulness exercises that teach people to be in the moment. Because most of their fear is caused by rehashing the past or worrying about future events that usually never happen.

Also, teach those you treat to turn off the news media. Regardless of which side is being watched, it is largely a fiction meant to make people hate each other and be frightened. As Mark Twain was reported to say "if I don't read the news I'm *uninformed*. But if I do read the news, I am *mis*informed!" This has not improved since then. Advise people that when media reporting starts feeling bad, turn it off.

Frequency Specific Microcurrent (www.frequencyspecific.com) is not only helpful for chronic pain but can also help balance vagal tone.

Brain Tap® exercises can be helpful, but specifically use the programs for "Quieting ANS."

Exercises in Stanley Rosenberg's book *Accessing the Healing Power of the Vagus Nerve: Self-Help Exercises for Anxiety, Depression, Trauma, and Autism* can also be very helpful approaches that the person can do on their own.

Once people you treat do these, they will be much better able to tolerate other treatments. And they will feel dramatically better!

The bottom line? Heal your mind, and your body *and immune system* will follow! ◆

Jacob Teitelbaum, MD, is one of the most frequently quoted integrative medical and CFS/fibromyalgia authorities in the world. He is the author of 10 books including the best-selling *From Fatigued to Fantastic!* and the popular free Smart Phone app Cures A-Z. He is the lead author of 8 studies on effective treatment for fibromyalgia and chronic fatigue syndrome, and a study on effective treatment of autism using NAET. Dr. Teitelbaum appears often as a guest on news and talk shows nationwide including *Good Morning America, The Dr. Oz Show, Oprah & Friends, CNN,* and *FoxNewsHealth*. Learn more at www.Vitality101.com .

Keys to Curing Autoimmune Disease

by Frank Shallenberger, MD

In order to cure any disease, the causes must be treated. So, what causes an autoimmune disease? Let me start with a case example.

The patient is a 58-year-old woman, I'll call her Susan, who has had asthma and allergies almost all her life. Over the years, she managed her symptoms fairly well on various medications, but none of her doctors had ever bothered to look into what was causing them. Six years ago, she started having severe pain, inflammation, and swelling in her joints. First, it was her knee, then that would stop, and her shoulder would act up. Then it was her ankle. She had what doctors call migrating joint disease. This is characteristic of an autoimmune condition. Ultimately, her symptoms became so bad that she could barely get around and had to quit working. Her doctors diagnosed an autoimmune disease called lupus.

When I first saw her, she was on immune-suppressive medications. Her symptoms were better, but she had gained 45 pounds and was feeling weak and run down from the medications. Her doctors had told her that there was no cure for her condition. They were wrong. All autoimmune diseases are curable provided that the causes can be found and treated.

The list of autoimmune diseases is long. And it gets longer every year. Lupus, rheumatoid arthritis, colitis, scleroderma, fibromyalgia, and thyroiditis are the old standbys. Now the list includes autoimmune diseases of the liver, pancreas, kidney, muscles, nerves – virtually every organ and system in the body. Specialists will say that autoimmune diseases are caused by an immune system running amuck. But what is causing that? And why are so many more immune systems running amuck now than just a few decades ago?

Two basic factors behind every autoimmune disease explain the answer to both these questions. First, in every autoimmune disease – no matter what the name is – there is something foreign to the body that the immune system is reacting to. And secondly, there is poor control of the reaction. Let's break apart these two concepts.

The Immune System Is Reacting to Something

Your immune system reacts to everything that comes into contact with your body. Everything that contacts your skin, everything you breathe, and everything you ingest causes an immune reaction.

In order for this system to work properly, there has to be a way to control these reactions. The body controls the reactions in two ways. First, it directs the reactions correctly. In other words, when my immune system is reacting to the broccoli I just ate, it needs to direct that reaction to broccoli molecules. If it mistakenly directs the reaction to my muscles, then I will start to have problems with my muscles every time I eat broccoli. So there needs to be controls in the immune system that properly direct every immune reaction to the correct target.

Next, there must be a way to limit the extent of the reaction to what is appropriate. For example, if I eat a small amount of broccoli, my immune system should react with a lesser reaction than if I ate a large amount. If it overreacts, then the overreaction will create problems. Allergies are an example of an overreacting immune system. So, in summary, in order for it to function properly, the immune system must correctly direct and properly limit its reactions. And here's the point.

When these controls are not working well, the result can be an autoimmune disease. This is true of every autoimmune disease. It doesn't matter what particular tissue or organ the autoimmune disease is focusing on. If it is focusing on the liver, we call that autoimmune hepatitis. If it is focusing on the skin, we call it scleroderma. In terms of curing the disease, it doesn't matter what the name of the disease is or what particular part of the body it is affecting. The factors causing the disease are always the same. The immune system is reacting to something. And it's not properly directing and limiting its reaction.

So, knowing this, it should now become obvious what needs to be done in order to cure an autoimmune disease. First, we should remove or limit the "something" that the immune system is reacting to. Second, we should eliminate the factors that are causing it to overreact.

Removing the Something

How can we know what the immune system is reacting to? It's not easy. And it takes time. We need to take an exhaustive history of what happened in the months to years prior to the first onset of the symptoms. Did the symptoms happen after an infection, surgery, concussion, blood transfusion, or trip to another country? After a vaccine or some other pharmaceutical?

After a root canal or some other dental procedure? Did the first symptoms start after a change in diet? How about a change in environment? Did they start to occur during a time of severe stress? If stress, then one of the causes might be adrenal exhaustion, which is present in every case of an autoimmune disease.

In some cases, laboratory testing might be helpful, but the most important source of information as to cause is an extensive, detailed, chronological history of the events leading up to the first symptoms of the disease. That said, the most common thing that the immune system is overreacting to in an autoimmune disease is a microbe such as a virus, a bacterium, a fungus, or a parasite. The name of the microbe can sometimes be determined by analyzing antibody levels of the various microbes and correlating that with the history.

For example, if the history points to an infection and the patient's antibody levels are high for rickettsia, mycoplasma, or borrelia, tetracycline might be called for. If antibody levels are high for streptococcus and the history points to a strep infection, penicillin might be the drug of choice. If a virus is suspected, ozone therapy is usually effective. If a parasite or a fungus is suspected, the appropriate drug for those microbes should be used.

The problem that you can run into when trying to identify the microbe is that it is often not at all clear what microbe is at fault. But one thing is for sure. Whatever the microbe is, it is very likely that it will be found in one of three places.

The most likely place is the intestines. That is for two reasons. First, the intestinal tract is by far the most contaminated area of the body. Secondly, the intestinal tract contains nearly 90% of all the immune reactive cells in the body. I am convinced that most diseases start in the intestinal tract; and when it comes to autoimmune diseases, this is usually true. The other two most likely places are the sinuses and the teeth. Once again this is because these areas are so vulnerable to infection. I think it would be a safe bet to say that microbes residing in one or more of these three areas cause over 90% of all autoimmune diseases.

Detoxifying the Intestines

The single most important thing to do in any patient with an autoimmune disease is to detoxify the intestinal tract. The best way to do this is by using colonic therapy along with ozone infusions directly into the colon. Combine that with oral ozonated oil capsules, probiotics, and antifungal, antibacterial, and anti-parasitic herbal and pharmaceutical medications. Blood tests and stool tests for these microbes can be helpful to determine exactly what medications are needed.

Food allergies or sensitivities are often a problem with autoimmunity. It works like this. Either stress, an infection, GMO or otherwise processed foods, drugs, vaccines, pharmaceuticals or other chemicals or toxins cause a breakdown of the mucin layer protecting the intestinal cells from potentially irritating foods. The end result of that mucin breakdown is that foods can then become irritating. We call this phenomenon a "leaky gut" situation. The irritating foods can in turn cause further breakdown in the mucin layer. The result is immune reactivity to foods that can then be misdirected to an autoimmune reaction. The treatment here is to start with a 5-7 day water fast followed by a diet that excludes commonly eaten foods. Additionally, L-glutamine (2 grams, 2-3 times per day) with N-acetyl glucosamine (700 mg, 2-3x times per day) will help repair the mucin level faster. Once the mucin layer is healed in 4-8 weeks, a normal diet can usually be re-established.

Detoxifying the Sinuses

If there is a history of repeated sinus infections or chronic sinus irritation, the sinuses must be aggressively detoxified. Ozone therapy is the best way to do this. Ozone can be easily injected into the sinus areas. Ozone can also be insufflated into the sinuses. Additionally, sinus irrigation is often critical. I like a device called a SinuPulse. You can get that online. Add ½ tsp baking soda, ½ tsp salt, 2 drops of Johnson's baby shampoo, and 10 drops of betadine solution to the irrigation water. Use it twice a day for 6 weeks and then 1-3 times per week as needed.

In cases of chronic sinus infections treated with antibiotics and/or steroid nasal strays, it is 100% sure that the sinuses are infected with fungus. In that case, a systemic antifungal is needed. The one I find the most useful is terbinafine (250 mg per day for three weeks).

Behind every autoimmune disease is something foreign that the immune system is reacting to and poor control of that reaction.

Detoxifying the Mouth

If there are root canals or any other source of dental infection, that needs to be treated as well. I always ask my patients if they have a history of dry socket after wisdom teeth extraction. Also, did they have a root canal or any other dental infection in the weeks to months before the onset of their symptoms? These are good clues. This is why it is so crucial to have a good ozone proficient biological dentist in your area who knows how to use ozone therapy to clear these infections up. I have literally seen complete cures of autoimmune diseases within days after having dental infections effectively treated.

Detoxifying the Whole Body

But what if the microbe is somewhere other than the intestines, sinuses, or teeth? What if you don't know where it is? And what if you know where it is or what it is, and the standard remedies don't work? In these cases, you need systemic ozone therapy followed by intravenous vitamin C. Once a week for two to three months should be adequate. This protocol activates the immune system to do what it is supposed to do – irradicate the infection. Another good way to do this is with UB Isode therapy. I describe that in the book I wrote for doctors titled, *The Principles and Applications of Ozone Therapy*.

Eliminating the Overreaction Factors

Okay, so that's it for doing what we can to remove the "something" triggering the immune reaction. The next step is to begin removing the factors that might be

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causing the immune system to misdirect and overreact. The most common factors are chronic stress resulting in adrenal exhaustion, heavy metals, hormone imbalances, vaccines and the TH1-TH2 immune system imbalance they cause, root canals and other dental infections, petrochemicals, GMO foods and other forms of toxicity, and drugs (including prescription drugs).

Chronic stress depletes the adrenal glands. And fully functioning adrenal glands are critical for preventing the immune system from over reacting. I find that almost every case of autoimmune disease is preceded by months of severe, sustained stress. In Susan's case, she had been under a tremendous amount of emotional stress for almost two years before she developed the disease. Chronic stress often comes from emotional causes. But it can also stem from physical causes such as pain, lack of sleep, a diet high in processed carbohydrates, and drugs and medications.

There is very little chance of anyone curing an autoimmune disease until the stress factors are eliminated and the adrenal glands are treated. This means ensuring adequate sleep, eliminating pain (ozone therapy is awesome for this), correcting a bad diet, and eliminating unnecessary drugs. It also means aggressively treating adrenal exhaustion.

In autoimmune diseases, aggressively treating immune system overreaction almost always means supplementing the body with the adrenal hormones hydrocortisone (10-60 mg/day) and dehydroepiandrosterone (DHEA 25-200 mg/day) along with adrenal-stimulating herbs and nutrients. The doctor should get baseline fasting ACTH and DHEA before initiating therapy. The doses should not suppress the ACTH level below 10 pg/ml or allow the DHEA to be greater than 400 µg/dL.

But stress is not the only factor causing the immune system to overreact. One of the most common problems is the effect of heavy metals such as mercury, arsenic, cadmium, and lead. The worst is mercury. It's not a question of whether or not you have these toxic metals in your body. You do. You can't avoid them. They are in everything you eat (including organic foods), in the air you breathe, and in the water you drink. The only question is what they are doing to your immune system. In many cases, they are at the heart of autoimmune disease. Although Susan almost immediately improved with the measures I mentioned above, she was not completely cured until she had her mercury-containing silver dental fillings removed and completed a course of mercury chelation therapy.

Another major factor in autoimmune disease is hormone deficiency. This fact should be obvious to anyone who looks at the statistics of autoimmune disease. It is mostly a woman's disease. For every man who develops an autoimmune disease, there are three women. And most of these women develop the disease after their menopause.

The reason is that sex hormones play a major role in how the immune system reacts. Why did Susan get autoimmune disease at the age of 37? It was because her uterus and ovaries were removed, and she was forced into a premature menopause at the age of 34. Making sure her hormones were adequately replenished was a critical part of her recovery. The other hormones that play a role are the thyroid hormones, which are often deficient in the over fifty group. And don't forget melatonin. Melatonin is a known regulator of the immune system. Melatonin is deficient in anyone over 50.

Beware of Vaccines!

Perhaps the single most common factor creating an imbalance in the immune system is vaccines. I will say right up front that I am opposed to all, and I mean all vaccines in otherwise healthy people. There are two reasons for this.

One, as we have all been witness to over the past two years, we simply cannot trust the purveyors of vaccines. Because they have no liability and because there is so much money involved, they have demonstrated that they have absolutely no problem with lying and falsifying data to further their sales.

Two, even if a vaccine is what the makers say it is, it will still always create an immune system imbalance. The reason is that the efficacy of all vaccines is based on how efficiently they stimulate the TH-2 part of the immune system to produce antibodies. But when the TH-2 system is stimulated, it produces cytokines (IL-4 and IL-10) which act to suppress the TH-1 innate system. In essence, vaccines are immune suppressive. And the worst part about them is that ironically by suppressing the TH-1 innate system, they suppress the very part of the immune system that is responsible for controlling viral infections. This is why they are so inefficient at protecting their recipients from future viral infections.

Although I cannot find one definitive study that can conclusively prove vaccines do or do not cause autoimmunity, the available data is very suspicious.

For example, according to the British Society for Immunology since the childhood vaccine schedule has been increased 700% over what it used to be, the incidence of autoimmune diseases has been steadily increasing from between 3-9% per year.[1] This includes a 7.0% increase per year in rheumatic diseases such as rheumatoid arthritis; a 6.3% increase in endocrinological conditions such as type 1 diabetes; a 3.7% increase in neurological diseases such as MS; and a whopping 4–9% increase every year in celiac disease. Keep in mind that these are not simply overall increases – they are annual increases. That means in any ten-year period the incidence of these diseases has close to doubled.

Additionally, a German survey first released in 2011, looked at the incidence of a variety of immune-related diseases in 8,000 vaccine-free children aged newborn to 19 years old.[2] The researchers then compared it to the reported overall incidence of the same diseases according to the national German KIGGS health study of all children. The survey results are alarming. They show that compared to the general population of children, children who are vaccine free are anywhere from 2-5 times less likely to have any of these diseases. Specifically, children in the general population were 18 times more likely to be diagnosed with an autoimmune disease than those who had never had one vaccine.

Avoiding Autoimmune Disease

I've always maintained that the best way to treat any disease is not to get it. And that works for autoimmune disease as well. So, what can you do to make sure that you don't become one of the fifty million Americans who have an autoimmune disease?

First of all, avoid vaccines. They are almost all loaded with mercury and other toxins. But worst of all, the very way they work throws the immune system into a state of imbalance. And this imbalance favors the development of the inappropriate reactions that lead to autoimmune disease. They have already been linked to the development of several autoimmune diseases, including lupus, rheumatoid arthritis, and neurological diseases such as Guillain-Barre, multiple sclerosis, Bell's palsy, and parasthesias. In this day and age, I see almost no need for any vaccines in first-world countries. This includes all children's vaccines and includes the vaccines that are being pushed for flu and pneumonia. And here's something else to consider.

Although the evidence isn't overwhelming yet, I am very concerned about the use of genetically modified foods (GMO). These "Frankenfoods" are toxic. They can cause a breakdown in the immune system regulation in the intestinal tract. Remember how important the intestinal tract is to the development of autoimmune diseases. A child's immune system is not fully functioning until the middle teens. Imagine the effect on their developing immune systems while they are being fed increasing amounts of genetically altered, heavily contaminated GMO "Frankenfoods." GMO foods are forbidden in every first-world country except the US!

Pay attention to what your dentist is putting into your mouth. Mercury-containing silver fillings have been banned in Canada and all the European countries. Why not here? If you have these fillings already, bite the bullet, get out your check book, and have them replaced with something not poisonous. And make sure that this is done by a biologic dentist certified by one of the biological dental associations. Improper removal of these toxic fillings can lead to complications. I have seen them. What about root canals?

Read the book by Robert Kulacz, DDS, and Thomas E. Levy, MD, JD, called *The Toxic Tooth*. This heavily referenced book makes a very good case for root canals being a scientifically flawed and potentially dangerous procedure. "Instead of solving a problem, root canals introduce a steady stream of dangerous – and even deadly – toxins into your body," says Dr. Levy. These toxins are often the "something" that starts a reaction leading to an autoimmune disease. I have seen several cases of autoimmunity completely disappear almost immediately after the removal of a suspicious root canal. If you have an autoimmune disease and have any root canals, I would advise you to have them all removed as a first step. I know it's drastic, but unless you know what the "something" is causing your disease, your root canals are a very likely culprit.

Americans love to treat everything with drugs. This is especially true of stress. No matter what kind of stress you have, Big Pharma has come up with some drug to help you avoid dealing directly with it. There are many natural ways to deal with stress. You don't need a drug. Get someone to help you eliminate the causes of your stress, and also strengthen and protect your adrenal glands. There is no stress reliever as effective as proper exercise regularly done. Get in shape and be sure to eat well and get enough sleep.

Two more things. Have your doctor check you for heavy metal toxicity. It can be done with a chelation challenge test and a UPPA (urinary porphyrin profile analysis). If you are high on any heavy metal, get it chelated out. This will not only help you to avoid autoimmune disease but also every other disease, including cancer.

Lastly, make sure your hormones are replaced as you get older. This is especially true of women going through the menopause. Only use bio-identical hormones. These are the ones natural to your body. Remember that replacing your sagging hormone levels is not just something that can make you feel better; it can also protect you from disease, especially autoimmune disease.

Does All This Sound Too Difficult or Complex?

I liken any chronic disease to a chain with 4-5 links broken. Fix one link and you get nowhere. Fix two links and the same result. That chain will not work until every single link is repaired. In the case of autoimmune disease there are often 4-5 links broken. This would include stress, sinus infections, imbalances in intestinal bacteria, toxicity, hormonal imbalances, drugs, vaccines, and everything I have discussed here. So yes, beating autoimmune disease can be very painstaking at first. Every case is different. Every detail must be attended to. That can take time and experimentation and money. That's the bad news. The good news is that relief is a definite possibility.

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Healing Chronic Back Pain

by Erik Peper, PhD, BCB, Jillian Cosby, and Monica Almendras

At the beginning of 2021, I broke my L3 vertebra during a motorcycle accident and underwent two surgeries in which surgeons replaced my shattered L3 with a metal "cage" (looks like a spring) and fused this cage to the L4 and L2 vertebrae with bars. I also broke both sides of my jaw and fractured my left shoulder. I felt so overwhelmed and totally discouraged by the ongoing pain. A year later, after doing the self-healing project as part of the university class assignment, I feel so much better all the time, stopped taking all prescription pain medications and eliminated the sharp pains in my back. This project has taught me that I have the skill set needed to be whole and healthy.

–J.C., 28-year-old college student

Chronic pain is defined as a pain that persist or recurs for more than three months.[1] It is exhausting and often associated with reduced quality of life and increased medical costs.[2] Pain and depression co-exacerbate physical and psychological symptoms and can lead to hopelessness.[3,4] To go to bed with pain and anticipate that pain is waiting for you as you wake up is often debilitating. One in five American adults experience chronic pain most frequently in back, hip, knee, or foot.[2] Patients are often prescribed analgesic medications ("pain killers") to reduce pain. Although, the analgesic medications can be effective in the short term to reduce pain, the efficacy is marginal for relieving chronic pain.[5,6] Recent research by Parisien and colleagues (2022) reported that anti-inflammatory drugs were associated with increased risk of persistent pain.[7] This suggest that anti-inflammatory treatments might have negative effects on pain duration. In addition, the long-term medication use is a major contributor to opioid epidemic and increased pain sensitivity.[8-10] Pain can often be successfully treated with a multidisciplinary approach that incorporates non-pharmacologic approaches. These include exercise, acceptance and commitment therapy, as well as hypnosis.[11] This paper reports how self-healing strategies, taught as part of an undergraduate university class, can be an effective approach to reduce the experience of chronic pain and improve health.

Each semester, about 100 to 150 junior and senior college students at San Francisco State University enroll in a holistic health class that focused on 'whole-person' holistic health curriculum. The class includes an assessment of complementary medicine and holistic health. It is based upon the premise that mind/emotions affect body and body affects mind/emotions that Green, Green & Walters (1970) called the psychophysiological principle[12]: "Every change in the physiological state is accompanied by an appropriate change in the mental emotional state, conscious or unconscious, and conversely, every change in the mental emotional state, conscious or unconscious, is accompanied by an appropriate change in the physiological state."

The didactic components of the class include the psychobiology of stress, the role of posture, psychophysiology of respiration, lifestyle, and other health factors, reframing internal language, guided and self-healing imagery. Students in the class are assigned self-healing projects using techniques that focus on awareness of stress, dynamic regeneration, stress reduction imagery for healing, and other behavioral change techniques adapted from the book, *Make Health Happen*.[13]

The self-practices during the last six weeks of the class focus on identifying, developing, and implementing a self-healing project to optimize their personal health. The self-healing project can range from simple lifestyle changes to reducing chronic pain. Each student identifies their project such as increasing physical activity, eating a healthy diet and reducing sugar and junk food, stopping vaping/smoking, reducing anxiety or depression, stopping hair pulling, reducing headaches, decreasing eczema, or back pain, etc. At the end of the semester, 80% or more of the students report significant reduction in symptoms.[14-17] During the last five semesters, 13 percent of the students focused on reducing pain (e.g., migraines, neck and shoulder pain, upper or lower back pain, knee pain, wrist pain, and abdominal pain). The students successfully improved their symptoms an average of 8.8 on a scale from 0 (No benefit) to 10 (total benefit/improvement). The success for improving their symptoms correlates 0.63 with their commitment and persistence to the project.[18]

The purpose of this paper is to describe a case example how a student with severe back pain reduced her symptoms and eliminated medication by implementing an integrated self-healing process as part of a class assignment and offer recommendations how this could be useful for others.

Participant: A 28-year-old female student (J.C.) who on January 28, 2021 broke her L3 vertebra in a motorcycle accident. She underwent two surgeries in which surgeons replaced her shattered L3 with a metal "cage" (which she describes as looking like a spring) and fused this cage to the L2 and L4 vertebrae with bars. She also broke both sides of her jaw and fractured her left shoulder. More than a year later, at the beginning of the

self-healing project, she continue to take 5-10 mgs of Baclofen and 300 mgs of Gabapentin three times a day to reduce pain.

Goal of the self-healing project: To decrease the sharp pain/discomfort in her lower back that resulted from the motorcycle accident and, although not explicitly listed, to decrease the pain medications.

Self-healing process*:* During the last six weeks of the 2022 Spring semester, the student implemented her self-healing practices for her personal project which consisted of the following steps.

To create a self-healing plan that included exploring the advantage and disadvantage of her illness.

To create a step-by-step plan with specific goals to relief her tension and pain in her lower back. This practice allowed her to quantify her problem and the solutions. Like so many people with chronic pain, she focused on the problem and feelings (physical and emotional) associated with the pain. As a result, she often feels hopeless and worried that it would not change.

To observe and evaluate when her pain sensations changed. She recognized that she automatically anticipated and focused on the pain and anxiety whenever she needed to bend down into a squat. She realized that she had been anticipating pain even before she began to squat. This showed that she needed to focus on healing the movement of this area of her body.

Through her detailed observations, she realized that her previous general rating of back pain could be separated into muscle tightness/stiffness and pain. With this realization, she changed the way she was recording her pain level. She changed it from "pain level" into two categories: tightness and sharp pains.

To ask questions of her unconscious through a guided practice of accessing an inner guide through imagery (For detailed instructions, see Peper, Gibney, & Holt, 2002, pages 197-206).[13]

In this self-guided imagery, the person relaxes and imagines being in a special healing place where you felt calm, safe, and secure. Then as you relaxed, you become aware of another being (wise one or guide) approaching you (the being can be a person, animal, light, spirit, etc.). The being is wise and knows you well. In your mind, you ask this being or guide questions such as, "What do I need to do to assist in my own healing?" Then you wait and listen for an answer. The answer may take many forms such as in words, a picture, a sense of knowing, or it may come later in dreams or in other forms. When students are assigned this practice for a week, almost all report experiencing some form of guide, and many find the answers meaningful for their self-healing project.

When we think or imagine something, it changes our physiology. Thus, *focus on processes that support healing*.

Through this imagery of the inner guide script, she connected with her higher self and the wise one told her to "*Wait*." This connecting with the wise one was key in accepting that the project was not as daunting as she initially thought. She realized that pain was not going to be forever in her future. She also interpreted that as reminder to have patience with herself. Change takes practice, time and practice such as she previously experienced while correcting her posture to manage her emotions and edit her negative thoughts into positive ones.[17] Whenever she would have pain or feel discouraged because of external circumstances, she would remind herself of three things:

- I need to have patience with myself.
- I have all the healing tools inside me, and I am learning to use them.
- If I do not make time for my wellness, I'll be forced to make time for my illness.

To practice self-healing imagery as described by Peper, Gibney, & Holt (2002)[13] and adapted from the work by Dr. Martin Rossman.[19] Imagery can be the communication channel between the conscious/voluntary and the unconscious/autonomic/involuntary nervous system.[20-22] It appears to act as the template and post-hypnotic suggestion to implement behavior change and may offer insight and ways to mobilize the self-healing potential.[23] Imagery is dynamic and changeable.

The process of self-healing imagery consists of three parts.

1. To inspect the problem and create a graphic illustration of the problem as it is experienced at that moment of time.
2. To illustrate graphically how that area/problem would look when being completely well/whole or disappeared.
3. To create a self-healing process by which the problem would become transformed into health.[13] The process focuses on what the person can do for themselves; namely, each time they became aware of, anticipated, or felt the problem, they would focus on the self-healing process. It provides hope – since the person now focuses on the healing of the problem and becoming well.

The drawings of inspection of the pain and problem she experienced at that moment of time are shown in Figure 1. The resolution of the problem and being well/whole are illustrated in Figure 2.

Although she utilized the first image of the muscles warm, full of blood, free of thorns and the muscles relaxed and flexible, her second image of her fully being healed was inspired through a religious statue of Yemaya that she had in her room (Yemaya is a major water spirit from the Yoruba religion Santeria and Orisha of the seas and protector of women). Each time she saw the statue, she thought of the image of herself fully healed and embodying the spirit Orisha. Therefore, this image remained important to her all the time.

Her healing imagery process by which she transforms the image of inspecting of the problem to being totally well are illustrated in Figure 3.

For five weeks as she implemented her self-healing project by creating a self-healing plan, asking questions of her unconscious, drawing her self-healing imagery. She also incorporated previously learned skills from the first part of the semester such diaphragmatic breathing, hand warming, shifting slouching to upright posture, and changing language. Initially she paired hand warming with the self-healing imagery and she could feel an increase in body warmth each time she practiced the imagery. She practiced the self-healing imagery as an in-depth daily practice and throughout the day when she became aware of her back as described in one of her log entries.

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I repeated the same steps as the day prior today. I did my practice in the early morning but focused on the details of the slowed down movements of the sun's hands. I saw them as they stretched out to my back, passed through my skin, wrapped around my muscles, and began to warm them. I focused on this image and tried to see, in realistic detail, my muscles with a little ice still on them, feeling hard through and through, the sun's glowing yellow-orange fingers wrapped around my muscles. I imaged the thorns still in my muscles, though far fewer than when I started, and then I imaged the yellow-orange glow start to seep out from the sun's palms and fingers and spread over my muscles. I imaged the tendons developing as the muscle tissue thawed and relaxed, the red of the muscle brightened, the ice on and within my muscles started to melt, and the condensation formed as it ran down into collected droplets at the bottom of my muscles. I imaged the thorns lose their grip and fall out, one at a time, in tandem with the droplets falling. I continued this process and imaged my muscles expanding with warmth and relaxation as they stayed engulfed in the warmth of the sun.

At the end of my practice, I did a small stretch session. I felt extremely refreshed and ready for yet another extremely busy day between internship, graduation, and school. I would say I felt warm and relaxed all the way into the afternoon, about 6 hours after my practice. This was by far the most detailed and impactful imagery practice I have had.

The self-healing imagery practice provided me with the ability to conceptualize more than my problem as it showed me the tools to (and the importance of) conceptualizing my solution, both the tool and end result.

Figure 1. Illustration of the problem of the pain. Thorns dug deep, muscles tight, and frozen vertebrates grinding.

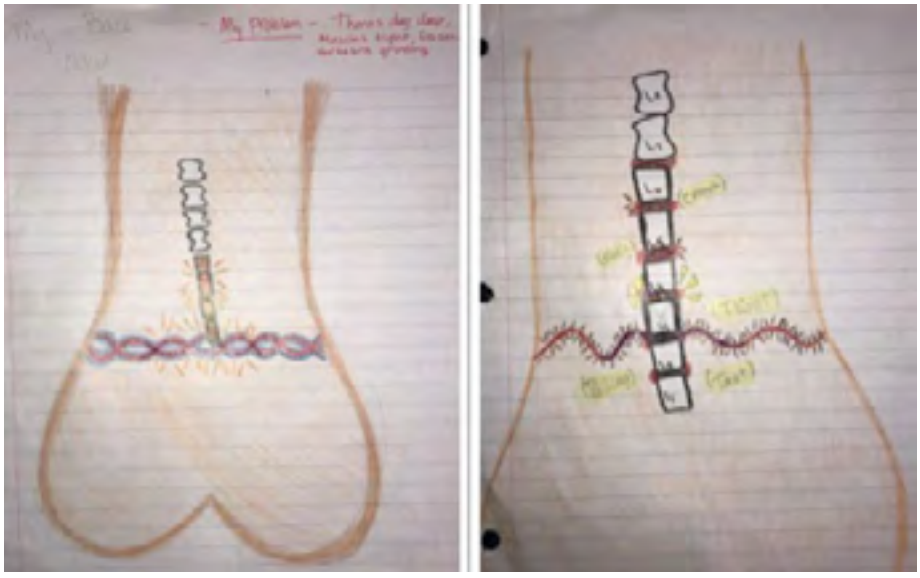
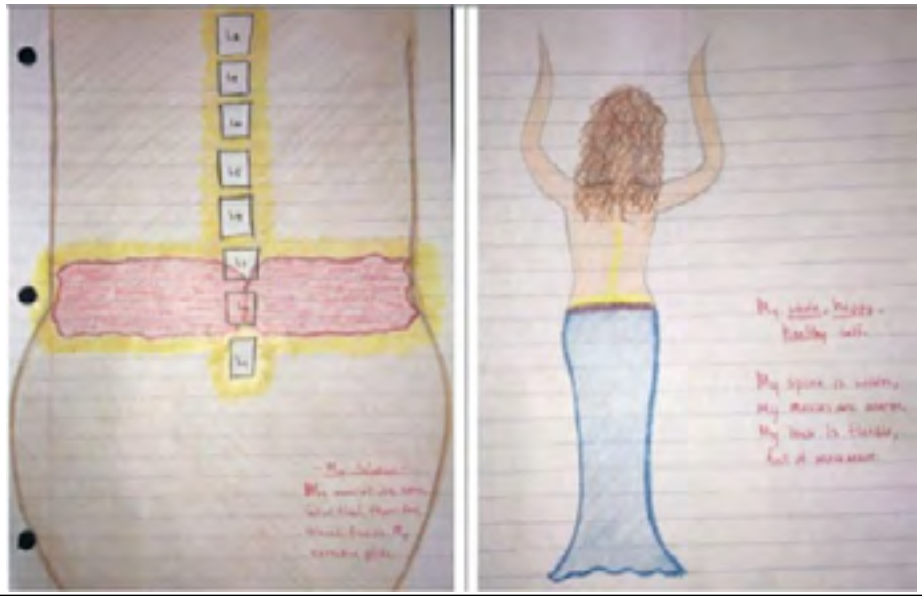


Figure 2. Resolution of the problem in which her muscles are warm, full of blood, free of thorns, relaxed and flexible and being whole happy and healthy in which her spine is warm, her muscles are warm, her back is flexible and full of movement.



Results

Pain and tightness decreased, and she stopped her medication by the third week as shown in Figure 4.

At the 14-week follow-up, she has continued to improve, experiences minimal discomfort, and no longer takes medication. As she stated, "I was so incredibly shocked how early on [in the project] I was able to stop taking pain medications that I had already taken every day for over a year."

Discussion

This individual case example provides hope that health can be improved when shifting the focus from pain and discomfort to focusing on actively participating in the self-healing process. As she wrote:

> The lesson was self-empowerment in regard to my health. I brought comfort to my back. There is metal in my back for the rest of my life and this is something I have accepted. I used to look at that as a horrible thing to have to handle forever. I now look at it as a beautiful contraption that has allowed me to walk across a graduation stage despite having literally shattered a vertebra. I am reintegrating these traumatized parts of my body back into a whole health state of mind and body. Doctors did not do this, surgeries did not, PT didn't and neither did pain medications. MY body and MY mind did it. I did this.

Besides the self-healing imagery and acting upon the information she received from the asking questions from the unconscious there were many other factors contributed to her healing. These included the semester-long self-practices and mastery of different stress management techniques, learning how stress impacts health and what can the person can do to self-regulate, as well as being introduced to the many case examples and research studies that suggested healing could be possible even in cases where it seemed impossible.

The other foundational components that was part of the class teachings included attending the weekly classes session and completing the assigned homework practices. These covered discussion about placebo/nocebo, possibilities and examples of self-healing with visualization, the role of nutrition, psychophysiology of stress, and factors associated with healthy aging across cultures. The asynchronous assignments investigated factors that promoted or inhibited health and the role of hope. The discussions pointed out that not everyone may return to health; however, they can always be whole. For example, if a person loses a limb, the limb will not regrow. The healing process includes acceptance and creating new goals to achieve and live a meaningful life.

The possibility that students could benefit by implementing the different skills and concepts taught in the class were illustrated by sharing previous students' successes in reversing disorders such as hair pulling, anxiety, psoriasis, and pain. In addition, students were assigned to watch and comment on videos of people who had overcome serious illness. These included Janine Shepherd's 2012 TED talk, "A broken body isn't a broken person,"[24] and Dr. Terry Wahl's 2011 TEDxIowaCity talk, "Minding your mitochondria."[25] Janine Shepard shared how she recovered from a very serious accident in which she was paralyzed to becoming an acrobatic pilot instructor while Dr. Terry Wahl shares how she used diet to cure her MS and get out of her wheelchair. Other assignments included watching Madhu Anziani's presentation, "Healing from paralysis-Music (toning) to activate health," in which he discussed his recovery from being a quadriplegic to becoming an inspirational musician.[26] The students read and commented on student case examples of reversing acid reflux, irritable bowel and chronic headaches.[27-32]

Although self-healing imagery appears to be the major component that facilitated the healing, it cannot be separated from the many other concepts and practices that may have contributed. For example, the previous practices of learning slow diaphragmatic breathing and hand warming may have allowed the imagery to become a real kinesthetic experience. In addition, by seeing how other students overcame chronic disorders, the class provided a framework to mobilize one's health.

Lessons Extracted from This Case Example That Others May Use to Mobilize Health

· Take action to shift from being hopeless and powerless to becoming empowered and an active agent in the healing process.

- Change personal beliefs through experiential practices and storytelling that provides a framework that healing and improvement are possible.
  - o Teach the person self-regulation skills such as slower breathing, muscle relaxation,

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Figure 3. The healing process: The sun's warm fingers thaw my muscles, lubricate my vertebra, thorns fall out, and blood returns.

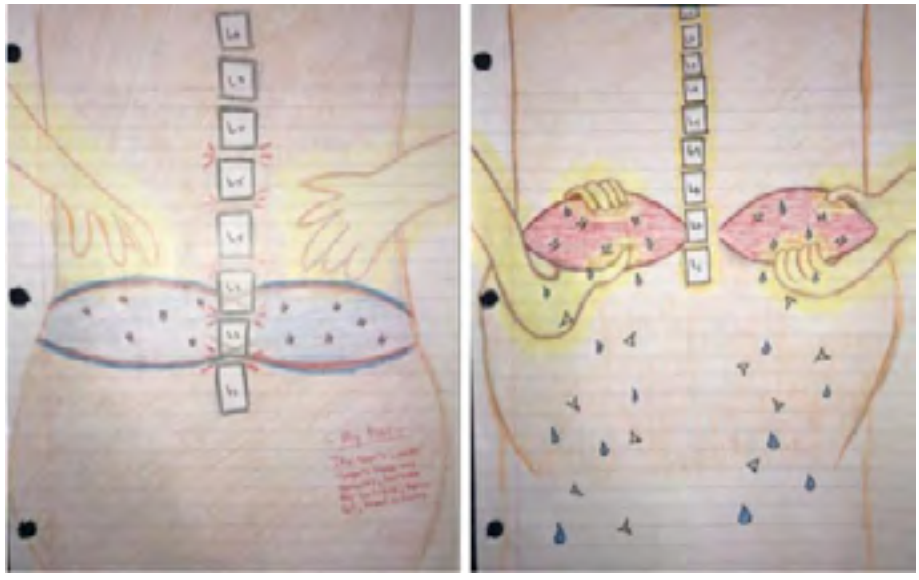
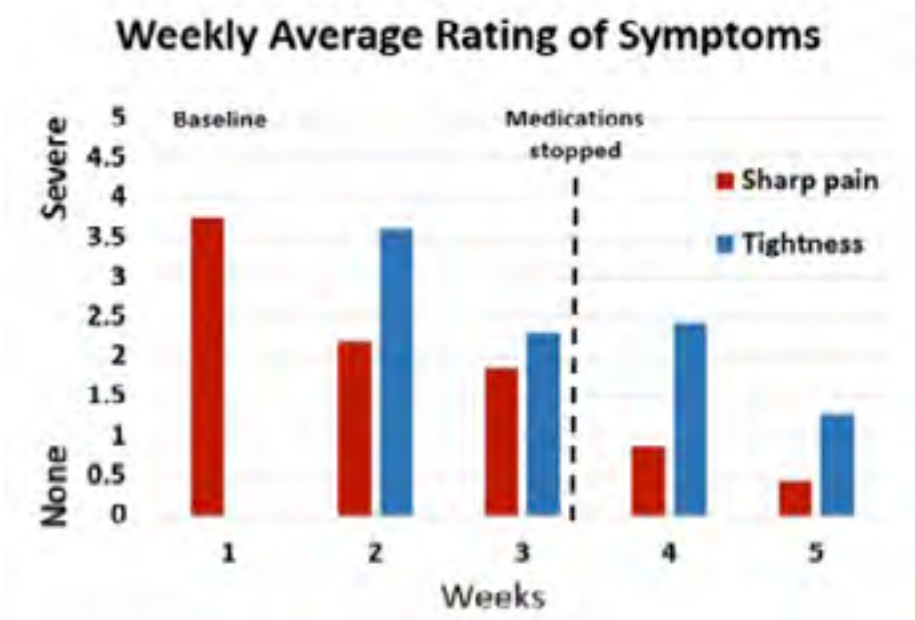


Figure 4. Self-rating of sharp pains and tightness during the self-healing project.



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cognitive internal language changes, hand warming by which the person experiences changes.

- o Provide believable role models who shared their struggle in overcoming traumatic injury, watch inspirational talks, and share previous clients' or students' self-reports who had previously improved.

- Transform the problem from global description into behavioral specific parts. For example, being depressed is a global statement and too big to work on. Breaking the global concept into specific behaviors such as, *my energy is too low to do exercise* or *I have negative thoughts*, would provide specific interventions to work on such as, increasing exercise or changing thoughts. In JC's case, she changed the general rating of pain into ratings of muscle tightness and sharp pains. This provided the bases for strategies to relax and warm her muscles.
- Focus on what you can do at that moment versus focusing on the past, what happened, who caused it, or blaming yourself and others. Explore and ask what you can do now to support your healing process and reframe the problem as a new opportunity for growth and development.
- Practice, practice, and practice with a childlike exploratory attitude. Focus on the small positive benefits that occur as a result of the practices. It is not mindless practice; it is practice while being present and being gentle with yourself. Do not discard very small changes. The benefits accrue as you practice more and more, just as many people have experienced when learning to play a musical instrument or mastering a sport. Even though many participants think that practicing 15 minutes a day is enough, it usually takes much more time. Reflect on how a baby learns to walk or climb. The toddler practices day-long and takes naps to regenerate and grow. When the toddler is not yet successful in walking or climbing, it does not give up or interpret it as failure or blaming himself that he cannot do it. It just means more practice.
- Have external reminders to evoke the self-healing practices. In JC's case, the small statue of Yemaya in her room was the reminder. It reminded her to think of the image of herself fully healed each time she saw it.
- Guide yourself through the wise one imagery, ask yourself a question and listen and act on the intuitional answers.
- Develop a self-healing imagery process that transforms the dysfunction to health or wholeness. Often the person only perceives the limitations and focuses on describing the problem. Instead, acknowledge, accept what was and is, and focus on developing a process to promote healing. *Many people do not realize that if they think/imagine how their injury/illness was caused, it may reactivate and recreate the initial trauma.* This can be illustrated through imagery. When we think or imagine something, it changes our physiology. For example, when one imagines eating a lemon, many people will salivate. The image affects physiology. Thus, *focus on processes that support healing*.
- While practicing the imagery, experience it as if it is real and feel it happening inside yourself. Many people initially find this challenging as they see it outside themselves. One way to increase the "felt sense" is to incorporate more body involvement such as acting out the imagery with hand and body movements.
- When having a relapse, remind yourself to keep going. Every morning is the beginning of a new day, do each practice anew. In addition, reflect on something that was challenging in the past but that you successfully overcame. Focus on that success. As JC wrote, "I was also successful in that I gave myself slack and reminded myself that relapses will happen and what matters more is the steps I take to move forward."
- Make your healing a priority that means doing it often during the day. Allow the self-healing imagery and process to run in the back of the head all the time just as a worry can be present in the background. So often people practice for a few minutes (which is great and better than not practicing at all); however, at other times during the day they are captured by their worry, negative thoughts or focus on the limitations of the disorder. When a person focuses on the limitations, it may interrupt the self-healing process. The analogy we often use is that the healing process is similar to healing from a small cut in the skin. Initially a scab forms and eventually the scab falls off and the skin is healed. On the other hand, if you keep moving the skin or pick on the scab, healing is much slower. By focusing on the limitations and past visualization of the injury, self-healing is reduced. This is similar to removing the scab before the skin has healed. As JC stated, *"If you don't make time for your wellness, you'll be forced to make time for your illness" was 100% a motivating factor in my success.*
- Explore resources for providers and people living with pain. See Dr. Rachel Zoffness' website, which provides a trove of high-quality articles, books, videos, apps, and podcasts. https://www.zoffness.com/resources.

In summary, we do not know the limits of self-healing; however, this case example illustrates that by implementing self-healing strategies health and recovery occurred. As JC wrote:

> To have broken a vertebra in my back and experience all the injuries that came with the accident when I already did not have the strongest mind-body connection was incredibly intense and really heartbreaking and discouraging in my life. And, that made things difficult because I was not able to 100% focus on my healing because I felt so overwhelmed by the feeling of discouragement that I felt. Experiencing this self-healing project, seeing the imagery that helped me not just feel so much better all the time but be able to stop taking all prescription pain medications and eliminate the sharp pains in my back has taught me that I have the skill set needed to be whole and healthy.

The interview with Jillian Cosby in which she describes her self-healing process is available at https://peperperspective.com/2022/07/31/healing-chronic-back-pain/.

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Monica Almendras holds a BSc in kinesiology, BA in German language and literature, and minored in holistic health. She also studied abroad at the Universität Heidelberg in Germany. She has a passion for helping people in all aspects of health and wellbeing to live life with no pain.

References are available online at www.townsendletter.com.

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Low-Level Laser Therapy and a Torn Meniscus: A Case Report

by Ryann McInturf and Bradford Case, ND, DC

Bastyr University, California

Abstract

Introduction: Meniscal tears can occur from excess rotation on the knee or degeneration associated with aging. Diagnosis is made by MRI and the standard of care is surgical repair. In this case, we consider the role of low-level laser therapy (LLLT) in the treatment of a torn meniscus.

Patient Information: XX is a 75-year-old female who presents with pain, swelling, and buckling in the right knee after walking downhill.

Clinical findings: McMurray's exam was positive on the right knee, indicating torn meniscus. All other tests performed were negative.

Diagnostic assessment: MRI was not possible. We diagnosed a torn meniscus by orthopedic testing. Given treatment compliance, we expect a good prognosis.

Therapeutic Intervention: Our primary treatment was LLLT for 15 minutes every week. Other treatments included curcumin, icing the knee, use of a knee brace, castor oil, and glucosamine sulfate.

Outcomes: After three treatments, orthopedic testing revealed 20% improvement and after four treatments, the patient-rated improvement was 5-10%. *Future*

Considerations: We hope to obtain an MRI to confirm our diagnosis.

Conclusion: LLLT has shown promise in reducing symptoms of a torn meniscus.

Introduction

Menisci are fibrocartilaginous structures composed primarily of type 1 collagen that are located in all articular surfaces throughout the body. In the knee, the lateral and medial menisci cover 70% of the articular surface and are located on the tibial plateau.[1] Menisci aid in shock absorption, load transmission, secondary stabilization and provide lubrication and proprioception to the knee joint.[1,2] The peripheral zones of the knee menisci are well-vascularized, while the medial zones receive nutrition via diffusion through the synovial fluid. A tear of the meniscus can occur from excess rotation or shear placed on the knee, especially when there is an increased load on the knee, such as is seen with kneeling, squatting, carrying heavy weights, and jumping. Medial meniscus tears are more common than lateral meniscus tears, and the incidence rate of meniscal tears in the United States is 61 per 100,000.

When a meniscus is torn, it is categorized by its shape and location via MRI. Horizontal tears are more likely in older populations with underlying degeneration where there may not be an originating event, while the various other forms of tears are related to specific injury-inducing events.[1] Often times in older populations, meniscal tears and osteoarthritis are strongly associated and the relationship between the two is complex, making it difficult to discern which caused the other.[3] Treatment of meniscus tears focuses on symptomatic relief, facilitating activities of daily living, and prevention of sequelae such as osteoarthritis and cartilage degeneration.[2,4] The current standard of care for a torn meniscus is arthroscopic surgical repair that involves partial meniscectomy or meniscal repair; however, surgeons are not able to restore the meniscal tissue or delay the development of osteoarthritis.[4,5]

Although surgical repair is the standard of care for a torn meniscus, there are a variety of low-force interventions that can be used to aid in meniscal repair. One such intervention is low-level laser therapy, also called photobiomodulation therapy, invented in 1967 by Endre Mester in Hungary.[6] Low-level laser therapy works by emitting an intense, monochromatic, coherent, and highly collimated beam of light within the red and near infrared portions of the electromagnetic spectrum. The photons from the laser are absorbed by cellular chromophores, undergo photochemical conversion, and are transferred to other molecules, causing chemical reactions and altering cellular metabolism without altering the temperature of the surrounding tissue. It is suggested that the mitochondria are most sensitive to near infrared light, and that LLLT increases production of ATP, increases DNA synthesis, modulates ROS, and induces transcription factors. Furthermore, near-infrared wavelengths lead to increased intracellular calcium.[7] These mechanisms stimulate tissue growth and repair and provide anti-inflammatory support to damaged tissues.[8]

This case involves a 75-year-old female who "tweaked" her knee one year ago. Orthopedic tests revealed

degeneration of the lateral meniscus of the right knee. In this case, we consider the role of low-level laser therapy in the treatment of a torn meniscus. This case is important because meniscal tears are very common and low-level laser therapy is a potential low force treatment option for cases where surgical repair may not be desired. This case study will look at whether or not low-level laser therapy is effective for reducing the severity of a torn meniscus.

Patient Information

XX is a 75-year-old female who presents to clinic with a chief complaint of knee swelling with occasional pain. Her knee pain started one year ago after she "tweaked" her knee while walking downhill and worsened with the new symptom of swelling one month ago after walking around a hilly area all day. Upon inspection, there is effusion in the superior lateral portion of the right knee. She experiences sharp pain and weakness when she walks downhill, and occasionally experiences buckling of her knees. She has been able to catch herself and prevent from falling when her knees buckle. Despite the onset of knee pain occurring about one year ago, this is the patient's first time presenting with this complaint and no past interventions have been attempted.

The patient's medical history reveals moderate lumbar scoliosis, which is being managed with chiropractic care and stretching. She also has a history of anemia, anxiety, skin cancer on the face, and hypertension. She is currently seeing a homeopathic doctor for depression, for which she has been prescribed *Sepia*.

The patient's family history reveals maternal arthritis, cancer, depression, hypertension, stroke, anemia, a blood transfusion, and osteoporosis. Her father had a history of heart problems, diabetes, stroke, and COPD. The patient's paternal grandfather had kidney disease, and her child has allergies.

Clinical findings reveal a non-antalgic gait. The right knee is positive for edema in the superior lateral quadrant of the right knee and active, passive, and resisted range of motion of the knee are within normal limits bilaterally. Additionally, the right knee was not tender to palpation.

Diagnostic Assessment

In order to diagnose and assess patient progress, we performed various orthopedic exams (Figure 2). Of note was McMurray's test, which was positive on the right knee. A positive finding on this exam indicates a torn meniscus and is the basis of our diagnosis. Definitive diagnosis of a torn meniscus is done by MRI imaging of the knee, but such imaging was not completed due to patient constraints.

Diagnostic constraints involved financial constraints as well as constraints related to patient preference. Due to financial constraints, the patient was not able to receive an MRI to confirm the diagnosis. Additionally, we advised the patient that treatment once a week was ideal, but coming to the clinic that often was not feasible for the first three treatments. Lastly, the patient did not want to participate in some of our treatment recommendations, namely wearing a knee brace when going for walks.

Our working diagnosis was "other tear of lateral meniscus, current injury, right knee" and our differential diagnosis included anterior cruciate ligament injury, iliotibial band syndrome, osteochondritis dissecans, lateral collateral knee ligament injury, patellofemoral joint syndrome, and posterior cruciate ligament injury. We were able to come to our working diagnosis by performing orthopedic exams, ruling in a torn meniscus and ruling out various other conditions.

Given the mild nature of this patient's injury, we feel the prognosis is good given that the patient is compliant with our treatment plan. Although the first three treatments were spread out because of patient time constraints, the patient has agreed to come in every week for treatment going forward. Moving to weekly treatment, we expect to see good improvement in symptoms within about two months.

Therapeutic Intervention

Our primary treatment was low-level laser therapy administered to the right knee in order to increase circulation for 15 minutes every week. We used ➤

Figure 1. Case Report Timeline

Figure 2. Orthopedic Exam

Orthopedic Exam	6/30/2021	8/4/2021
Apley's compression	Negative b/l	Negative b/l
Apley's distraction	Negative b/l	Negative b/l
Varus stress	Negative b/l	Negative b/l
Valgus stress	Negative b/l	Negative b/l
Anterior drawer	Negative b/l	Negative b/l
Posterior drawer	Negative b/l	Negative b/l
Lachman's	Negative b/l	Negative b/l
McMurray's	Positive on R Negative on L	Positive on R, but to lesser degree Negative on L

➤

the muscle/tendon/ligament for increased circulation setting set to chronic continuous with a 13 diode. The specifics of this treatment are listed in Figure 3.

We also recommended several other treatments. We recommended consumption of 1 gram of curcumin per day as an anti-inflammatory. The patient was very compliant with this treatment. We also recommended icing the knee when painful and wearing a knee brace during walks, neither of which the patient was compliant with. Application of castor oil to the knee once per day was recommended to support healing of the joint. Additionally, we recommended 1.5 grams of glucosamine sulfate per day to further support joint repair. The patient was compliant with both the castor oil and the glucosamine sulfate.

Follow-up and Outcomes

After three treatments with low-level laser therapy, we re-performed orthopedic exams to assess treatment outcome. McMurray's exam remained positive on the right knee, but there was a 20% reduction in clicking and grinding, indicating some degree of improvement. Additionally, the patient reported that she no longer experiences pain when walking and her knees are no longer buckling as often. Overall,

Figure 3. Therapeutic Intervention

Item	Description
Low Level Laser Therapy (LLLT)	A non-invasive treatment involving a single wavelength of light. It does not emit heat, sound, or vibration. LLLT affects the function of connective tissue cells, accelerates connective tissue repair, and acts as an anti-inflammatory agent.
Proprietary information	Chattanooga Group low-level laser, Model 27814, SN T1040
Authorization	This product is licensed in the USA
Qualitative Testing	Not applicable
Preparation methods	Not applicable
Route of administration	topical
Dosing regimen	15 minutes every other week
Recipient	75-year-old female with torn meniscus in right knee
Rationale	LLLT was chosen because of its ability to stimulate healing of connective tissue and reduce inflammation
References	Stausholm MB, Naterstad IF, Joensen J, et al. Efficacy of low-level laser therapy on pain and disability in knee osteoarthritis: Systematic review and meta-analysis of randomised placebo-controlled trials. *BMJ Open*. 2019;9(10). doi:10.1136/bmjopen-2019-031142
Practitioner	Ryann McInturf, NMS4 student
Instructional materials	Not applicable
Procedures	Plug machine in, then press power button. Enter passcode (1111), then click the folder symbol. Select clinical indications then select M/T/L increase local circulation. Select chronic continuous. Hit the start button, and then the laser button. Repeat last step until 15 minutes has been completed.
Delivery Setting	Intervention was applied to the patient's right knee. The mode of delivery was face-to-face
Tailoring	Not applicable
Modifications	Not applicable
Planned Adherence	Adherence was achieved at each appointment by performing the intervention during the appointment
Actual Adherence	Not applicable
Funding/Conflicts of interest	There were no conflicts of interest

Intervention	Compliance
1 gram curcumin per day	Compliant
Icing the knee when painful	Not Compliant
Wearing a knee brace when walking	Not Compliant
Castor oil topically on knee QD	Compliant
1.5 grams glucosamine sulfate per day	Compliant

the patient feels she has seen 5-10% improvement in her symptoms. Given that treatment is ongoing and the patient has only recently started to come for treatment weekly, we feel this degree of improvement is expected and indicates good prognosis.

On August 4, 2021, the patient presented an x-ray report ordered by her primary care provider. The x-ray results revealed chondrocalcinosis in the right knee. While this expands our understanding of the factors contributing to the patient's picture, it does not rule out the possibility of a torn or degenerated meniscus. Additionally, this finding reinforces our treatment plan, as chondrocalcinosis can also benefit from low-level laser therapy. Furthermore, the patient stated that she received a physical therapy referral from her primary care provider but has not yet had her first appointment with the physical therapist.

Overall, the patient was fairly compliant with her at-home treatment plan. As previously described, she was not compliant with icing her knee or wearing a knee brace, but all other home treatment recommendations were followed regularly. Additionally, the patient tolerated her low-level laser therapy treatments well and felt more relaxed after each treatment. Despite noticing a 5-10% improvement in symptoms, the overall patient-rated severity is unchanged (3/10).

There have not been any adverse events associated with the patient's knee symptoms or our treatment plan.

Future Considerations

As we continue care with this patient, we hope to obtain an MRI. Given that the patient has received an x-ray, an MRI is the next step in confirming our diagnosis of a torn meniscus. Furthermore, the patient has recently agreed to come in every week for treatment rather than every other week, which was her original preference. We feel that with continued treatment, and increased frequency of treatments, we will see good improvement in the patient's symptoms within two months.

Discussion

Torn meniscus is a common condition seen in primary care that is most often related to an excess force injury or increasing age. In this case, low-level laser therapy has shown some promise in reducing symptoms of a torn meniscus by stimulating circulation to the area of injury. Over the course of four treatments, the patient noticed a 5-10% improvement in symptoms. Additionally, McMurray's test, while still positive, shows a reduction in the degree of clicking and grinding in the knee. These results indicate that the use of low-level laser therapy may have some benefit for those experiencing a meniscal injury.

Conclusion

In this case study, we assessed the effectiveness of using low-level laser therapy to treat a torn meniscus in the knee over the course of three treatments. Our results reveal that low-level laser therapy does lead to improvement in patient symptoms and objective measures. While the improvement is small, it does indicate that low-level laser therapy may be a viable low-force intervention for a torn meniscus.

Acknowledgements

Verbal and written consent were obtained from the patient and are on file. We would like to thank her for her compliance with her treatment plan and willingness to participate in this case report. We would like to thank Dr. Case for his supervision and approval of this case report.

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He taught in the clinical sciences department at NUHS-Florida for two years as part of their Doctor of Chiropractic program. He now teaches naturopathic medicine at Bastyr University-California and is a clinical supervisor at Bastyr University Clinic in San Diego. While he claims no true specialty, GI health, physical medicine, AK/muscle testing, and whole food concentrates are mainstays of his practice life. He's also a veteran, serving in the Army National Guard for six years, retiring as a staff sergeant.

Biological Rhythms of Human Beings

by Raul Ibarra, MD*

Introduction

What is a Rhythm?

- Chronobiology: science that studies biological rhythms.
- Cycle: Pattern that repeats itself continually. Each one of the specific recurring events that happen with a determined periodicity.
- Frequency: Number of cycles that happen in a certain time. Number of successions of a certain kind of event per time unit.
- Period: Duration of a complete rhythmic cycle. Time that a wave requires to complete a cycle and go back to the starting point. Interval between two cycles
- Photoperiodicity: Response of a certain organism to the relative duration of day and night.

Some Examples in Plants and Animals: In plants, the leaves "rise" at the beginning of the day and go "down" at the sunset. Heliotrope rotates its stem so that its branches and leaves can always face the sun. Linnaeus described a Floral Clock, by which botanists could know the hour of the day, according to the moment at which the plants open their flowers. French astronomer de Mairan (1729) found that heliotropes locked in a dark closet kept moving their leaves with a 24-hour rhythm, proving clearly the existence of an **internal clock**. Bunning described the genetic characteristic of the internal clock in the pea leaves.

During the Greek era, Aristotle described the swelling of sea urchin ovaries during the new moon. Also, Cicero and Pliny observed that the number of oysters and other shellfish "increase and decrease" according to the moon´s phases.

(*) Guadalajara, Jalisco, Mexico

Crustaceans collected at the coast, even within a lab, keep their "activity cycles" according to the tides. In Panama there lives the "3 hours bird," that signals exactly at that time, either day or night. In Germany, Kramer (1950) found that diurnal birds guide themselves by the sun (solar compass); afterwards Sauer (1955) described that night birds use the stars as compass. Also, it has been seen that flies are more sensitive to the sprays at evening.

First Research in Humans

In 1614, Italian physician Sanctorius sketched a giant balance to measure his weight. During 30 years he made the observation that it "fluctuated" with a monthly rhythm parallel to a 30-day cycle in his urine turbidity. In 1842, Gierse described for the first time that the body`s normal temperature reaches a minimum (approx. 36.5 d.C.) at early morning, and a maximum (approx. 37.5 d.C.) at night.

In 1927, the Swedish physician Forsgreen described the periodic formation of bile and glucogen in human liver; the quantity changing with the hour of the day; and with an inverse relationship between them. In 1937, five physicians, one botanist, and a zoologist created the International Society for the Biological Rhythms. In 1938, researchers Kleitman and Richardson spent 32 days in the Mammoth Cave in Kentucky. In 1950, Hallberg used normal and blind mice to study the cyclic changes in their temperature and leukocytes. He also proposed the term "circadian" to refer to cycles of approximately 14 hrs.

The first Congress of Biological Rhythms was at Cold Spring Harbor, Florida, in 1960. In 1962, the French researcher Michel Siffre spent two months alone in a cave, with observation on changes in some of his rhythms. In Germany, Professor Aschoff used arranged bunkers for studies of total isolation during 16 to 30 hours.

Rhythms and the Normal Functions of Human Beings

For their study, thythms are divided as follows:

- Ultradians: less than 24 hrs. Like the cellular functions, heart beat, or brain waves.
- Circadians: Around 24 hrs. Sleep/ Awake. Changes in blood components, hormones. Body temperature.
- Infradians: More than 24 hours, including the Circaseptal (7 days), Circamensual (30 days), etc.

Internal (Endogenous) Rhythms are controlled by an "external environment," (also called external or exogenous cycles, geophysical, or periodic environmental factors): day/night (light/darkness) cycle, season changes, different Earth meridians, Earth´s rotation and translation; tides (moon´s attraction), changes in atmospheric pressure, solar flares, cosmic radiation.

In mammals, internal rhythms are controlled by the suprachiasmatic nucleus, which are located in the brain´s basement, at the anterior hypothalamus. From there, two branches emerge; one goes to the hypophysis (pituitary) gland, which elaborates several hormones that travel to the general circulation and regulates all the endocrine system. Afterwards, the different hormones produced at the thyroid, suprarenal, ovaries, and testes arrive through the general circulation to stimulate the hypophysis, and so, "close the circuit" in what is known as the hormonal feedback.

The other branch controls the functions of the sympathetic, and the

parasympathic systems, which are part of the autonomic nervous system. Also, at the brain´s basement is the pineal gland, which works as a mediation between the sunlight, retina, optic nerve (retino-hypothalamic path) and finally the central/endocrine nervous system.

In order to develop this activity, the pineal produces melatonin, a hormone which is liberated to the general circulation, but primarily works as neurotransmitter in the central nervous system (mostly upon the suprachiasmatic nucleus), affecting the oscillatory phase of the circadian and the reproductive rhythms. Its secretion reaches a peak at night, between 2 and 6 a.m.; this "secretory rhythm" depends upon the daylight intensity.

Among the conditions that control the amplitude in the melatonin´s secretion rhythm are the following: age, kind of work (diurnal/nocturnal), menstrual cycle (melatonin´s secretion decreases during the pre-ovulatory phase), season, sunlight, certain drugs, stress/exercise. For all the previous concepts, melatonin can be considered the seasonal synchronizer of the yearly endogenous rhythms.

Some examples of rhythms in the human body are brain waves (alpha, beta, theta and delta), cardiac rhythm (80 beats/minute) and the everyday/day-to-day fluctuations in arterial pressure and body temperature.

Applications of Rhythms in Our Daily Life

From the point of view of chronobiology, there are two kinds of persons: the Early Risers and the Noctambulists. The first ones, work better in the morning, being the contrary to the others, and vice versa.

Based in all the previous concepts, it has been found that the "worst" hour for a visit to the dentist is at 6 p.m. because the endogenous analgesic mechanisms (as for example, the endorphin production) reaches its "minimum" around this hour. Also, the tolerance for alcohol is greater in the afternoons.

Related to nutrition, the best hour for glucose assimilation is in the mornings, so the optimal metabolic conditions for losing weight are when the greater intake of food is done during breakfast. On average, the maximum intellectual performance is between 10 a.m. and 3 p.m.

In contrast, the maximum physical performance is on the afternoon. The greatest amount of mistakes occur with night workers, and also, after lunch hours (having eaten) or adapting to a new schedule (jet-lag).

Actually, sleeplessness is considered an internal desynchronization (the same as in chronic diseases), and the remedies are called re-synchronizers.

Some diseases "predominate" at certain time of day or season:

- Mornings: Rheumatoid arthritis, stroke, myocardial infarction and allergic rhinitis.
- Afternoon: Anxiety and essential hypertension.
- Nights: Asthma, biliary colic, and peptic ulcer.
- Spring: Migraine, allergic rhinitis
- Summer: Asthma
- Autumn: Arthritis, Asthma, myocardial infarction, migraine.
- Winter: Arthritis, Depresion/suicide, myorcardial infarction.

And Florida surgeons found that the post-tonsillectomies bleedings is "greater" during the full moon (14th. Day).

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Mercury Chelation: What Ever Became of OSR#1®?

by David C. Kennedy, DDS

Abstract

OSR#1®, also known as **NBMI**, is a lipophilic chelator and potent antioxidant. NBMI chelates irreversibly most toxic metals, notably mercury. Mercury is an insidious toxicant whose broad molecular mechanism – binding to sulfur – creates multiple toxic effects that interact to create a biochemical train wreck. The resulting dysregulation of multiple organ systems causes or contributes to most chronic illnesses as well as to aging. As an oxidative-stress remedy, NBMI employs two key mechanisms. 1) It scavenges hydroxyl radicals, three per molecule. 2) By chelating both mercury (Hg^{2+}) and free iron (Fe^{2+}), NBMI prevents the Fenton reaction and its resulting cascade of oxidative stress. As a result, NBMI boosts levels of reduced glutathione, the body's main intracellular antioxidant, and also improves the ratio of reduced to oxidized glutathione. Since 2010, NBMI's developer has been pursuing drug approval before the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), and recently the regulatory body, INVIMA, in Columbia, South America.

In 2008, following a decade of effort, retired chemistry professor Boyd Haley, PhD, introduced OSR#1® (Oxidative Stress Relief) as a doctor-dispensed, antioxidant dietary supplement, under pharmacovigilance. The compound is made from two natural, dietary ingredients – dicarboxyl benzoate and cysteamine, found in cranberries and meat, respectively – thus meeting the criteria of the US Food and Drug Administration (FDA) for dietary supplements in effect at that time (i.e., any natural ingredient or combination of two, without claims of treating a disease). But in 2010, after multiple blog claims by physicians and parents of autistic children that OSR#1® alleviates many symptoms of autism, the FDA changed its dietary-supplement rule specifically to exclude OSR#1®. Thus, despite consumer accolades and no evidence of harm, Haley was forced to cease and desist all sales. Haley's dismayed dentist and physician clients urged him to seek formal drug approval, and nearly one hundred of them offered early financial support for the lengthy and expensive undertaking.

As a chemist, Haley had long known that mercury's molecular mechanism of toxicity – binding to sulfhydryl (–S-H, one of the most useful and ubiquitous functional groups in biochemistry) – was upstream of most bodily processes; therefore, mercury had the potential to cause a metabolic train wreck that could produce myriad symptoms across multiple organ systems. Mercury also binds selenol (–Se-H), an important but less ubiquitous functional group.

Early in his career, Haley's research had convinced him that mercury and its associated oxidative stress played a key role in many neurological conditions, including Alzheimer's disease. Eventually he would identify mercury as a promoter of Fenton chemistry – a destructive chain reaction of oxidative stress, in which free iron (Fe^{2+}) catalyzes the production of hydroxyl radicals, the damage from which begets more damage. Mercury promotes Fenton chemistry by displacing iron, liberating it from critical binding sites often within mitochondria, leading to mitochondrial damage.

By 1989, Haley's experiments with Alzheimer's brain homogenates had uncovered a neurochemical mechanism – dysregulated tubulin polymerization resulting in microtubule disintegration – that is found in the brains of most Alzheimer's patients.[1] (Tubulin subunits, upon binding to the energy nucleotide, GTP, normally self-assemble into polymers, which associate laterally to form microtubules – crucial structures that provide intracellular transport and cytoskeletal strength, which are particularly important in nerve axons.) This research at the biochemical level would be validated at the cellular level by colleagues in 2001; cultured neurons exposed to infinitesimal doses of mercury suffered impairment of normal tubulin polymerization, thus causing microtubule disintegration.[2]

Upon publishing his numerous research studies linking mercury in brain homogenates and Alzheimer's disease, Haley was invited to speak at a conference of the International Academy of Oral Medicine and Toxicology (IAOMT), a professional medical/dental organization whose mission is to develop and disseminate the science related to the biological impacts of dental materials, including mercury. There, Haley explained his *in vitro* findings linking mercury and Alzheimer's disease using brain homogenates. Haley also noted his failed attempts to reproduce his findings *in vivo* by injecting lab animals with mercury chloride ($HgCl_2$). Murray Vimy, DMD, a founder of the IAOMT and professor at the University of Calgary, remarked that mercury chloride, as an ionic (charged) compound, will not cross the blood-brain barrier, whereas mercury vapor (Hg^0) readily will.

At the time, Haley was unaware that so-called "silver" fillings release significant amounts of elemental mercury vapor (Hg^0), particularly upon stimulation, such as chewing. This author, as an IAOMT officer attending the meeting, used a Jerome 411 mercury vapor analyzer to show Haley exactly how much mercury vapor was off gassing from the scientist's own "silver" fillings. Haley remained skeptical, presuming the FDA would not condone widespread use of a toxic implant. Upon returning to his lab, Haley confirmed that dental amalgam fillings are indeed a significant source of mercury – a fact that became generally recognized soon after.[3] Haley's lab lacked the capacity to expose animals to mercury vapor, so he began a collaboration with Vimy and the Calgary team to investigate *in vivo* the effects of elemental mercury vapor (Hg^0).

In a seminal paper published in 1997, the Haley and Vimy team document that mercury vapor (Hg^0), when inhaled by lab animals at levels intended to mimic human exposure to a mouthful of fillings, does indeed cause tubulin depolymerization – the same neurochemical pathology found in 80% of Alzheimer's brains.[4] The authors find that "chronic inhalation of low-level Hg^0 can inhibit polymerization of brain tubulin essential for formation of microtubules." They note that Alzheimer's research has not targeted environmental etiological factors and conclude that "Based upon our data, we believe one such factor could be Hg^0, to which the majority of individuals are continuously exposed." After this publication, Haley, who for 24 years had been continuously funded by NIH through renewable grant applications, found that his federal funding was not renewed.

A 2001 publication[2] and related four-minute video[5] by the Calgary team provide dramatic verification of Haley's work. Using time-lapse microscopy, cultured neurons are allowed to sprout neurites and are then exposed to various toxicants. Low-dose mercury causes the neurites to shrivel. As the authors explain, mercury rapidly and selectively inhibits the binding of GTP to tubulin, causing the disintegration of microtubules, leaving denuded neurofibrils that aggregate to form "neurofibrillary tangles," like those observed in Alzheimer's brain samples. Only mercury – not aluminum, lead, cadmium, or manganese – causes this dramatic alteration in neurite growth and structure, consistent with tubulin damage and disassembly. The authors conclude that "this visual evidence and previous biochemical data strongly implicate Hg as a potential etiological factor in neurodegeneration."

Additional research has confirmed links between mercury exposure and other hallmarks of Alzheimer's pathology. Nanomolar levels of mercury produce both beta-amyloid peptides, the main component of Alzheimer's brain plaques, and hyperphosphorylated tau, a microtubule-associated protein also associated with Alzheimer's.[6,7] In addition, micromolar levels of mercury inhibit activity of the amyloid-degrading enzyme, neprilysin.[8]

Haley describes, in a 2007 review, the variety of mechanisms by which mercury causes or contributes to the neurochemical pathologies and clinical symptoms of Alzheimer's disease.[6]

- Mercury inhibits many key enzymes in addition to tubulin that are recognized to be inhibited in Alzheimer's, including creatine kinase, which provides local energy storage, and glutamine synthetase, which mediates excitotoxicity.
- Mercury inhibits enzymes that synthesize heme, a functional building block that is deficient in Alzheimer's and is necessary for oxygen transport in red blood cells, for energy production in mitochondria, and for detoxification (via cytochrome P-450) in most cells, especially the liver.
- Mercury causes protein abnormalities, including misfolding, cross-linking, aggregation, and altered solubility, which are found in Alzheimer's and other diseases. Protein function – the essence of biochemistry and health – depends on three-dimensional molecular structures that are stabilized by disulfide bonds, which are targeted by mercury.
- Mercury blocks the production and recycling of glutathione – the body's key antioxidant defense molecule, known to be depleted in Alzheimer's – by inhibiting production of the necessary nucleotides, ATP and NADH.

NBMI (OSR#1) binds toxic metals, including free iron (Fe^{2+}) and mercury (Hg^{2+}), for excretion through the bile.

- Mercury promotes oxidative stress, known to be elevated in Alzheimer's, by displacing iron from its critical binding sites, thereby allowing free iron to catalyze the Fenton reaction in a self-perpetuating cascade of oxidative radical production. Thus, mercury both increases oxidative stress and depletes antioxidant defenses.

Haley describes mercury as a "retention" toxicant. An unethical seven-year study known as the Children's Amalgam Trial illustrates this phenomenon.[9] As expected, children who received mercury dental amalgam fillings demonstrated increased urinary mercury levels in the first two years – as much as twice that of the unexposed controls. But after the second year, excretion declined, such that by year seven the mean excretion of the exposed children (µg mercury per g creatinine) actually fell below their initial mean excretion before exposure. In other ➤

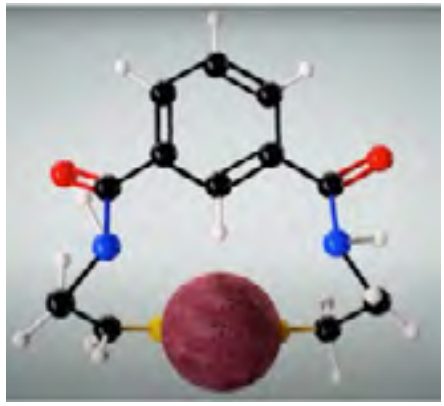

Figure A: NBMI is a stable, uncharged, lipid-soluble, intracellular heavy-metal chelator/antioxidant that passes the blood-brain barrier and biomembranes and is virtually nontoxic at levels that remediate mercury toxicity.

➤

words, exposures increased while excretion decreased. (See the infamous Figure 2 from the 2006 JAMA publication, "Neurobehavioral Effects of Dental Amalgam in Children."[9]) This finding suggests that routine exposures to dental mercury can cause retention toxicity, in which detox pathways become impaired – an inference not acknowledged by the study authors.

Haley notes that modern medicine has been unable to determine the etiology of the most important neurological diseases – autism, Alzheimer's, Parkinson's, ALS, and MS. The iatrogenic mercury hypothesis is ignored by the major research programs in the US and Europe despite ample evidence. Haley opines on the need for more research to investigate the extreme synergies of mercury with other toxicants. Haley notes that porphyrin profiles could be used to reveal the role of toxicant exposures in conditions such as Alzheimer's and autism, which both may be versions of iatrogenic mercury toxicity.

In his 2007 review paper, Haley summarizes, "Exposure of neurons in culture to nanomolar levels of Hg^{2+} has been shown to produce three of the widely accepted pathological diagnostic hallmarks of AD [Alzheimer's disease]. These AD hallmarks are elevated amyloid protein, hyper-phosphorylation of tau, and formation of neurofibrillary tangles." Furthermore, "....mercury is the only toxicant that has been shown able to reproduce many of the biochemical abnormalities and pathologic diagnostic hallmarks of AD."[6] In addition, ".... simultaneous exposure to other toxicants or factors can enhance the toxicity of mercury and hasten the onset of AD, especially in those individuals who are genetically susceptible."[6] Finally, "The presence of synergistic toxicity factors and genetic susceptibility factors prevent any simple correlation of mercury exposure or tissue levels to the onset of mercury-induced illness."[6]

Haley's research had evolved from investigating the role of toxicants in Alzheimer's to targeting mercury dental amalgam as the prime suspect. His work had revealed that inhalation of low-dose elemental mercury vapor (Hg^0) – but not the injection of mercury chloride ($HgCl_2$) – caused Alzheimer's-like aberrancies in test animals. From his association with the IAOMT dentists, Haley knew that dental amalgam was used worldwide to fill cavities; thus, exposure to elemental mercury vapor was, and is, ubiquitous. At the same time, the leading dental trade association, known for its powerful political lobby,[10] claimed – and to this day continues to claim – that mercury dental amalgam is "safe and effective"[11] despite an abundance of evidence to the contrary.

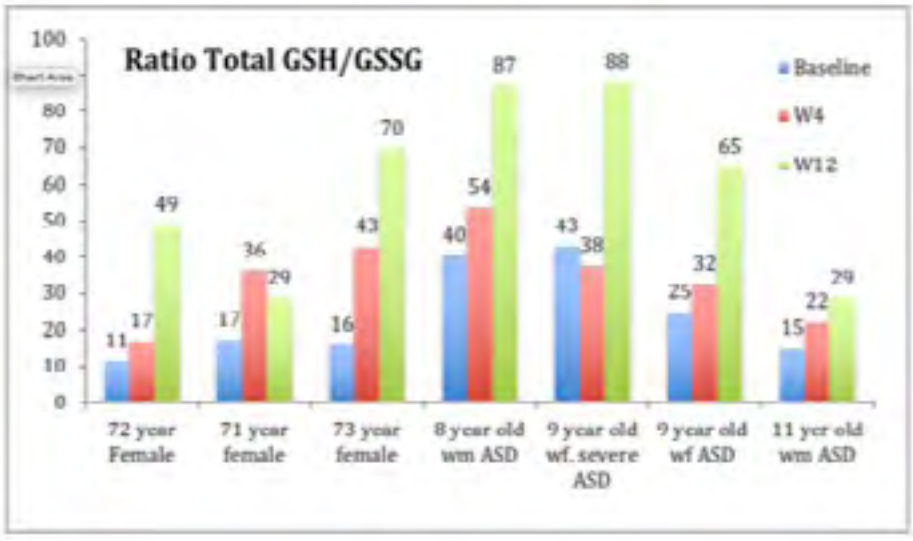

Figure B: The ratio of total reduced glutathione to oxidized glutathione, GSH/GSSH, improved by 245% in older women and autistic children after 12 weeks of NBMI at 100 mg/day. EmeraMed study done while OSR was a low-cost supplement.

By 1995, Haley had begun to envision the ideal mercury "chelator" – a compound that chemically binds a metal ion at two or more points, to facilitate elimination. It should be:

1. totally nontoxic;
2. made from natural substances to allow sale as a dietary supplement;
3. uncharged and lipid-soluble, in order to cross biomembranes and the blood brain barrier, so as to enter all cells and organelles of the body to which mercury would migrate;
4. capable of forming strong, thermodynamically irreversible semi-covalent bonds with the toxic metals, to eliminate toxicity upon binding and thereby prevent redistribution;
5. minimally attracted to essential metals to prevent their depletion (a major toxic effect of most charged chelators);
6. chemically inert and harmless even after binding the toxic metal;
7. effectively excretable, with and without a bound metal, through the bile and bowel via the naturally occurring cytochrome P-450 detox system, so as to prevent buildup in any organ or cell.

NBMI meets all seven requirements. It had been a compound initially developed at the University of Kentucky for treating contaminated mine wastewater but was deemed ineffective due to its relatively low solubility in water and difficulty in synthesizing. By 2005, Haley had succeeded in identifying and manufacturing this compound in a pure form, and in 2008 he introduced it as OSR#1® (Oxidative Stress Relief).

In 2014, Haley's company, CTI Science (formerly Chelator Technologies, Inc.), reorganized as EmeraMed LLC, headquartered in Ireland. Its chelator, NMBI, has received "orphan drug" designation by the FDA and the European Medicines Agency (EMA) for the treatment of mercury toxicity. This designation gives EmeraMed exclusive rights ("marketing authorization") to treat the orphan indication, upon approval, for seven years. Under the US Orphan Drug Act of 1983, Congress also intended the FDA to encourage development of effective treatments for rare, neglected diseases via incentives

such as fee waivers and grants, although for NBMI such help has not been available in the US. The EMA, on the other hand, provided a small grant for a fraction of the cost of a Phase 2 trial for Atypical Parkinsonism, a disorder linked to iron overload in the brain.

Biochemistry

NBMI, an abbreviation of the chemical name, **N**^{1}N^{3}-**B**is (2-**M**ercaptoethyl) **I**sophthalamide, comprises a dicarboxyl benzoate ring and two cysteamine arms, coupled to the ring by amide linkages, as shown in Figure A. The cysteamine arms function on opposite sides of the ring as two flexible appendages that fully rotate 360^{0} at each carbon or nitrogen atom, allowing the sulfhydryl hands of cysteamine to bind optimally a variety of toxic metals, forming an inert complex, as shown in an animated video.[12]

The dicarboxyl benzoate ring provides a site for both Phase I (cytochrome P-450) oxidation, yielding a soluble product for urinary excretion, as well as Phase II conjugation, to allow transport of the nontoxic, P-450-modified intermediate, out of the cell, into the blood, and then into the bile for fecal excretion.

This molecular structure allows NBMI to relieve oxidative stress via two key mechanisms. It binds toxic metals, including free iron (Fe^{2+}) and mercury (Hg^{2+}), for excretion through the bile. Alternatively, NBMI scavenges three hydroxyl radicals per molecule of NBMI, thereby becoming negatively charged and thus hydrophilic, for rapid excretion through the urine. As a result of these two mechanisms, intracellular glutathione is spared, and the ratio of reduced to oxidized glutathione is improved, as shown in Figure B.

Chelation

The two toxic-metal chelators frequently used in urine challenge testing – DMSA (dimercaptosuccinic acid; succimer; Chemet®) and DMPS (2,3-dimercapto-1-propanesulfonic acid; Dimaval®) – are hydrophilic; they are charged molecules at physiological pH, thus their access is extracellular only, primarily via blood. Furthermore, despite their di-thiol structure, these two "chelators" cannot form a true chelate complex due to the unfavorable stereochemical properties of their inflexible sulfhydryl groups. These so-called chelators are thus unsuitable for clinical use.[13] Another di-thiol, alpha lipoic acid, is a naturally occuring cofactor for the key metabolic enzyme pyruvate dehydrogenase, among others, as well as a transcription factor for the beneficial NRF2 pathway. As a potential chelator, alpha lipoic acid is both hydrophilic and lipophilic thus can access all cellular compartments, but like DMSA and DMPS, its unfavorable stereochemistry permits labile bonding and translocation of the toxic metal. The result can be toxic redistribution, especially in cases in which biochemical individuality has exacerbated poor detoxification and excretion.

Laboratory binding experiments have found that NBMI irreversibly binds mercury, arsenic, lead, cadmium, and uranium as well as free iron and free copper. A 2022 study on brain iron overload in an animal model shows NBMI to be superior in safety and efficacy as compared to the conventional treatment for brain iron overload.[14] Anecdotally, NBMI appears to chelate gadolinium, a rare earth metal used as a contrast agent in medical MRI (Magnetic Resonance Imaging).

Safety and Efficacy Studies

The regulatory approval process requires, first, a demonstration of safety in animals, followed by "Phase 1" clinical safety trials. When Phase I trials are complete, the sponsor may apply for Investigative New Drug status (IND), which allows the sponsor to conduct human Phase 2/3 (smaller/larger) clinical trials to evaluate safety and efficacy for treating the "indicated condition." NMBI received IND designation in 2015. When all Phase 2/3 studies are complete, the sponsor may submit a new drug application (NDA). If the agency accepts the application as complete, an FDA review team is assigned.

From 2008–2010, approximately 2.5 million doses of NBMI were sold as OSR#1® without prescription, under pharmacovigilance through about 1000 medical and dental offices, with no serious adverse events reported. Throughout its history, the only known adverse events have been exacerbation of sulfur sensitivity, described below.

Safety and efficacy studies in animal models. Haley's initial series of animal studies, reported in 2012, addressed acute and cumulative toxicity in several species of rats and concluded that NBMI

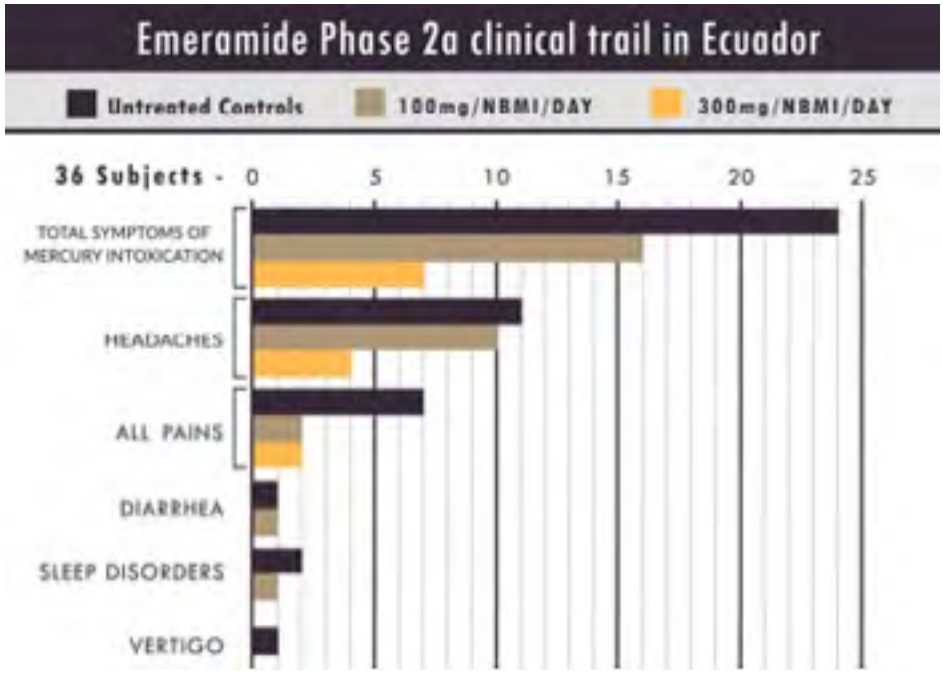

Figure C: Symptoms of mercury intoxication in Ecuadoran gold miners improved after two weeks of NBMI treatment.[16]

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was virtually nontoxic.[15] For example, an assessment of NBMI toxicity could not determine an LD_{50} (the lethal dose needed to kill 50% of the test animals); therefore, if an LD_{50} exists, it is above 5000 mg/kg-of-body-weight. In fact, this amount, which is roughly 1000 times the recommended dose for humans, failed to kill even one test animal. (The recommended dose for humans of 300 mg/day is equivalent to about 3–5 mg/kg-of-body-weight for a 60–90 kg, i.e., 130–200 lb. person.)

In rats poisoned with mercury both acutely and chronically, all animals treated with NBMI appeared to recover completely, except in a study of supra-lethal mercury exposures. In that study, the most unfortunate group of six rats received a mercury dose of 14 times the lethal level, then received a single dose of NBMI, 250 mg/kg-of-body-weight, 25 minutes after exposure. Four of the six rats actually survived the supra-lethal poisoning.[15]

In a fate and distribution study in animals, NBMI was well tolerated, easily absorbed and widely distributed; after four hours, NBMI was found throughout the body in all tissues, including the brain, and in organelles, including the mitochondria. Results of a bioaccumulation study of radiolabeled NBMI found that the compound was excreted to non-detectable levels in 72 hours.

Clinical trials for safety and efficacy. The Phase 1 clinical trial for safety and pharmacokinetics found no serious adverse events and no depletion of essential minerals when dosed at 300 mg/day for four weeks followed by 600 mg/day for 10 days.

In a Phase 2 field trial of 36 Ecuadoran gold miners who were severely ill with mercury intoxication, investigators tested a two-week course of NBMI at either 300 mg, 100 mg, or 0 mg per day, with a one-month follow-up. The 300-mg group demonstrated a statistically significant improvement in energy and drop in urine mercury, despite a daily cloud of mercury vapor wafting over the community, as well as the short duration and small sample size of the study.[16] The 300-mg group also demonstrated improvements in numerous other symptoms, most notably pain, as well as excessive salivation and tremors, as shown in Figure C**.**

A recent two-week, phase 2 trial of NBMI for Atypical Parkinsonism, an iron overload disorder, showed efficacy as measured by free iron (Fe^{2+}) levels. Subjects whose free-iron levels had steadily increased over the preceding years found their levels stabilized during the two-week treatment with NBMI. Results are being prepared for publication.

ORAC in vitro *study*. A remarkable ORAC score (Oxygen Radical Absorbance Capacity) of 199,000 Tolox units per 100 g[15] was measured for NBMI, as shown in Figure D.

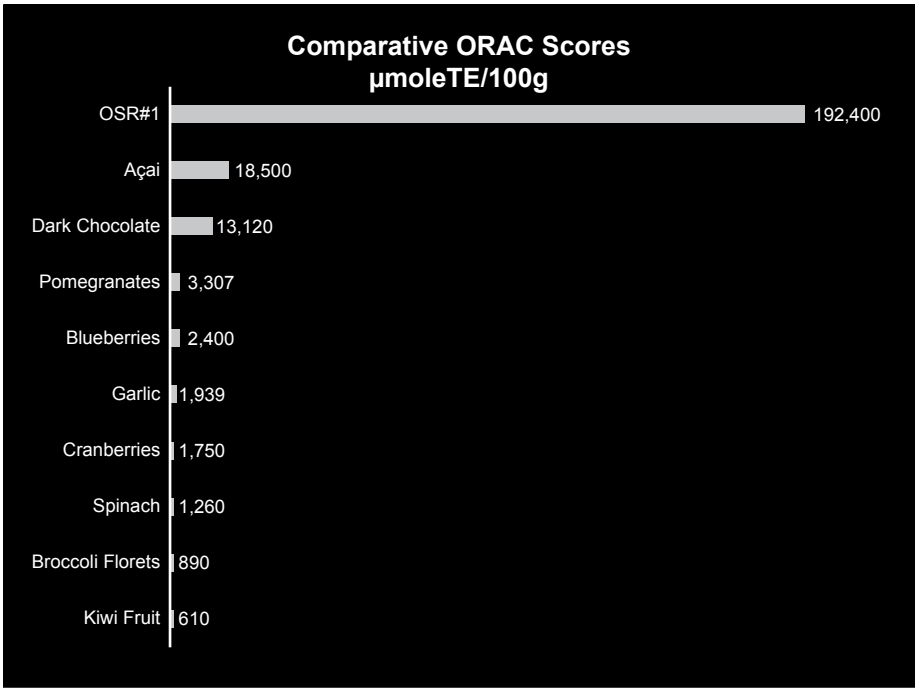

Figure D: Oxygen Radical Absorption Capacity (ORAC) score.[15] Note that scores are standardized based on 100 grams, although the recommended dose for OSR is only 300 mg.

Regulatory Status

In April 2019, Haley was encouraged by the results of a meeting with the oversight panel of the FDA's Division of Cardiology and Nephrology. The panel acknowledged the safety and effectiveness of NBMI for acute mercury exposure but wanted more information on NBMI's efficacy in treating chronic mercury toxicity. Since such a study in humans would be technically and ethically infeasible, a rat model was selected as appropriate, under the so-called Animal Rule. But in April 2021, the FDA inexplicably reassigned its oversight of the NBMI drug approval process to its Division of Non-Malignant Hematology – even though this medical discipline has little applicability to mercury toxicity. So far, the new panel has acknowledged the safety and efficacy of the product in two recent animal studies, one on reproductive toxicity in two species showing no evidence of harm to the fetus, and one on treating chronic mercury intoxication. The new panel even noted the apparent 100% protection conferred by NBMI when given to test animals prior to mercury injections. But the new panel demanded a large Phase 3 clinical trial in the US on patients with chronic mercury intoxication – despite the rarity of this diagnosis. This appears to the author to be yet another FDA effort to stall approval of this safe and effective heavy-metal chelator. Indeed, chronic mercury toxicity is virtually unrecognized in the US, aside from rare occupational exposures, and treatment endpoints are difficult to identify or measure. For over a year the agency has failed to provide guidance on an acceptable study design for this new requirement, leaving NBMI languishing in regulatory limbo, at least in the US.

In summary, as of 2022, Haley and his company, EmeraMed LLC, continue navigating the drug approval process to obtain marketing authorization in the US, the EU, and South America, for the treatment of mercury toxicity in humans, and in the US and the EU for animals. Fortunately, EmeraMed has been approved by Colombia's regulatory agency, INVIMA, to begin a Phase 2 trial in mid-2022 that will first enroll about 50 mercury-poisoned persons and then morph into a Phase 3 (larger) trial, enrolling a total of 120 subjects, with a simple endpoint – to evaluate urinary mercury excretion levels, with consideration of any mercury from dental amalgam exposure. Columbia is home to artisanal goldmining with its inevitable mercury exposures; consequently, regulators are familiar with the illness. According to Haley, the Columbia trial will likely lead to approval in South America well ahead of US FDA approval. In South America, approved drugs are registered to be dispensed by pharmacists, who assess a patient's needs independently of physicians. With approval in South America, it may also be feasible to obtain approval in Asia, the Philippines, and Africa.

In the US, on the other hand, where countless patients continue to suffer and die of treatable illnesses involving oxidative stress, even when a mercury burden is not apparent, the regulatory standstill is baffling. Haley has expressed frustration about the FDA's delays, rule changes, moving goalposts and lack of clarity on what additional steps are needed for approval. But he acknowledges that clinical trials on mercury toxicity in humans can be difficult to assess because, according to the FDA, this condition does not exist in the US. And if it does exist, it's a complex mix of interacting mechanisms, synergistic toxicities, genetics, and defenses, resulting in myriad, nonspecific symptoms that vary with the individual and are difficult to measure. Haley has acknowledged that providing proof of efficacy for treating a chronic illness can be difficult when there are no clear endpoints to identify or measure. Subjective improvement is not considered proof.

Practitioner and Patient Info

NBMI is not yet available; FDA approval remains chimeric. When NBMI is finally available, it is expected to provide significant benefits for any chronic illness involving oxidative stress, which is a sizeable target indication, because virtually every disease known has an oxidative-stress component. By treating oxidative stress in general and heavy-metal toxicity in particular, NBMI removes the body's impediments to healing, thereby allowing reversal of symptoms in many cases. NBMI on its own, however, does not reverse acquired damage such as tissue loss or scarring. The chronically injured patient will need a personalized recovery plan addressing genetic and metabolic hurdles as well as safe removal of mercury dental amalgams, such as the IAOMT Safe Mercury Amalgam Removal Technique.[17]

NBMI, once known as OSR#1®, goes by the generic name, emeramide and the proprietary name Irminix® in the EU. Counterfeit versions from unregulated suppliers, which have been sold on the internet since 2010, carry the warning label "not for human consumption" and may be contaminated. EmeraMed's product, made in the US, is pharmaceutically pure, with virtually no contamination, and unlike some counterfeits, will readily dissolve in 95% ethanol or dimethylsulfoxide (DMSO).

The most consistent side effect reported has been exacerbation of underlying sulfur sensitivity. As a sulfur-containing compound, NBMI may indirectly overload the enzyme, sulfite oxidase, which metabolizes sulfite to sulfate using molybdenum as a cofactor, and which is often impaired in mercury toxicity. The enzyme can usually be restored by supplementing with molybdenum, thereby alleviating symptoms of sulfur sensitivity.

OSR#1®

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David Kennedy is a retired dentist, who serves as the public information officer and a past president of the International Academy of Oral Medicine and Toxicology (IAOMT). His presentations on the health impacts of dental materials, including mercury and fluoride are available on his YouTube channel. He is an investor in Boyd Haley's company, EmeraMed, LLC.

On the Cover

Recent Research on Membrane Lipid Replacement with NTFactor Lipids®: Enhancement of Nutrient Bioavailability and Reductions in Symptom Severities in Chemically Exposed Veterans

by Garth L. Nicolson, PhD, MD (H)[1]*, Robert Settineri, MS[2] and Paul C. Breeding, DC[3]

Abstract

Membrane Lipid Replacement with protected membrane glycerolphospholipids (NTFactor Lipids®) enhanced the bioabsorption of three test nutrients (quercetin, curcumin and coenzyme Q10) in an *in vitro* Caco-2 gastrointestinal epithelial cell permeability model. *In vivo* oral use of NTFactor Lipids® in an open label study showed reduced multiple, self-reported symptoms in chemically exposed Gulf War veterans with multi-symptom chronic illnesses. In the patients that fully complied and completed a six-month study there were gradual and significant reductions of symptom severities in categories related to fatigue, pain, musculoskeletal, nasopharyngeal, breathing, vision, sleep, balance, urinary, gastrointestinal and chemical sensitivities. Membrane Lipid Replacement with protected membrane glycerolphospholipids is a simple, safe and potentially effective method of slowly reducing the severities of multiple symptoms in chemically exposed veterans. In addition to potentially promoting the increased absorption and transport of nutrients through intestinal epithelial cells, Membrane Lipid Replacement has its own health benefits in reducing symptom severities in chronically ill patients.

Introduction

Membrane Lipid Replacement (MLR) using dietary protected polyunsaturated glycerolphospholipids, such as NTFactor Lipids®, results in the systemic replacement of damaged cellular membrane glycerolphospholipids with undamaged, unoxidized lipids to ensure the proper function of cellular membranes, such as mitochondrial membranes.[1-3] By blending the glycerolphospholipids with antioxidants and membrane-protecting fructooligosaccharides, MLR supplements have proven to be effective in reducing multiple, chronic illness symptom severities and age-associated loss of function, while providing mitochondrial and other membrane support.[1-5] The MLR supplement NTFactor Lipids® has been used in several clinical studies that demonstrate its safety and efficacy.[3-7] Here we show that NTFactor Lipids® can improve nutrient transport in an intestinal epithelial bioabsorption model.[8] In addition, in chemically exposed veterans, this supplement can reduce the severity of several chronic signs and symptoms.[9]

MLR and Intestinal Bioabsorption Models

Prior to clinical studies on the effects of various nutrients on health indicators, cell-based assays are often used to provide evidence for human intestinal absorption and bioavailability of oral supplements.[10] I*n vitro* cultured cell models have been used for epithelial absorption and bioavailability, and these have been found to compare well with *ex vivo* organ absorption.[10,11] In such *in vitro* models various lipids have been added to oral supplements to enhance epithelial cell absorption and bioavailability.[12] Although other factors can affect gastrointestinal transit, digestion, dissolution and epithelial absorption, this last event is critical for the overall bioavailability of oral nutrients.[12]

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One of the most widely used cell models for bioabsorption and bioavailability is based on the human colon epithelial cell line Caco-2.[13] The differentiated Caco-2 epithelial cells are used in polarized monolayer cell cultures to mimic an epithelial cell barrier.[8-11] Caco-2 cell monolayers express a wide range of properties that mimic an intestinal epithelial cell layer and have been used as uptake/bioavailability models.[9,10] In these models Caco-2 intestinal monolayers are grown on a supportive membrane surface that separates two compartments in a trans-well where test substances can be sampled.[11,13] Caco-2 uptake studies have been used as the reference standard in the pharmaceutical and nutraceutical industries for the *in vitro* prediction of *in vivo* human intestinal absorption and bioavailability of orally administered nutrients.[11,13,14]

We used the Caco-2 intestinal monolayer test system to see if NTFactor Lipids® can improve nutrient transport. First, the reliability of the Caco-2 test system was confirmed in a control study.[8] The results indicated that the trans-well permeability system worked as expected during the assay. A low-permeability molecule, talinolol, control showed a Papp value of <0.5, and a high permeability molecule, warfarin, control was found to have a Papp value of >100, as expected.[8]

For studying the effects of MLR on bioabsorption and bioavailability of test nutrients, each nutrient was tested with three concentrations of NTFactor Lipids® (provided by Nutritional Therapeutics, Inc.).[8] For each nutrient, the mean response versus dose level and the standard deviation for the mean are shown in Table 1. For example, in Caco-2 bioabsorption studies of CoQ10 (with 0 to 1% NTFactor Lipids®) transport was increased 2.01-times over controls with 1% NTFactor Lipids® ($p= 0.0011$).[8] Although there were positive dose-dependent responses of curcumin and quercetin absorption with NTFactor Lipids®, these did not reach the same level of significance as seen with CoQ10.[8] However, when the overall combined dose increase was compared with all three nutrients, ANOVA analysis indicated a significant collective enhancement of absorption by NTFactor Lipids® ($p< 0.001$).[8]

The above study demonstrated that the bioavailability of nutrients, especially those with more lipophilic structures, when combined with NTFactor Lipids®, should result in increased absorption and transport through intestinal epithelial cells compared to the nutrients without added glycerolphospholipids. This suggests strongly that NTFactor Lipids® can promote oral nutrient bioavailability.[8]

Effects of NTFactor Lipids® on Symptom Severities in Chemically Exposed Veterans

Many veterans of the first Gulf War in 1991 returned and slowly displayed multiple signs and symptoms related to their deployment.[15,16] The most common signs and symptoms found included chronic fatigue, arthralgia, myalgia, headaches, gastrointestinal problems, sleeping difficulties, dermatological symptoms, breathing problems, loss of concentration and cognition, depression, muscle spasms, nervousness, blurred vision, anxiety, chest and heart pain, dizziness, nausea, stomach pain, loss of balance, hives, frequent coughing, chemical sensitivities, eye pain, vision problems and photophobia, bleeding gums, and other symptoms.[15-18] This multi-symptom chronic illness has been called Gulf War Illness or Gulf War Illnesses (GWI).[19,20] Many of these veterans appear to have their diagnoses linked to chemical exposures, such as oil spills and fires, smoke from military operations, chemicals on clothing, pesticides, chemoprophylactic agents (pyridostigmine bromide), chemical weapons and other possible exposures.[18-22] However, the apparent spread of a similar illness to immediate family members in the absence of environmental exposures suggests that a minority of veterans were exposed to an infection(s).[19,23,24]

Membrane lipid replacement has been used to slowly remove hydrophobic toxic molecules.

In addition, fine sand exposure was rather ubiquitous during deployment, and continued pulmonary exposure to fine sand particles can result in hyperergic lung conditions and pneumonitis.[25] The exposures to different, multiple agents and toxicants have made the successful treatment of GWI quite difficult.[19,26]

Treatment of GWI has been complicated by multiple toxic exposures (chemical, biological, and in a few cases radiological as well as stress) and the lack of available methods to successfully treat or remove offending substances.[19,26] MLR has been used to slowly remove hydrophobic toxic molecules, and possibly some of the toxic chemicals implicated in some cases of GWI.[19,21,26,] This removal process is thought to occur by a concentration-dependent process, driven by a bulk flow or mass action mechanism. Hydrophobic molecules are slowly sequestered into small glycerolphospholipid droplets, vesicles and other structures and eventually removed from cells and tissues by mass action, transported by the blood circulation, and deposited into the gastrointestinal system for elimination.[27,28]

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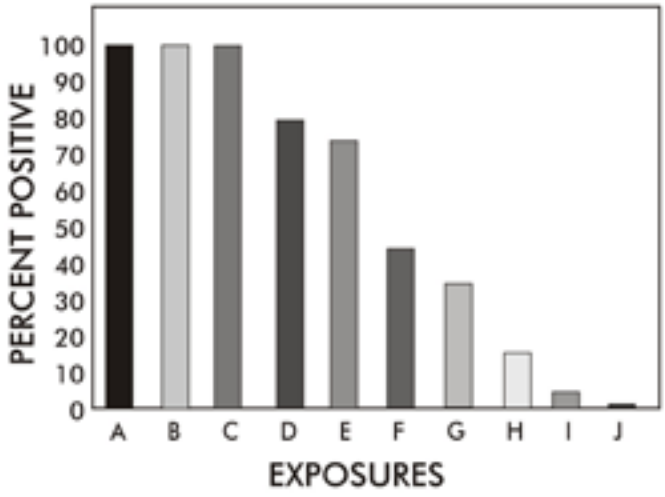
Figure 1. Trial participant-reported exposures during the 1991 Gulf War. Percent of trial participants exposed to: (**A**) Direct contact with fuel and/or oil, (**B**) Smoke from burning oil wells, (**C**) Smoke from burn pits, (**D**) Ingestion of pyridostigmine bromide, (**E**) Exposure to pesticides, (**F**) Exposure to raw sewage, (**G**) Exposure to insects, (**H**) Direct contact with dead bodies, (**I**) Presumed exposure to chemical warfare agents, and (**J**) Exposure to herbicides. (Modified from Nicolson and Breeding.[9])



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Most uses of MLR do not require the higher doses of NTFactor® or NTFactor Lipids® (usually 2-4 g per day) to affect the severity of multiple signs and symptoms. For example, several studies on various clinical conditions and aging have used the 2-4 g per day dose range.[3,4] However, to drive the removal of hydrophobic, toxic chemicals and support the health of Gulf War veterans higher dose levels were required (6 g per day) in case studies.[29,30] Also, most non-GWI clinical studies indicated that reductions in symptom severities found with MLR occurred much sooner than found in most cases of GWI. Although the reasons for this are not clear at this time, they may be related to deeply embedded, toxic chemicals in veterans that appear to be difficult to remove and are only removed slowly from their hydrophobic sites.[9]

Case reports previously suggested the usefulness of MLR in Gulf War veterans to lower symptom severities and improve health.[29,30] In these case reports the daily dose of NTFactor Lipids® was increased to 6 g per day in order to improve the rate of removal of toxic chemicals. Thus an open-label, Institutional Review Board-approved, preliminary clinical study was initiated to study the clinical effects of a glycerolphospholipid chewable wafer supplement containing NTFactor Lipids® (provided by Nutritional Therapeutics, Inc.) on the severities of signs and symptoms of GWI patients. Five supplement wafers providing a total of 6 g of NTFactor Lipids® were taken each day for six months, and various signs and symptoms were self-reported at various times (0, 0.25, 1, 3 and 6 months) using a validated patient symptom survey form.[9] The symptom severities in the survey form were scored numerically based on a linear scale from 0 to 10 or lowest (0) to highest (10) severity of symptoms. The symptom severity survey form contained approximately 120 signs and symptoms that were later merged into 22 symptom categories to more easily assess the effects of NTFactor Lipids®.[9] The patients were male US Marines and US Army veterans who were chemically exposed during their deployment, had been ill since their deployment without relief, and had signed informed consent documents. The average age in years of participants that fully completed the study was 53.1±3.2. Each patient was diagnosed with GWI based on their deployments and diagnosis of Gulf War Illness using the chronic multi-symptom illness standards developed by the US Government and the State of Kansas.[15,31] Inclusion criteria in the study included at least three of six symptom categories: fatigue, pain, neurological, skin, gastrointestinal, respiratory symptoms.[31] Exclusion criteria included diagnosis of a serious medical condition not usually associated with deployment to the Persian Gulf region or a psychiatric condition that could account for some symptoms, or an illness that could interfere with accurate scoring of sign/symptom severity.[9]

Study participants were exposed to a variety of environmental conditions and toxicants in the Persian Gulf

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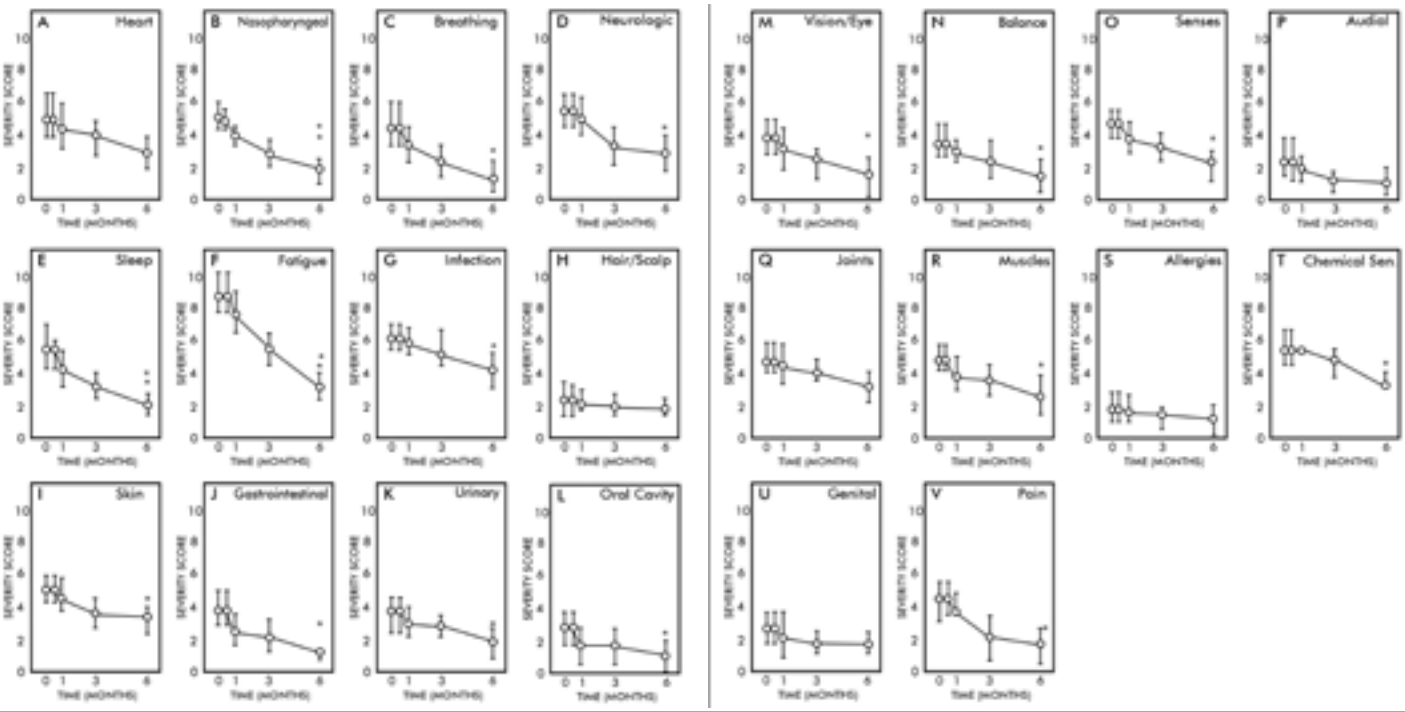
Figure 2. Symptom category scores with time reported by trial participants who took the oral MLR supplement NTFactor Lipids®. The mean symptom category severity scores (±standard deviations) of trial participants at day 0, one week, one month, 3 months and 6 months of 6 g/day oral NTFactor Lipids®. (**A**) Heart symptoms, (**B**) Nasopharyngeal symptoms, (**C**) Breathing difficulties, (**D**) Neurologic symptoms, (**E**) Sleep disturbances, (**F**) Fatigue, (**G**) Infection(s), (**H**) Hair/scalp disturbances, (**I**) Skin disturbances, (**J**) Gastrointestinal symptoms, (**K**) Urinary symptoms, (**L**) Oral cavity disturbances, (**M**) Vision/eye disturbances, (**N**) Balance disturbances, (**O**) Sense disturbances, (**P**) Audial disturbances, (**Q**) Joint symptoms, (**R**) Muscle symptoms, (**S**) Allergies, (**T**) Chemical sensitivities, (**U**) Genital disturbances, and (**V**) Pain. (*, p<0.01; **, p<0.001). (Modified from Nicolson and Breeding.[9])



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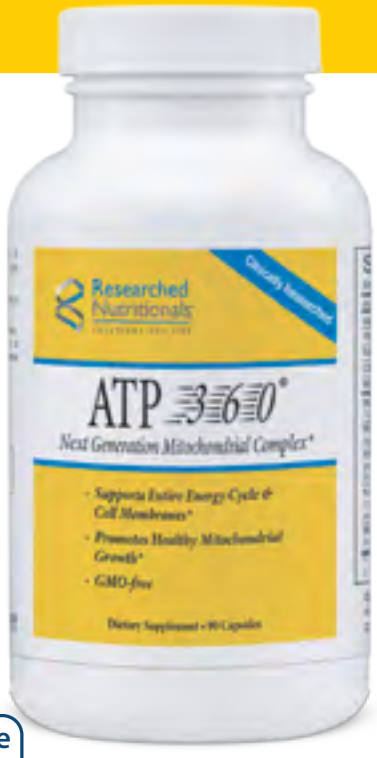

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region.[9] For example, all of the participants reported exposures to oil well fires and burn pit smoke, fuels, and crude or refined oils (Figure 1).[9] In addition, all of the participants took oral chemoprophylactic agents (pyridostigmine bromide) during the conflict. Most participants reported that they were also exposed to pesticides, but only a few to insects. Some trial participants also reported exposure to raw sewage and dead bodies.[9] A few participants may have been exposed to chemical warfare agents, and there was a very low incidence of reported exposure to herbicides (Figure 1).[9]

At the beginning of the study, veterans reported a variety of signs and symptoms severities that were unique for each patient. In Figure 2 the self-reported symptoms and severities of the study participants were grouped into symptom categories, and the reported category severities and their change over time were different and collected for each patient.[9] The mean changes in the study group's self-reported symptom categories with time during the study are shown in Figure 2 along with the standard deviations of symptom severities. Although there were differences in the symptom category severities and responses to the test supplement in individual subjects, the group mean data indicated that there were gradual and significant responses to the test supplement. Specifically, there were significant reductions in symptom category severities related to fatigue, pain, musculoskeletal, nasopharyngeal, breathing, vision, sleep, balance, gastrointestinal, chemical sensitivities and other symptom categories (Figure 2).[9]

As expected, the reductions in certain symptom severities were gradual and significant ($p<0.01$ to $p<0.001$) with time as shown in various symptom categories, such as fatigue (Fig. 2F), sleep disfunction (Figure 2E), gastrointestinal symptoms (Figure 2J), pain (Figure 2V) and other symptoms. In the present study we also considered self-reported changes in chemical sensitivities (Figure 2T). In general, there were significant reductions in certain symptom categories that have been related to GWI.[9]

Discussion

We have briefly presented some recent data on the use of MLR with the dietary supplement NTFactor Lipids®. This supplement has the structure and properties to improve the transport and bioabsorption of many nutrients as well as enhance cellular energy by repairing free radical damage to mitochondrial and other cellular membranes.[1-8] MLR with NTFactor Lipids® has been used to reduce symptom severity in patients with fibromyalgia, chronic fatigue, chronic pain and other chronic conditions that have pain and/or fatigue as major symptoms.[1-7] Some symptoms, such as fatigue and pain, also occur during normal aging, and they are important as secondary symptoms in many if not most chronic diseases.[32-34]

MLR with oral glycerolphospholipids have been used successfully in several clinical studies to reduce symptom severity and improve quality of life assessments.[1-7] The MLR supplement NTFactor Lipids® with fructooligosaccharides (to protect the phospholipids from disruption, degradation and oxidation in the gut) and antioxidants have significantly reduced symptom severity in various chronic illness patients (see reviews[1-7]). The membrane glycerolphospholipids are quickly and almost completely absorbed and transported into tissues and cells without excessive oxidative damage.[2,3] There the undamaged, replacement membrane phospholipids can exchange with damaged membrane phospholipids, resulting in replacement of the damaged molecules and in the process also remove other hydrophobic molecules. In addition, MLR glycerolphospholipids provide important precursors for specific membrane molecules, such as mitochondrial cardiolipin.[2,3]

Oral MLR supplements such as NTFactor Lipids® have been designed to reduce fatigue and protect cellular and especially mitochondrial membranes from damage.[1-7] By combining NTFactor Lipids® with vitamins and minerals (such as Propax™ with NTFactor Lipids®), cancer patients have shown reductions in the adverse effects of cancer therapy, such as chemotherapy-

Table 1. Analyses of nutrient bioabsorption assays in controls and with different concentrations of NTFactor Lipids® using the Caco-2 test system (n=3). (Data from Settineri et al.[8])

Nutrient	NTFactor Lipid dose	n	Mean	Std. dev.	Minimum	Maximum	Absorption increase
CoQ10	Control (0%)	3	0.90	0.10	0.81	1.00	–
	0.1% (1 mg/mL)	3	1.00	0.20	0.83	1.22	1.11
	0.25% (2.5 mg/mL)	3	1.17	0.23	1.01	1.43	1.30
	1.0% (10 mg/mL)	3	1.81	0.23	1.64	2.07	2.01
Curcumin	Control (0%)	3	0.56	0.06	0.51	0.62	–
	0.1% (1 mg/mL)	3	0.58	0.12	0.49	0.71	1.03
	0.25% (2.5 mg/mL)	3	0.96	0.22	0.72	1.14	1.71
	1.0% (10 mg/mL)	3	1.25	0.68	0.78	2.03	2.23
Quercetin	Control (0%)	3	1.42	0.13	1.29	1.55	–
	0.1% (1 mg/mL)	3	1.53	0.22	1.29	1.73	1.08
	0.25% (2.5 mg/mL)	3	1.71	0.42	1.25	2.08	1.20
	1.0% (10 mg/mL)	3	1.83	0.35	1.42	2.05	1.29

induced fatigue, nausea, vomiting and other adverse side effects.[33] MLR with NTFactor Lipids® have also been used in other illnesses to reduce symptoms, especially fatigue.[1-7] One combination supplement, ATP Fuel (Researched Nutritionals, Inc.) with NTFactor®, CoQ10, NADH and other nutrients has been used to significantly reduce fatigue in patients with intractable chronic fatiguing illnesses.[34] Indeed, the use of NTFactor® and NTFactor Lipids® in conjunction with several other natural supplements to restore mitochondrial function has many potential uses.[35] Finally, the most universal use of MLR supplements like NTFactor Lipids® may be as a completely safe anti-aging supplement to increase the performance of cellular membranes, especially mitochondrial membranes, that functionally decline with advanced age.[2-7,30]

Patient Consent

The data collection and patient evaluations were approved by an independent institutional review board. Patients consented to use their clinical information via informed consent.

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Managing Persistent Pain

by William Longton, MD

Anesthesiology & Pain Medicine

Chronic pain is one of the most debilitating conditions we experience. We can't exercise or sleep or focus. We may gain weight and become irritable, if not downright depressed. Yet the ability to perceive pain is vital to species survival and protects us by helping us detect injury and by initiating the body's response to acute damage. Our longevity is made possible by the ability to heal, restoring traumatized tissue and calming inflammation. Unfortunately, this ability diminishes over time. When this healing capacity is disrupted, it can play a role in the development of chronic tissue degeneration and pain.

Acute and Chronic Pain

Sudden, immediate pain is a response to tissue trauma, detected in the tissues by nociceptors that can identify thermal, pressure, or chemical injury and transmit that information along ascending sensory nerves to the spinal column and the brain. An accurate diagnosis of the cause of the pain is critical because if recognized and diagnosed early on, that can prevent the development of chronic pain.

Treatment of acute pain. Pain control for acute pain generally involves a series of steps, including reduction of inflammation with ice and anti-inflammatory medications, interruption of pain signals with an anesthetic nerve block or cortisone injections, and stronger opioid pain medication, used in the short term to mask the pain, temporarily allowing some degree of increased mobility and activity.

Pain brain. In the case of repeated trauma, nerve damage, and/or chronic inflammation, the pain pathway can go awry, resulting in increased pain sensitivity, nerve inflammation, and the development of chronic neuropathic pain sometimes referred to as "pain brain."

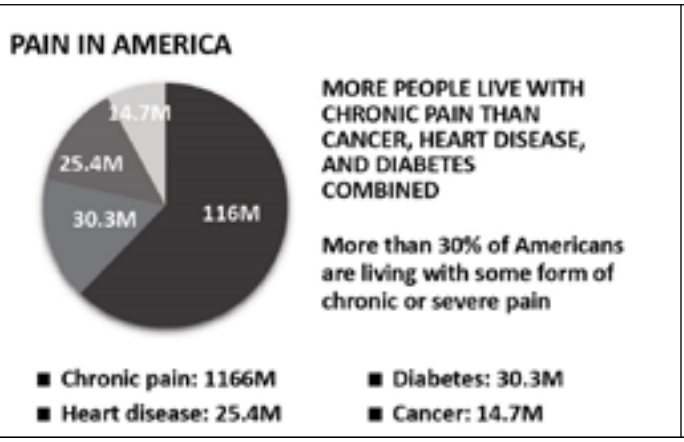
Unchecked chronic pain. In these disorders, multiple segments of the pain pathway have become dysfunctional or neuropathic, reflected in chronically swollen tissue, pain receptors that have become hypersensitive to pain, nerve endings that preferentially pass along pain signals, and central/brain processes leading to depression.

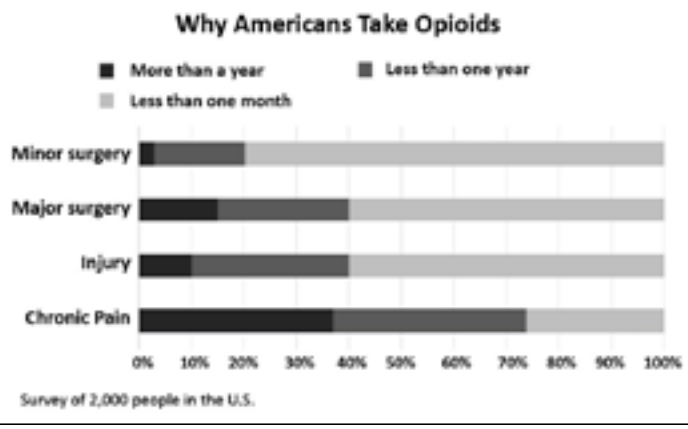
Incidence. Pain disorders increase as we age, with 7% of chronic pain sufferers between the ages of 18 and 24, growing to 22% between 45 and 64. From at least 65 on, 27% of the population is afflicted by chronic pain, which is an enormous economic burden costing over $500 billion (2010 US), including direct healthcare costs, and disability programs, as well as incalculable human cost.

Pain Syndromes

A detailed listing of all the causes of chronic pain and chronic pain syndromes is beyond this article's scope. However, we can draw many commonalities from familiar pain syndromes, including lumbar disc degeneration and osteoarthritis.

Low back pain. Estimates of the prevalence of low back pain have ranged from 22% to 48%, with surveys that found 26% of respondents reported low back pain lasting at least one day in the last three months. Risk factors associated with back pain complaints include smoking, obesity, age, physically strenuous work, sedentary employment, psychologically strenuous work, workers' compensation insurance, and job dissatisfaction.





Psychological risk factors include anxiety, depression, and somatization disorder (stress and emotions expressed through the mind-body connection).

The most common diagnosis is non-specific low back pain. These are conditions in which no specific tissue injury can be diagnosed, but the underlying cause is likely to be a combination of muscle, disc, tendon, and/or ligament strain. The vast majority of patients will recover within two weeks with brief episodes of rest (but avoid bed rest), NSAIDs, and muscle relaxants. If sciatica is present, a short course of oral steroids may be appropriate and may provide relief.

If the pain persists beyond two to four weeks and is not improving, then medical evaluation is needed with possible referral for physical therapy, massage, and chiropractic treatment, as well as a review of imaging studies and pain management referral.

Disc pain. Nearly everyone experiences some level of lumbar pain from disc degeneration by the age of 40. Initial causes are usually related to repeated strains and overuse. There is emerging evidence that infection may also play a role in the development of lumbar disc degeneration. Younger men tend to suffer more from disc and vertebral joint inflammatory processes, whereas older men will suffer more from spinal stenosis (see Sidebar).

Osteoarthritis. This is a classic age-related disorder of the joints, a form of chronic degeneration. In osteoarthritis, degradation and loss of joint cartilage are central features of wear and tear on the joints. The prevalence of osteoarthritis increases from 10% at age 45 to 30% at age 60 and 50% by the age of 80.

Effects of aging. In all degenerative diseases, cell and tissue aging results in age-related loss of the ability to heal and repair cells. Those who have excess weight gain or joint misalignment will develop a maladaptive response to joint stress resulting in osteoarthritis.

Smoking as a trigger of chronic pain. Cigarette smoking is strongly associated with increased chronic pain, including low-back pain from lumbar disc degeneration. Less well known is the negative effect of cigarette toxins on immune response and tissue regeneration (due to carbon monoxide, nicotine, and other chemical additives), which weaken discs and joints, inhibit cell growth within the disc, cause localized constriction of blood vessels surrounding the lumbar disc, damage collagen production, and weaken the outer lining of the disc (the annulus).

Obesity as a factor in inflammation. Addressing obesity is key in preventing and treating chronic pain because excess weight contributes to chronic inflammation (increasing pro-inflammatory mediators such as tumor necrosis factor – TNF-alpha). We know that patients undergoing gastric bypass procedures have a measurable decrease in inflammatory markers within 12 months of surgery.

The links between stress, depression, and inflammation. Both stress and depression are common in people with chronic pain. There is considerable evidence that those with diagnosed depression have higher markers of pro-inflammatory mediators, suggesting a link between depression and inflammation: Vagal nerve tone is reduced, diminishing opportunities to reduce inflammation. This results in increased stress response, which dials down the relaxation response and slows cellular healing.

Lifestyle Strategies

Exercise. It may seem like common sense to exercise, thereby reducing the risks of cardiovascular disease and obesity, improving metabolism, and strengthening the heart, muscles, and bones. Studies have also shown that as little as 20 minutes a day of exercise can reduce blood levels of pro-inflammatory chemicals, allowing the body to heal injured tissues more efficiently.

Breath work. The use of breathing techniques to improve the control and tone of the vagus nerve is a simple approach that can be practiced by anyone. As humans, we breathe up to 20,000 times per day, so we have ample opportunities to perfect this pain-relieving skill.

Mindfulness meditation. Functional MRI studies have found that mindfulness meditation rapidly increases the ability to tolerate pain. This has been demonstrated in research studies involving patients with no prior experience with meditation. Imaging studies have shown that meditation improves blood flow to critical brain areas involved in pain processing. Efforts at meditation can be supported by an app on the phone (such as The Headspace), books, podcasts on meditation, and HeartMath devices and software.

*Anti-inflammatory diet***.** Dietary interventions to manipulate or optimize the gut flora (the microbiome) could play an increased role in inflammation control. The goal is a simple diet of anti-inflammatory foods, such as the Mediterranean diet, which is high in fresh fruits (berries and stone fruit such as cherries and peaches), vegetables and leafy greens, whole grains, healthy oils such as olive oil, nuts (almonds and walnuts), and fatty fish. These foods are rich in natural antioxidants, polyphenols, and other protective compounds that reduce inflammation. Coffee, which contains polyphenols and other anti-inflammatory compounds, can also reduce free radicals and protect against inflammation.

The gut-inflammation connection. Recent studies have focused on the role of the gut microbiome on osteoarthritis:

- We now have evidence of a genuine relationship between certain gut bacteria and low-grade inflammation in the knee (as well as arthritic knee pain, independent of obesity).

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The lumbar spine has a normal aging process that accelerates as the disc loses cushioning:

- Tears occur in the disc's outer annulus surface.
- Subsequent damage results in the inner disc nucleus.
- Ultimately this trauma induces loss of water content from the disc
- The resiliency and cushioning of the disc are reduced.
- The disc then loses height.
- Vertebra may shift, and inflammation ensues.
- Nerves and spinal joints become inflamed, causing pain and/or spasms.
- Nerve compression can occur, resulting in sciatica and nerve injury.
- As the spine ages further, degenerative arthritis and bone spurs result.
- This narrows the spinal canal (spinal stenosis). which further compresses spinal nerves.

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- Differences are also evident in the spine suggesting that certain gut flora may be more favorable in minimizing disc inflammation.
- It also suggests that disc *infection* may be one possible initiator of lumbar disc disease.

Foods to avoid. The goal is to find healthy substitutes for refined carbohydrates, fried foods (such as French fries), sodas, red meat, processed meat such as luncheon meat, margarine, and lard. By modifying the Western diet, it is possible to facilitate a healthier gut microbiome, cutting down on unhealthy fats and eating significantly more fiber-rich foods (such as fresh fruits and vegetables). Healthy lifestyle habits that promote a more diverse gut microbiome also include fermented foods such as sauerkraut and miso, probiotics, the avoidance of unnecessary antibiotics, reducing stress, and getting adequate sleep.

Medications

NSAIDS. Nonsteroidal anti-inflammatories are commonly used to treat acute and chronic inflammation pain. Diclofenac 150 mg/day has been reported in some studies as the most effective NSAID for pain relief for osteoarthritis or rheumatoid arthritis. The studies compared diclofenac with naproxen (1000 mg/day), ibuprofen (2400 mg/day), celecoxib (200 mg/day), and acetaminophen (4000 mg/day). Since side effects include renal and hepatic toxicity and gastrointestinal (GI) bleeding that can be potentially fatal, diclofenac is not available over the counter and physician-directed lab monitoring will be required periodically.

Over-the-counter NSAIDS such as 200 mg naproxen 1-2 capsules as needed every 12 hours may be preferable due to naproxen's longer duration of action.

Antidepressants and anti-seizure medications. Gabapentin (Neurontin) and pregabalin (Lyrica) are prescribed for neuropathic pain. These medications work by reducing nerve transmission along the pain pathway of the central nervous system, but can cause side effects of drowsiness.

Topical preparations. These medications include topical Voltaren, lidocaine, capsaicin, and Traumeel to reduce pain of painful joints, the lumbar region, or smaller areas of inflammation. Diclofenac 1% in a topical formulation can be effective for smaller joints near the skin surface, such as those of the hands, elbows, and knees. Formulated as a gel, there is less systemic uptake, so the risk of toxicity is less when taken at the prescribed dosage.

Supplements and Botanicals

Meta-analysis of nutritional supplements for osteoarthritis (the knee, hip, or hand) reported pain reduction in the short term (less than three months). Clinically significant effects were reported for several supplements: L-carnitine (an amino acid), pycnogenol (an extract of the peeling of passion fruit), and collagen hydrolysate.

Note that, in the long-term, no supplement was found to have clinically significant effects on pain.

Magnesium deficiency. Insufficient levels of magnesium are often a major contributor to chronic low-grade inflammation, and a magnesium oxide supplement in a 500 mg dose has been shown to reduce inflammatory markers such as IL-6 (interleukin 6). Magnesium supplements have also been shown to improve endurance in magnesium-deficient athletes.

Zinc. This critical mineral appears to support the immune system, while reducing several markers of inflammation.

Curcumin. The key ingredient of turmeric, curcumin has been shown to benefit inflammatory conditions and pain. It is a polyphenol that has antioxidant and anti-inflammatory effects. A typical dose is 400-600 mg, three times daily.

Frankincense. Studies have shown that frankincense (*Boswellia serrata* resin) can reduce both inflammation and pain and is a relatively fast-acting supplement that may help with osteoarthritis pain within as little as five days. The typical dosage is an extract containing 30% to 40% boswellic acids, 300–500 mg doses two to three times per day.

Curcumin and frankincense in combination. Using these two botanicals together increases potency, suggested in studies on patients with knee osteoarthritis. Patients sensitive to the gastrointestinal side effects of NSAIDs may tolerate this supplement combination better and still get meaningful pain relief.

Prescription Opioids

The use of opioids to treat chronic non-cancer pain is controversial due to limited evidence of long-term efficacy and the potential risk of serious harm. For patients with chronic non-cancer pain, opioids should only be used when non-opioid therapies have not provided sufficient pain relief, resulting in reduced function and/or compromised quality of life. In terms of decision-making, the potential benefits of opioid therapy should outweigh potential harms.

Risk factors. The use of opioids for pain relief requires additional levels of monitoring to assess medication misuse or abuse. Risk factors for misuse of opioids include a personal or family history of substance use disorder, younger age (less than 45 years of age), more severe pain, and/or co-occurring mental health disorders.

Complementary therapies. To minimize the amount of opioids required, opioids should be provided in tandem with non-opioid medication and physical treatments, including acupuncture, chiropractic, and physical therapy. Treatment should be accompanied by improved physical functioning.

Alternative medications. A variety of medications are typically prescribed before a trial of opioids, including NSAIDs, and certain antidepressants (Cymbalta-duloxetine, Elavil-amitriptyline) or antiseizure medications (Gabapentin, Lyrica-pregabalin) to target neuropathic pain.

*Intrathecal administration***.** For patients who require particularly large doses of opioids, resulting in intolerable side effects such as fatigue or drowsiness, implantable spinal delivery systems that provide intrathecal administration of opioids can be considered. Intrathecal analgesic therapy should be reserved for intractable severe pain with significant impact on quality of life that is resistant to all other appropriate treatments.

Newer formulations. Opioids that stimulate opioid kappa receptors in peripheral tissue (for example, kappa receptors in knee joints) and do not cross the blood-brain barrier may be more effective and safer than traditional opioid drugs and are currently in development.

Working with a Pain-Management Physician

Seek out a physician who is fellowship-trained and board-certified in pain medicine. Other credentials relevant to pain medicine include residency training in fields such as anesthesiology, neurology, physical medicine and rehabilitation, family medicine, psychiatry, or radiology.

A qualified pain management physician will be comfortable performing a number of different interventional procedures, including nerve blocks, joint injections, and spinal injections. They will be able to evaluate and treat a variety of acute and chronic pain problems, prescribe or optimize appropriate medications, and refer patients for physical therapy and rehabilitation. No single physician is an expert in every treatment and technique, so a qualified doctor should also know when to refer to other experts and subspecialty physicians.

Preparing for a visit. Patients should be prepared in advance to discuss their medical history and pain symptoms in detail:

- When the pain started
- Where it is located
- The quality, intensity, and timing of the pain
- The radiation pattern, if any
- Aggravating and alleviating factors.

Medical records. The patient should collect relevant imaging studies and have a list of treatments, surgeries, and medications tried thus far. Important considerations include the diagnosis, the prognosis, and appropriate treatment, starting with the most conservative options.

*Assessing the physician's expertise***.** The patient should make sure that the physician is highly skilled in performing any interventional treatments being offered. The patient should get an understanding of what needs to be done to optimize his health and lifestyle to prevent or minimize further pain episode.

Pain Management Interventions

Injecting local anesthetics and cortisone. Injections, applied along nerve pathways, interrupt the pain signal, allow restored mobility, and can "reset" a dysfunctional pain pathway. Spinal injections include epidural and facet joint injections that reduce inflammation around compressed spinal nerves and joints due to herniated discs, vertebral degeneration, or spinal stenosis.

Nerve blocks. These are relatively brief treatments that often take only a few minutes to perform. If specialized x-ray equipment is involved and a number of nerves are being injected, the procedure usually takes 10 to 15 minutes. X-rays are usually taken using a fluoroscope, which creates a live image with different viewing angles. Imaging makes the injection process much safer and faster. Most nerve blocks and injections are not overly painful and can be performed in an office setting with just a local anesthetic. However, some spinal injections are performed at a surgery center with light intravenous sedation combined with local anesthetic for patient comfort.

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Pain relief should occur relatively quickly, even before you leave the office, because of the rapid onset of the local anesthetic. The addition of a steroid is designed to promote a longer-lasting anti-inflammatory effect on inflamed nerves and tissues.

Shockwave therapy. Treatment of greater trochanteric pain syndrome, patellar tendinopathy, and Achilles tendinopathy, as well as plantar fasciitis and calcific tendinopathy of the supraspinatus or Achilles tendon, with ESWL shockwave therapy can provide meaningful pain-relief. This is typically performed by a sports medicine doctor.

Minimally invasive surgical treatments. This type of treatment includes nerve ablation (with radiofrequency energy applied through a small needle) and neurostimulation (using small, implanted electrodes to minimize nerve transmission along the pain-pathway without causing weakness). Delivery of imperceptible electrical stimulation pulses at specific frequencies across the spinal cord can inhibit the pain circuitry responsible for the transmission of pain. This stimulation reduces the hyperactivity of neurons implicated in chronic pain. Spinal cord and peripheral nerve stimulation is used in a variety of pain syndromes, including persistent spinal or sciatic pain after failed spinal surgery, persistent nerve pain syndromes such as chronic regional pain syndrome (CRPS), extremity pain from ischemia, post-amputation pain, and other peripheral nerve pain syndromes.

Advancements in spinal neurostimulator technology and algorithms. High-frequency spinal stimulation can be provided at a level that is imperceptible yet offers substantial pain relief in a variety of chronic nerve pain conditions, including peripheral neuropathy and chronic spine and sciatic pain. This type of treatment also includes PRP (platelet rich plasma) injections to facilitate improved local tissue healing and remodeling and to promote nerve axon healing and recovery.

Implanted vagal nerve stimulators. Targeted vagal nerve stimulation (VNS) has been demonstrated to reduce pain. A decrease in severity of a variety of pain conditions has been documented in pelvic pain, visceral pain, headaches, chronic rheumatoid arthritis pain and inflammation, epilepsy, and depression.

The vagus nerve is the longest of the cranial nerves, extending from the brain to the abdomen. Many important autonomic functions in the brain and the body are affected by vagal function. Influencing the vagus nerve can normalize neurotransmitter levels, reduce inflammation levels, and regulate metabolism. While implantable vagus nerve stimulation (VNS) is an emerging technology, there are a number of commercially available non-invasive devices that externally stimulate the vagus nerve at the ear or at the neck. The mechanism of VNS pain relief points to anti-inflammatory effects working in conjunction with both central and peripheral pain pathways.

Radiofrequency energy. This type of treatment creates heat generated by radio waves, which can be directed through small needles to lesion sensory nerves, for example to the knee (genicular nerve ablation). Radiofrequency energy can also be applied to lesion areas of inflammation inside spinal discs and vertebral bodies (intradiscal nerve ablation and basivertebral nerve ablation).

Minimally invasive spinal surgery. Other surgical and radiographic advances have allowed the development of minimally invasive spinal surgery (MISS), which can be performed with 3D CT guidance, using small incisions and specialized techniques to minimize tissue disruption and promote rapid recovery.

Conclusion

Pain tolerance is an interesting area of study. The research involving experimental pain has found measurable differences in individual pain tolerance, apparently related to mutations in proteins responsible for opening sodium channels on nerve endings. Some patients may simply transmit pain signals much more readily than others. On the other end of the spectrum, certain mutations of the sodium channel gene SCN9A, for instance, result in the inability to perceive pain, termed congenital insensitivity to pain (CIP).

Chronic pain is extremely common, especially in midlife, and can lead to significant distress and lifestyle limitations. Lifestyle factors that minimize chronic inflammation and promote tissue healing and restoration are key in mitigating the risks of developing or worsening chronic pain. Emerging high-tech devices, medications, and lifestyle behavioral therapies focus on reducing chronic cellular inflammation. The continued development of the biology of longevity will hopefully allow for the means to prevent the development of chronic pain in the first place.

This article is excerpted from *The 21st Century Man,* curated by Judson Brandeis, MD, reflecting emerging perspectives in men's health, sexual healing, and rejuvenation medicine.

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Post-Acute Covid Therapies

by Ronald Steriti, ND, PhD©

Post-acute coronavirus syndrome (PACS), also known as long-hauler syndrome, presents a challenge and unique opportunity for naturopaths and alternative medicine practitioners. This article presents a few research studies that may help guide therapy for these patients.

Adaptogens – Rhodiola, Eleutherococcus, and Schisandra

A randomized, quadruple-blind, placebo-controlled trial published in *Pharmaceuticals* assessed the efficacy of adaptogens on the recovery of patients with long-covid symptoms. The Tbilisi State Medical University, Georgia, conducted the study. The study included 100 patients with long-covid symptoms that were randomly assigned a fixed combination of adaptogens for two weeks: Rhodiola, Eleutherococcus, and Schisandra (Chisan®/ADAPT-232).

Chisan® decreased the duration of fatigue and pain by one and two days, respectively, in 50% of patients. The number of patients with lack of fatigue and pain symptoms was significantly less in the Chisan® treatment group than in the placebo group on Days 9 (39% vs. 57%, pain relief, p = 0.0019) and 11 (28% vs. 43%, relief of fatigue, * p = 0.0157).

Adaptogens can increase physical performance in long covid and reduce the duration of fatigue and chronic pain.[1]

Pycnogenol and Centellicum Improve Lung Healing

A study published in *Minerva Medica* evaluated the combination of Pycnogenol® (150 mg/day) and *Centella asiatica* (Centellicum® 3 x 225 mg/day) (PY-CE) for eight months in 19 subjects with sequelae of idiopathic interstitial pneumonia (IIP) plus 18 subjects with post-covid-19 lung disease. The Chieti-Pescara University and Sonderborg Hospital, University of South Denmark, conducted the study.

Preliminary results show that symptoms associated with post-covid-19 lung disease after four weeks were significantly improved with the supplement combination ($p<0.05$). Oxidative stress and the Karnofsky performance index scale were significantly improved in the supplements group as compared with controls ($p<0.05$).[2]

Pycnogenol and Cardiovascular Risk Factors

An open supplement study evaluated the effects of Pycnogenol® (150 mg in 3 doses of 50 mg) on symptoms of post-covid-19 syndrome over three months in 60 symptomatic subjects recovering from covid-19.

Patients, supplemented with Pycnogenol® showed significantly better improvement compared to the control group patients.

Endothelial function, low in all subjects at inclusion, was significantly improved in the Pycnogenol® group after one month and after three months ($p<0.05$ vs controls).

The rate of ankle swelling (RAS) by strain gauge decreased significantly in the supplemented group ($p<0.05$) in comparison with controls showing an improvement of the capillary filtration rate.

High sensitivity CRP (hs-CRP) and Il-6 plasma levels decreased progressively over three months with a significant more pronounced decrease in the supplement group ($p<0.05$). The number of patients with normal plasma IL-6 levels at the end of the study was higher ($p<0,05$) with the supplement. ESR followed the same pattern with a progressive and a more significant decrease in the supplemented subjects ($p<0.02$).

Pycnogenol® may offer a significant option for managing some of the signs and symptoms associated with post-covid-19 syndrome.[3]

Palmitoylethanolamide and Luteolin for Olfactory Dysfunction

A multicenter double-blinded randomized placebo-controlled clinical trial published in *Current Neuropharmacology* investigated recovery of olfactory function after covid-19. The Humanitas University conducted the study at three referral hospitals (Fano, Naples and Sassari).

Participants were randomized to daily oral supplementation with ultramicronized palmitoylethanolamide and luteolin (770 mg) plus olfactory training (intervention group) or olfactory training with placebo (control). Sniffin' Sticks assessments were used to test the patients at baseline and 90 days. A total of 185 patients, including intervention (130) and control (55) were enrolled.

The intervention group showed significantly greater improvement in olfactory threshold, discrimination, and identification scores compared to controls ($p=0.0001$).

Overall, 92% of patients in the intervention group improved versus 42% of controls. Magnitude of recovery was

significantly greater in the intervention group versus control (12.8 + 8.2 versus mean 3.2 + 3), with >10-fold higher prevalence of anosmia in control versus intervention groups at the 90-day endpoint.

Combining palmitoylethanolamide and luteolin with olfactory training resulted in greater recovery of smell than olfactory training alone among individuals with olfactory dysfunction post-covid-19.[4]

Alpha-Lipoic Acid for Post-Viral Olfactory Loss

A study published in *Laryngoscope* investigated the potential therapeutic effects of alpha-lipoic acid in olfactory loss following infections of the upper respiratory tract. The University of Dresden Medical School, Germany, conducted the study.

A total of 23 patients participated. Alpha-lipoic acid was used orally at a dose of 600 mg/day; it was prescribed for an average period of 4.5 months. Olfactory function was assessed using olfactory tests for phenyl ethyl alcohol odor threshold, odor discrimination, and odor identification.

Seven patients (30%) showed no change in olfactory function. Two patients (9%) exhibited a moderate decrease in olfactory function; in contrast, six patients (26%) showed moderate and eight patients (35%) remarkable increase in olfactory function. Two of the four patients with functional anosmia reached hyposmia; five of 19 hyposmic patients became normosmic. Overall, this resulted in a significant improvement in olfactory function following treatment (P =.002).

At the end of treatment, parosmias were less frequent (22%) than at the beginning of therapy (48%). Interestingly, recovery of olfactory function appeared to be more pronounced in younger patients than in patients above the age of 60 years (P=.018).

The results indicate that alpha-lipoic acid may be helpful in patients with olfactory loss after upper respiratory tract infection.[5]

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Monkeypox Infection: To Fear or Not to Fear?

by Thomas E. Levy, MD, JD

Orthomolecular Medicine News Service

As of the writing of this article, multiple news reports have recently addressed the occurrence of monkeypox virus infections in humans. In the current setting of the entire planet dealing with the covid pandemic over the last two and a half years, fear is readily stoked that another pandemic with a virus that comes from the same family of viruses as smallpox could be poised to inflict widespread suffering and death. This article will present the significant scientific data and literature surrounding monkeypox infection in humans, which clearly demonstrates that the monkeypox virus presents **NO** threat of a pandemic or even a large epidemic.

Monkeypox Characteristics

Although many have never heard of it until recently, monkeypox infection is not the result of the emergence of a new virus. Rather, it was first identified in captive cynomolgus monkeys in Denmark in 1958.[1] The first documented human infection was reported in 1970 in a nine-month-old in the Congo. After clinically recovering from the infection and its associated rash over a month-long period, this baby then contracted the measles and died six days later.[2] While not found exclusively in remote populations in Central and West Africa, limited monkeypox outbreaks appear to have occurred most commonly in such areas of the world, where advanced malnutrition can potentially make some otherwise benign infections life-threatening.[3] This initial case also serves to highlight the fact that underlying chronic malnutrition with moderate to severely depleted vitamin and mineral stores in those living in such remote areas of Africa literally sets the stage for contracting any infectious disease. Quickly contracting measles upon the resolution of the monkeypox virus is the logical result of such an advanced depletion of nutrients in the body. The typical mild to moderate clinical presentation of the measles can easily evolve into a fatal infection when a chronic state of nutrient depletion is still further depleted by a month-long bout with the monkeypox virus.

Monkeypox cases have only occurred as very limited outbreaks, never as an epidemic or a pandemic. Such an outbreak is a cluster of cases in a given area from a pathogen with a limited contagion risk. An epidemic/pandemic requires a pathogen that is very easily spread. This is not the case with the monkeypox virus. The United States has already had an outbreak of monkeypox infection in 2003, involving 47 human cases felt to be secondary to the importation of infected wild rodents from Ghana. No secondary larger outbreak or epidemic resulted, however. Furthermore, no human-to-human transmission was documented.[4] Typically, while human-to-human transmission is certainly possible, it is the exposure to and/or the consumption of infected animals, as well as their consumption of each other, that both spreads this virus and serves as a reservoir for it. This is an additional reason for its primary presence in Africa, in addition to the overall poor nutrition on much of this continent.[5,6]

Monkeypox is characterized as a zoonotic infection, meaning it can transmit from animal to human, or vice-versa.[7] Asymptomatic monkeypox infections are very common, as ***over half*** of the healthy persons in an area of Ghana, which actually had ***no*** reported clinical human cases of monkeypox at the time of this study, had positive immunoglobulin G (IgG) antibodies against the monkeypox virus genus.[8] A similarly large percentage of the healthy residents in a region of the Congo had circulating antibodies as well.[9] Another study in Cameroon found these antibodies in slightly over a third of the subjects tested.[10] This indicates that monkeypox is not typically severe in its clinical course, much less fatal, in any human population. And this would especially be the case in the United States or in a comparable country with a relatively high-quality level of nutrition as well as a relatively widespread intake of vitamin and mineral supplementation.

Ebola, another virus that has been largely limited to African countries, resulted in a substantial outbreak in West Africa from 2014 to 2016, but it never approached pandemic or even significant epidemic proportions. Nevertheless, in the nutrition-depleted populations in which it emerged, death resulted in those individuals demonstrating clinical infection between 25% and 90% of the time, enough to generate a great deal of fear that it could spread and kill easily throughout the world.[11] And even though Ebola killed many who became infected, a substantial number of those individuals exposed developed natural immunity

(IgG antibody) response without ever becoming clinically ill. Depending on the location of the African community and the conditions of the testing protocol itself, up to 50% of exposed individuals, including those living with clinically infected individuals, showed the development of natural antibodies to Ebola without ever becoming ill.[12-18] And in spite of the initial fear that was generated, no pandemic, epidemic, or even minor outbreak of Ebola ever occurred in the United States, even though international airline travel reliably introduced infected individuals into the country.[19,20]

Most of the fear currently seen with the potential spread of the monkeypox virus is due to the fact that both monkeypox and smallpox comes from the same genus of DNA viruses.[21] Smallpox has been estimated to have killed between 300 and 500 million people in the 20th century.[22] Understandably, then, anything that is remotely related to smallpox can be expected to generate a great deal of concern.

While the smallpox vaccine is credited for the effective eradication of smallpox, it is also believed by some that waning vaccine immunity is currently leaving over 70% of the world's population unprotected against smallpox, as this vaccine has not been routinely administered since 1980.[23] Some estimates indicate that the smallpox vaccination has offered roughly an 85% protection against monkeypox infection.[24] And since the vaccine immunity against smallpox is felt to be waning, the associated cross-immunity against related viruses like monkeypox is felt to be fading as well.[25]

However, *monkeypox is simply not smallpox*. The evidence presented above indicates that many asymptomatic infections occur with monkeypox, and that it is far less contagious than smallpox, with human-to-human transmission being decidedly uncommon. Concurrent epidemics or outbreaks of smallpox and monkeypox have not been reported, and smallpox is not a zoonotic infection like monkeypox, but infects humans only.[26]

In the more well-fed and healthy populations in the world, monkeypox is simply not a killer virus.

Finally, in the more well-fed and healthy populations in the world, monkeypox is simply not a killer virus once contracted. The typical clinical course of monkeypox in such populations much more resembles chickenpox than smallpox. Even if the presumed waning protection of the old smallpox vaccinations results in some increase in human monkeypox cases, it will not turn monkeypox into the highly contagious and deadly killer that is smallpox.

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Monkeypox

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Easily Prevented, Readily Resolved

While some viruses are much more contagious and much more capable of causing severe illness and even death than others, they all share therapeutic susceptibilities. As devastating as Ebola has been to many of the individuals in Africa who have contracted it, bio-oxidative treatment readily resolves it as well as any other virus that is treated before too much advanced organ damage has already taken place. At the height of the Ebola scare in 2014, Drs. Robert Rowen and Howard Robins were so convinced of their ability to cure Ebola infections that they put themselves directly in harm's way by traveling to Sierra Leone, a West African epicenter of Ebola infection at that time. Of note, many physicians and other healthcare providers in this area of Africa were dying from the infection at that time.

The primary therapy they used to treat the Ebola patients was ozone. And even though great local resistance was met in gaining access to patients, four individuals were successfully treated with ozone therapy. The cornerstone ozone application was direct intravenous ozone gas injection. Supplemental oral vitamin C therapy was administered as well to address its infection-induced deficiency, to bolster immune function, and to minimize the impact of any possible pro-oxidant Herxheimer-like rapid virus kill-off reactions. All four patients improved *immediately* after the first treatment and complete resolution of their infections was seen between two to five days. Furthermore, no progression of any Ebola-related symptoms was seen after the first ozone treatments were administered.[27]

Other acute viral syndromes that have initially had much of the world on edge in recent years have also been proven to be readily curable, although not with any known prescription drugs. In 2014, Chikungunya virus received a lot of attention, and some outbreaks with this virus were sizeable, although never really reaching epidemic proportions. This viral infection typically left those infected with debilitating symptoms, often resulting in severe pain in many of the joints in the body. The most immunocompetent individuals would often resolve their most severe symptoms in about a week, but in some the joint pain would become chronic and last as long as five years. Separate *one-time* intravenous infusions with two bio-oxidative agents (vitamin C and hydrogen peroxide) in 56 patients were highly effective in both completely resolving this viral infection, as well as in immediately alleviating much of the chronic pain that remained long after the acute phase of the infection.[28] Treatment with just high-dose vitamin C intravenously (as much as *100 grams daily*) in the acute stage of viral infection with Chikungunya, influenza, Zika, and dengue has also been reported to be similarly curative.[29-32]

In a nutshell, unless the patient has advanced organ damage and is very near death, intravenous vitamin C, *in sufficient doses*, can always be expected to save the patient from succumbing to an advanced infection, especially viral. As the primary electron-donating nutrient in the body, enough vitamin C must be administered to both neutralize the new, ongoing infection-derived pro-oxidants (toxins) while restoring (reducing) the physiological function of those biomolecules that have already been oxidized. A sizeable number of integrative medicine practitioners who appreciate the therapeutic value of IV vitamin C remain needlessly wary of 50- to 100-gram infusions of vitamin C. This unnecessary caution too often results in a total daily dose of vitamin C of 25 grams or less that proves insufficient to save the patient with severe and widespread oxidative damage secondary to an advanced infection. Nevertheless, even such lower doses can oftentimes suffice, just not as reliably so.

The experience at the Riordan Clinic alone in Wichita, Kansas clearly establishes the safety (and efficacy) of even the highest dosing regimens of vitamin C on a routine basis. Over the past 32 years, over 150,000 intravenous infusions of vitamin C have been administered at Riordan campuses. Doses have varied from *7.5 to 250 grams daily*, with 50 grams being the most common dose administered. ***NO*** significant adverse side effects have occurred, and ***NO*** kidney stones have resulted. For more information on the vitamin C-related research and results of the Riordan Clinic, see: https://riordanclinic.org/journal-articles/.

The primary bio-oxidative therapies (vitamin C, hydrogen peroxide, ozone, ultraviolet blood irradiation, and hyperbaric oxygen) have all been shown to eradicate any viral infections for which they have been properly administered. As noted above, intravenous ozone can promptly resolve even an advanced viral infection whenever access to it is available. Properly dosed intravenous hydrogen peroxide is comparably effective, and as long as the healthcare practitioner is willing to use it, its expense is nominal and it is available literally everywhere. Vitamin C, ultraviolet blood irradiation, and hyperbaric oxygen therapy are incredibly effective as well, but less available and anywhere from slightly to substantially more expensive to apply than the hydrogen peroxide and/or the ozone therapies. These therapies, along with other supportive antipathogenic measures, are discussed in greater detail elsewhere.[33]

Another great option for dealing with any virus once contracted is a combination vitamin C-cortisol approach, especially when the intravenous administration of bio-oxidative agents is not readily available, if at all. A sizeable oral dose of vitamin C (3 to 5 grams, liposome-encapsulated or as sodium ascorbate powder) along with 20 mg of cortisol (hydrocortisone) is dramatically effective in its clinical impact, often resulting in a prompt cessation of infection evolution followed shortly thereafter by complete resolution. As a very general guideline, the vitamin C/cortisol should be taken three times daily until baseline health is restored. Complete clinical resolution is typically seen in 12 to 36 hours. A more prolonged treatment plan is only required when the pathogen has had a longer time to replicate and clinical illness is more pronounced when therapy is initiated.[34,35]

Recap

Monkeypox virus should never be confused with smallpox, even though the viruses have some common family roots. Smallpox is a human infection, and monkeypox is primarily limited to infections in susceptible animal populations. When monkeypox does infect a human, its clinical course is little more than that of a typical case of chickenpox, as long as the infected individual is not grossly malnourished. And even in populations with significant nutrient depletion, monkeypox is very often a completely asymptomatic infection, as high levels of protective antibodies to monkeypox have been documented in significant percentages of these populations. Also, unlike smallpox, monkeypox has both a very low level of contagion and only rarely results in a fatal outcome, even in the most susceptible of populations.

A good level of nutrition, along with judicious supplementation with vitamins and minerals, will almost completely prevent the transmission of monkeypox, from either an infected animal or human. And when it is contracted, the application of any of a number of bio-oxidative and other therapies will give a rapid resolution to this infection. This ease of prevention and susceptibility to rapid cure should be kept in mind before deciding to proceed directly with any monkeypox vaccinations that end up being offered to the public.

The views presented in this commentary are the author's and not necessarily those of all members of the Orthomolecular Medicine News Service Editorial Review Board.

Monkeypox

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References are available online at www.townsendletter.com.

Clinical Uses of CBD for Minor Medical Conditions

by Sabrina Brunner, DACM

As a doctor of Traditional Chinese Medicine in Cincinnati, my patients are looking for ways to help themselves without using over-the-counter medication. Not only do individuals want to limit their OTC pain relievers, but they also choose not to explore the use of medical marijuana. I have found a way to help my patients without using OTC medications for minor medical conditions. What I have found with clinical experience is to apply the CBD salve on the area of acute or chronic pain after my patient has been treated by acupuncture, cupping (cupping opens the pores of the skin allowing the CBD salve to penetrate the skin), then medical massage (rubs the salve into the fascia and muscle itself) on the localized area of pain. The patient can take the 1,000 mg tincture under the tongue and apply the salve for pain management for up to three days after treatment, then as needed for flare-ups. My patients are guided to use CBD for short-term use.

According to National Institute of Health (NIH), cannabidiol (CBD) is "a Phyto-cannabinoid derived from Cannabis species, which is devoid of psychoactive activity with analgesic, anti-inflammatory, antineoplastic and chemo-preventive activities."[1] This is why CBD is such a complement to alternative medicine and provides a safe and organic way to extend treatment at home. I tried five different CBD product lines before I found Dao Zen. My patients love the effects of Dao Zen. The Dao Zen line that I use provides a salve (topical containing 300 mg of CBD and 30 ml) and a tincture (sublingual containing 1,000 mg of CBD and 30 ml). Prior to using CBD salves on clients, I explain the product and ask for their permission to use it in their care. One caution that has been found is that CBD oil interacts in the metabolism of medications such as blood thinners.[2] Some working professionals and professional athletes are not allowed to use CBD products due to random drug testing.

The State of Ohio uses the NIH definition of hemp as "The plant cannabis sativa L. and any parts of that plant, including the seeds thereof and all derivatives, extracts, cannabinoids, isomers, acids, salts, salts of the isomers, whether growing or not with a delta-9 tetrahydrocannabinol concentration of no more than 0.3% on a dry weight basis."[1] This definition provides support to the low amounts of THC in CBD, making CBD products more easily accepted than medical marijuana.

Cannabinoid receptor 1 (CB1) is found in the bones, ligaments, tendons, cartilage, adipose tissue, and surrounds muscle tissue. Cannabinoid receptor 2 (CB2) is found throughout the brain, central nervous system, and peripheral nervous system.[3] CBD products work very well for people due to the harmonizing effect shared between the CBD salves and CB1 receptors, CBD tinctures, and CB2 receptors. CBD products can be used for several conditions in conjunction with alternative medicine. Treatments for some of these conditions are described below.

Headaches and Migraines

Use acupuncture points Li4, 11, Lr 3, St 36, Sj5, Gb 43, 34 and local head points to address the headache/migraine.[4] Next cup, and then apply a pea-sized amount of CBD salve to the upper back, shoulders, and neck, followed by medical massage. At home, the patient is reminded that CBD salve can be applied to the base of the skull, top of the neck, and shoulders every four to six hours as needed. At night, one may add three to six drops of CBD tincture under the tongue. The patient is cautioned not to use CBD tincture more than three days in a row.

It has been concluded that "Cannabinoids appear to modulate and interact at many pathways inherent to migraine, triptan mechanisms of action, and opiate pathways suggesting potential synergistic or similar benefits."[5]

Low Back Pain

Apply Si 3, Ub 40, 62, 24, 23, 22 and Du 3 to address the low back pain.[6] Cup the lower back area once the needles are removed, then add CBD salve to the needled area, then perform medical massage. The patient is guided to apply the salve every four to six hours as needed for pain. Patients can also add three to six drops of CBD tincture under the tongue before bed.

Menstrual Cramps

Provide acupuncture points P6, Sp 4, 6, 9, Gb 26, Ren 2, 3 and Zigong to address the menstrual cramps,[7] followed by CBD salve on the skin over the uterus. Cupping and medical massage is not provided on the abdomen or over the uterus for menstrual cramps. If the patient is experiencing low back pain from menstruating, then one can apply cupping, CBD salve, and medical massage to the localized area of pain. At home, the patient may apply CBD salve to the skin over the uterus every four to six hours as needed and take three to six drops of CBD tincture until the menstrual cramps have ceased. Armour, et al. found that

"Hemp/CBD oil was the most highly rated in terms of self-reported effectiveness in pain reduction" in a study for Australian woman with endometriosis.[8]

Anxiety

Provide acupuncture P6, H7, Sp6, K3, St36, Ren14, 17 and Sishencong (four points on the crown of the head) to address the stress/anxiety.[9] Apply cupping, CBD salve, and medical massage to the Shu points on the back to help soothe the patient. Patient can take three drops of CBD tincture at night two hours before bed for up to three nights. Also, recommend the patient follow up with a visit to their therapist. When I am treating teenagers and young adults for anxiety, I obtain the consent of the parent. I will also only sell the CBD tincture to the parents if their child is working with a therapist. I explain to the young patient that CBD tincture is not a substitution for therapy but rather a complement to therapy.

Generalized Aches or Pain: Home Use

When CBD treatment is being used for generalized aches or pains, the products are most often used together at home. Such conditions would result from overuse of muscles in gardening, yardwork, housework, or other more strenuous home projects. Place CBD salve to localized areas of aches or pain before bed while taking three drops of CDB tincture sublingually; reapply CBD salve in the morning for up to three days. I always recommended three days for the salve and tincture together and then as often as needed. Depending on the patient's preference, the salve and tincture can be taken separately. However, my patients have reported that they have more success using the two products together within a shorter duration of time with pain.

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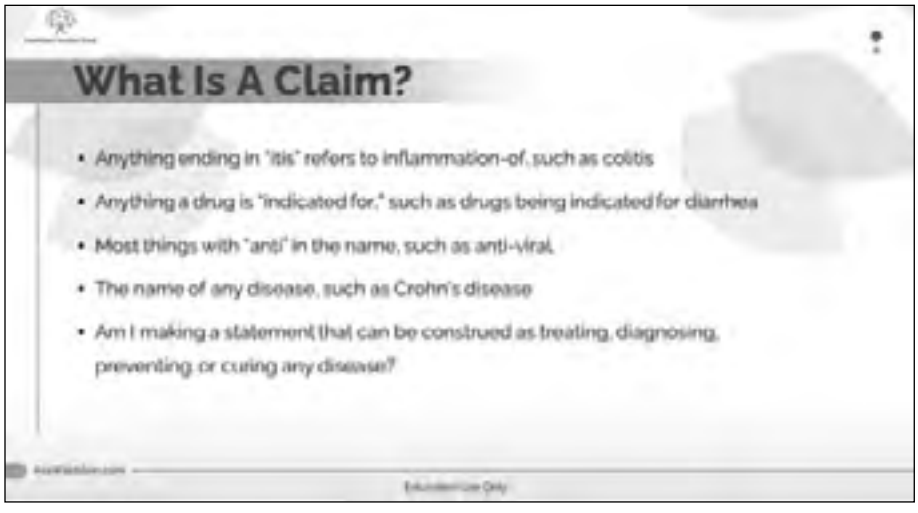
Common Practitioner Pitfalls to Avoid When Marketing Dietary Supplements

by Asa Waldstein

Practitioners selling dietary supplements can easily cross the line into FDA/FTC trouble. This article reviews common marketing mistakes and discusses lower-risk ways to sell supplements while maintaining a thriving practice.

We often hear about not making disease claims, but it can be confusing to know what a claim is. Here are a few general rules.



Education Versus Marketing

Education is okay, but there is a thin line between educating about health concerns and making uncompliant marketing claims. Here are a few scenarios.

Scenario #1 Citing ingredient research and benefits.

- Low Risk: A doctor's website discusses the dangers of high blood pressure and provides information about alternative therapies such as diet, exercise, and meditation. There is also research on ingredients used for high blood pressure.
- High Risk: This scenario above becomes a high risk if the doctor's website sells supplements for high blood pressure or contains discussed ingredients. For example, discussing ingredient research is a marketing claim if that ingredient is contained in any product sold on the website.

Scenario #2 Testimonials

- Low Risk: Client testimonials do not refer to supplements and only reference the therapeutic nature of the practitioner's practice, such as dietary interventions and acupuncture results.
- High Risk: This same scenario above becomes a high risk if the client testimonials include product reviews with disease words such as "Product ABC worked great for my arthritis."

Disease Words

Practitioners are accustomed to using medical and drug terminologies such as anti-inflammatory, hypertension, or anti-viral in their practice. However, these words do not translate into compliant marketing, and it's a common practitioner mistake to use these risky words to describe supplements. If truthful and not misleading, "Marketing Differences" on page 67 shows some alternative ways to discuss these words.

Follow Enforcement Trends

Following the ever-changing enforcement trends is a great way to ensure dietary supplement marketing is compliant. One example is the word "hangover," which would have been a relatively low risk in the past, but in July 2020, the FDA issued seven warning letters to companies making hangover claims. Companies that were paying attention removed this word from their online marketing and social media, thus significantly reducing their risk of a future warning letter. The FDA is looking at several-year-old blogs and social media posts in the same manner as current posts.

I recently conducted a review of diabetes and blood sugar-related FDA warning letters. Since January 2021, there have been 56 diabetes-related letters. These findings provide a snapshot of where the FDA is finding and perhaps looking for risky words. We can learn a lot from this, and it's an excellent reminder for companies to re-evaluate these areas to ensure

no disease statements are lurking on their website or social platforms. Here is what I found.

- 62% include claims made on social media. This is an excellent reminder to scan for high-risk words on socials, including old posts.
- 26% involve claims made in blogs. This is a strong enforcement trend to watch as the FDA continues to cite claims made in blogs. Many of these blogs may be "forgotten"on company websites. All marketing material on a commercial website is "fair game." This is an important reminder to scan all blogs for risky words such as diabetes, cancer, and depression.
- 23% include claims made in testimonials.
- 25% involve claims made in hashtags.

A good resource to stay on top of trends is my weekly Warning Letter Wednesday post (https://www.asawaldstein.com/warning-letter-wednesday), where I review interesting FDA enforcement trends.

What Are the Repercussions of Not Complying

The most common agency action is a warning letter from the FDA, FTC, or sometimes both. Here are some reasons to avoid a warning letter.

- Requires legal resources to respond
- Public record
- Repeat warning letters can lead to an injunction
- Scares away investors and partnerships
- Alerts class action attorneys

Too Small to Be on the FDA's Radar

Some companies feel they are "too small" to be on the FDA's radar. Based on numerous practitioner warning letters, this is untrue. One example of this is a recent warning letter that mentioned a claim made in a YouTube video. When I reviewed this video, it only had about 60 views, demonstrating that the authorities may scrutinize any marketing.

Best Practices for Compliant Marketing

Step one in reducing risk is to remove risky words from all marketing platforms. If accurate, finding truthful ways to talk about products without disease words is a good next step. For example, replacing "anxiety" with "balanced mood support" and "anti-inflammatory" with "discomfort" may be suitable options. The key to compliant marketing is to make the point without disease words while being truthful. This can be done by using substantiated structure-function statements such as "supports heart health" or talking about a quality-of-life discussion about "feeling resilient" or "refreshed in the morning."

Disclaimer: These are for informational purposes and are not intended to replace competent legal or regulatory advice. Have a qualified attorney or consultant review your marketing for compliance.

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Healing with Homeopathy

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A Rare Homeopathic Remedy for a Case of Diverticulosis and Depression

Choosing One Remedy Among Over 8000

In my last column, I began by pointing out the mind-boggling task of choosing a single homeopathic medicine for a patient at any point in time. I described *The Sensation Method* of Dr. Rajan Sankaran as one effective approach to doing just that. Here is a case in point. I began seeing this woman, 47 years old, a nurse, in 2003. Let me call her Vicki. Her chief complaint was depression, and she had been treated by another homeopathic practitioner for a number of years. She shared a longstanding sense of failure and terror. When I look back at her original case, I see clues of the remedy that has helped her many years later. Fortunately, she returned four years ago, and I have had the opportunity to help her at a deeper level. Looking back at the original case, there were clues, but I didn't put them together as I did years later.

Way back in 2003, she shared with me her fear to the point of paralysis. Having grown up with an alcoholic father, terror was instilled in her early on. That tremendous fear stuck with her, despite therapy. She never felt that she fit in, and she was convinced there was something terribly wrong with her. She pursued many therapies, including EMDR, without any lasting improvement. Alcohol only made her feel worse. Sometimes more information is not necessarily helpful, and, in retrospect, I was overwhelmed by the depth of information and her degree of suffering.

The initial case taking in 2003: "As a kid into adulthood, I had this nightmare: I would be lying on my bed. All around the corners of the walls at the ceiling, there would be faces. I would feel like a two-dimensional stick person. Like I couldn't get back into my body... it was horrible. I couldn't make it go away. Couldn't get back into my body." Among other remedies, I did prescribe *Cannabis indica* LM1. But she never took the remedy, but rather *Argentum nitricum* (a very different remedy, prescribed by her previous homeopath, that does cover a sense of panic and claustrophobia).

When she returned again to see me a year later, having just turned 50, she was traumatized, depressed, and sobbing. She felt torn between seeing her previous homeopath, who had helped the family for years when her children were small, and me. At that point I encouraged her to continue taking the I*gnatia* prescribed by the other homeopath, and which she considered helpful. I could understand the rationale: "sobbing, sighing, and shock." She suffered through menopause, continued taking the *Ignatia*, and disappeared from my practice for another three years.

When she returned, she had experienced tremendous grief due to family losses, and described herself as "paralyzed," "in cement." Again, there were clues of the remedy she ultimately needed: "I feel heavy.... I'm just heavy." She was suffering from hip and buttock pain and stiffness, which caused her to keep shifting, moving around. I gave her *Rhus tox*, then didn't hear from her again for three years. She was now turning 60 and was again, or still, experiencing a sense of panic and grief. I prescribed *Ignatia* 10M with improvement, then another hiatus.

Finally Putting the Pieces of the Puzzle Together

It wasn't until October of 2018 that I was able to piece together the case. She had pursued other avenues of healing, experienced more grief, and thyroid problems. But she was able, after all that time, to really communicate, and I was able to grasp accurately, her homeopathic picture and ended up prescribing an unusual remedy that I hadn't given before and haven't since. That was three and a half years ago, I prescribed

a remedy I had never before used, and it continues to be quite effective.

October 2018. Vicki was now 66. Dealing with her aging, sick father, she felt overwhelmed and stuck. "Mostly I'd like you to figure out how to unstick me... It's all floating around in my head.. I feel paralyzed, stuck.... heavy." I asked further about these sensations. "Mostly just my mind... I'd like to feel free, lighter... I feel overwhelmed, dragged down...It's all floating around in my head." She complained about her breathing and described feeling paralyzed and heavy. I asked Vicki about the opposite of feeling paralyzed, stuck, heavy. "I'd feel lighter, not overwhelmed and dragged down." This struck me as the same sensation Vicki had described for years, going way back to her initial case taking when I prescribed *Cannabis indica*, which she never took.

Assuming the remedy family was, indeed, *Hamamelidae,* characterized, like *Cannabis*, by the sensations of heaviness/dragging and, the opposite, light, floating, it would explain her ongoing feeling, over so many years, of paralysis. By this time, Vicki had a diagnosis of diverticulosis, as well as longstanding depression, and various diagnoses in the interim. She focused more on her mental, rather than her GI, sensations. "Everything feels too hard. I want to get up, but I don't move. I feel paralyzed." To differentiate plant sensations, we inquire about the opposite. What would Vicki feel like if she weren't stuck, heavy, and paralyzed. "I'd feel free, lighter, not in pain rather than overwhelmed and dragged down.. I feel paralyzed and heavy... barely breathing."

This certainly sounded to me like the *Hamamelidae* family, just like *Cannabis indica*, which I had prescribed in 2003, but she had never taken. But, which member of the *Hamamelidae*? We look at the miasm in order to select the best remedy. I chose a remedy I had never before prescribed because the miasmatic feeling seemed to be one of restriction, intermittent attacks, stuckness, misfortune, misery, and periodic rage: *Myrica* (bayberry or wax-myrtle, also called candleberry or tallow shrub). I was looking for a *Hamamelidae* with a focus on mucous membranes. The mental/emotional picture included "irritable with a constant desire to find fault," "condemned herself for imaginary faults" (Vicki was always very self-critical), a great depression of mind and feeling of gloominess/depression, a nasal obstruction, and many GI symptoms. It was a leap of faith, since I knew nothing previously about this remedy. *Myrica* is an evergreen shrub growing in thickets near swamps and marshes with an odor similar to laurel. The fruits have an exceptionally high wax content and, in fact, has been used for making sealing-wax. I prescribed *Myrica 1M* (2 doses 12 hours apart) and LM5 daily.

Follow-Ups Since the Myrica

Six Weeks: "It's either a placebo or I'm much better. I'm not miserable (this is a word to describe the malarial miasm). I'm getting things done. I'm definitely not as melancholy. My family situation has not changed... in fact it's worse. Nothing has changed outwardly, but it's shifted inside me." Vicki continued the *Myrica LM5* daily.

*Ten Weeks: "*I'm exhausted. I have bronchitis. It's cold, and the wind is icy. I got the flu. I was feeling weak. I did have pneumonia three years ago." I looked up *Myrica*, and it did cover Vicki's cough symptoms. I prescribed four doses of *Myrica 1M* 12 hours apart, another four doses to hold in case she needed them.

Five Months: "They found polyps on colonoscopy and diagnosed diverticulosis. I guess the Myrica helped because I got better."

Eleven Months: "I feel better after I take the Myrica. I'm not good about taking the LM5." I prescribed *Myrica* 1M up to once a week along with the daily LM5.

Thirteen Months: "I feel better mentally and emotionally. I definitely don't feel depressed like I did before... I'm doing way, way better." I prescribed *Myrica* 1M to hold and asked Vicki to continue the daily LM5.

Twenty-One Months: "I asked to go back on my natural thyroid medication. My mother is 85 and father is 92 and I help take care of them. I feel that I am slowly sinking." I repeated the *Myrica* 1M, two doses to take, and to continue the LM5.

Twenty-two and a Half Months: "Had a horrible blowup with my mother, but doing okay."

Twenty-three and a-Half Months: Doing well. Continue *Myrica LM5* and *Myrica* 1M to hold.

Twenty-Five and a Half Months: "I haven't needed the Myrica 1M I'm holding."

Three and a Half Years: "Yesterday I had a really big diverticulitis flare. The remedy has worked really well for it, but I didn't have any." I prescribed four doses of *Myrica* to take and four to hold as well as a daily LM6.

Conclusion

You can see that this patient has not had consistent follow-ups, but the remedy has definitely helped her. She has not mentioned the dragging sensation and her moods do not dip like they did in the past. She is more stable mentally and emotionally, despite the stress of caretaking two elderly parents. She still calls me inconsistently and has continued with treatment periodically over all of these years.

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The Lobay Viewpoint

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Hyaluronic Acid Knee Injections

I could see the bright neon lights of Las Vegas in the distance as I hobbled up the stairs on the tarmac to my connecting flight. I had just returned from a weekend seminar with the Dr. Dietrich Klinghardt on prolotherapy in Albuquerque, New Mexico. It was November 1994, and I was just three years graduated from Bastyr College of Naturopathic Medicine. I was now practicing as a licensed naturopathic physician in British Columbia. I was eager for practical knowledge and skills that I didn't acquire in school. I was enthusiastic to learn some invasive naturopathic treatments with one of the gurus of chronic pain treatment. It was a small, intimate group of about thirty practitioners at an airport hotel meeting room. The revered Dr. Klinghardt explained his approach to neural therapy, prolotherapy, and chronic pain. He asked for volunteers to demonstrate his techniques. At some point I stuck up my hand and said I had a bad knee. He examined my knee, confirmed my suspicion and proceeded to inject my knee with a P2G solution of phenol, glycerin, and glucose. He peppered my anterior cruciate ligament attachment to the tibia plateau. He told me it was okay to use a stationary bicycle at the hotel after the treatment and to take it easy. Some inflammation and swelling would be normal for a few days after the treatment. After leaving Albuquerque, I really felt the inflammation for a few days. Needless to say, my knee got better and the prolotherapy treatment was a key part of my recovery.

I have bad knees. I played competitive hockey when I was younger and my knees took the brunt of many hits. I originally injured one knee, can't remember which one, when I was playing squash as an undergraduate student at the University of British Columbia in Vancouver. Running, planting, pivoting and twisting and snap. I tore my anterior cruciate ligament. I saw a sports medicine doctor and he recommended surgery. I had arthroscopic surgery and it seemed to help. Another time I was taking judo classes and had a match with bigger, stronger opponent. My other knee gave out and pop I tore my meniscus. I later had arthroscopic surgery on that knee. As I pass the half century mark, I still play old-timer's hockey and recreational tennis. I am particularly fond of taking good care of my aging knees as I get older.

More recently I injured my knee while playing mixed doubles tennis at the Lakeview Heights Tennis Club. My knee was inflamed, swelled up, and was painful to walk on for a while. I used a cane, applied ice, lathered copious amounts arnica cream and took a combination of over-the-counter and herbal anti-inflammatory medicine mainly as turmeric. I was pretty sure that I had a meniscal tear. I went to a walk-in-clinic, was examined by a doctor and went for some obligatory knee x-rays. The x-rays showed some narrowing joint space and some age-related degeneration. When the acute swelling had diminished, I embarked on an aggressive rehabilitation program that included swimming, biking, and the use of some physiotherapy devices that I had at the office. In the true spirit of "physician heal thyself," I gave myself a series of generalized intra-articular prolotherapy injections with hyaluronic acid and procaine. While I am not advocating that anyone should give themselves intra-articular knee injections, I can attest that it was only slightly unnerving – after all I have given numerous shots like this to many of my patients. The shots seemed to help a lot, decreased the pain almost immediately and accelerated healing to the point at which I am now back playing tennis.

Prolotherapy is a generic term that involves the use of proliferants to help stimulate growth of new connective tissue in cartilage, ligaments, and tendons. Proliferants include any substance that would help to proliferate or stimulate the growth of new tissue. Substances used as proliferants include dextrose or glucose, saline, glycerin, phenol, sodium morrhuate or a mixture of the sodium salts of the saturated and unsaturated fatty acids of cod liver oil, dimethylsulfoxide, glucosamine sulphate, growth hormone, hyaluronic acid, plasma rich platelets (PRP) and other minerals and substances. Some of the substances such as phenol and sodium morrhuate are strongly irritating and provoke inflammation. Other substances such

as hyaluronic acid and PRP tend to be less irritating and less inflammatory. Prolotherapy is a quintessential natural healing therapy.

Synovial fluid is a thick viscous straw-colored fluid that lubricates joint space between two bones. A typical knee joint contains between 0.5 to 4.0 milliliters of this fluid. The fluid can expand and contract depending on internal and external pressure, temperature and other rheological factors. The purpose of synovial fluid is to lubricate the joint between two bones, reduce friction, and act as a shock absorber. Synovial tissue is considered to be a sterile environment that can also supply nutrients and remove waste products and act as a molecular sieve. The synovial lining is composed of several cells, including chondrocytes, fibroblasts and monocytes. Chondrocytes produce collagen proteins that line the surface of bones in a joint. Lubricin is a glycoprotein produced by chondrocytes that coats and protects the outer surface of joint collagen. Fibroblasts produce hyaluronic acid and monocytes are active in removing debris produced in the joint space. Hyaluronic acid is a disaccharide polymer of repeating units of glucuronic acid and N-acetyl glucosamine. Synovial fluid is also composed of a filtrate of blood plasma mixed with hyaluronic acid and lubricin and different proteinase and collagenase enzymes. With osteoarthritis or degenerative joint disease there is a breakdown of the connective tissue, including collagen and hyaluronic acid and deterioration of the quality of synovial fluid lining the joint space.[1]

A search of the medical research database PubMed revealed over 28,000 listings on hyaluronic acid. I found that some of the most informative articles on this site belong to the area of veterinary medicine. Hyaluronic acid is widely used on horses, dogs, rabbits, sheep, and other animals with arthritic degeneration. The biochemistry and pharmacology of hyaluronic acid has been studied more extensively in this group. Intra-articular injections of hyaluronic acid appear to be safe and effective in the treatment of degenerative arthritis in animals and humans.[1]

Hyaluronic acid (HA) is a large, heavy molecule that exists with different molecular weights. Hyaluronic acid is typically measured in Daltons. A Dalton is a unit of atomic mass that is exactly 1/12 the weight of a carbon-12 atom. Native hyaluronic acid usually exists between 4 to 10,000 kilodaltons in joint space. Hyaluronic acid is composed of repeating units of glucuronic acid and N-acetylglucosamine in different chain lengths. Different lengths and size of the chain account for the different atomic weights of the molecule. Injectable hyaluronic acid can be made from animal tissues such as shellfish and rooster combs but is more typically made from bacterial production commercially. Injectable hyaluronic acid can exist in different molecular weights. Low molecular weight hyaluronic acid ranges from 500 to 730 kilodaltons. Intermediate molecular weight hyaluronic acid ranges from 800 to 2000 kilodaltons. High molecular weight hyaluronic acid ranges greater than 6000 kilodaltons. Some studies suggest that injectable high molecular weight hyaluronic acid is more effective than smaller subunits. All weights seem to have beneficial effects.[1]

Some commercially available injectable hyaluronic acid products include Hyalgan, Orthovisc and Synvisc. The exact ingredients and weights of the hyaluronic acid are proprietary and non-disclosed. Some compounding pharmacies will make up generic hyaluronic acid preparations. The compounding pharmacy I am currently using makes up an intermediate molecular weight hyaluronic acid at 10 milligrams per milliliter.[1]

Animal studies show that injectable hyaluronic acid can directly improve lubrication of synovial fluid shortly after injection. Also, local hylauronidases break down some of the hyaluronic acid into smaller chains and subunits which can then be reassembled into nascent hyaluronic acid. Injectable hyaluronic acid has been shown to decrease inflammatory cytokines like prostaglandin E2, interleukin-1 beta and tumor necrosis factor; decrease oxidative stress; decrease chondroctyte and fibroblast apoptosis; increase fibroblast and chondroctye growth factors; decrease proteolytic enzyme activity; and block pain receptors. These effects summarily improve joint lubrication, preserve joint function, and prevent degenerative deterioration.[1]

An overview of hyaluronic acid injections showed improved lubrication, anti-inflammatory activity, chondro-protective effects. Hyaluronic acid further significantly reduced pain in the affected joints. It was further suggested that HA should be mixed with other drugs or substances to maximize potential benefits. Additionally, it was noted that HA was generally non-toxic and biodegradable.[2] Seventeen papers, including seven randomized controlled trials and ten cohort studies, evaluated intra-articular HA injections for knee osteoarthritis. Repeated injections of HA appear to be safe, effective, and well tolerated for most patients.[3] In one randomized controlled trial with eighty patients, low molecular weight HA injections were compared to high molecular weight HA injections. Both solutions showed about the same benefits in terms of reduced pain and inflammation and improved range of motion. There was no clear benefit of one molecular weight of HA compared to the either one.[4]

In one larger study, three hundred and sixty patients with osteoarthritis of the knee were divided into four treatment groups. One group received just plasma rich platelets (PRP) injections, one group received just HA injections, a third group received PRP plus HA injections and a fourth group received normal saline injections. The group that received the combination of PRP plus HA simultaneously showed the best improvement in terms of pain reduction and joint healing. Decreased cytokines, decreased tumor necrosis factor, decreased interleukin-1 beta, increased interleukin-6, and increased vascular endothelial growth factor were observed. Side effects to the treatments were closely monitored and were noted to include such symptoms as fatigue, high blood pressure, proteinurea, and high triglycerides. In some patients a reduced dose of medicine was more tolerable.[5]

Thirteen studies, including three prospective studies and ten randomized controlled trials, compared PRP to HA intra-articular injections in patients with knee osteoarthritis. Both treatments were equal after three months post-treatment.

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PRP was shown to be slightly more effective than HA after six months follow up but was not obviously superior. More high-quality studies suggested the benefits of these two treatments.[6]

A meta-analysis of fifteen randomized controlled trials with 1,314 patients showed the plasma rich platelet therapy was better than hyaluronic acid in pain reduction. Plasma rich platelets is an autologous highly concentrated solution made from the patient's own blood that contains a variety of growth factors that promotes healing in ligaments, tendons, and cartilage. Some of these growth factors include platelet derived growth factor, fibroblast growth factor, transforming factor B, vascular endothelial growth factor and bioactive proteins that increase cartilage repair and production. There was a lack of clarity in terms of the number and frequency of injections to achieve maximum results and the ideal treatment regime for different areas.[7]

A randomized controlled trial of 120 patients compared intra-articular injections of cortisone, hyaluronic acid and PRP. After three months post injection treatment all patients showed basically the same improvement rate. However, after six, nine and twelve months the PRP-treated group was slightly superior to either the cortisone or hyaluronic acid groups.[8]

A systematic review and meta-analysis of three randomized controlled trials with 258 patients showed positive and beneficial effects of prolotherapy with a dextrose solution. Positive benefits included decreased pain and improved range of motion.[9] In one study twenty-four women with knee osteoarthritis received monthly injections of a 20% dextrose solution. Patients were monitored at four, eight, and 24 weeks. A significant improvement in pain reduction, range of motion and stiffness was noted. Two patients left the study because of pain from the injections.[10] In another study seventy-six patients with knee osteoarthritis received four intra-articular injections at 0, 4, 8 and 16 weeks consisting of 1.0 milliliter of 1.0% Xylocaine and 5.0 milliliters of a 25% dextrose solution. Patients were instructed that it was ok to take acetaminophen if needed for post-injection pain but were advised not to take non-steroidal anti-inflammatory drugs (NSAIDS). Significant reduction in pain and inflammation in the treated joint was observed.[11]

In a double blinded study of 54 patients, intra-articular glucosamine was compared to 0.9% sodium chloride injections into degenerative joints at a frequency of once per week for five weeks. The glucosamine-treated group showed a marked increase in recovery, decrease in pain, increased range of motion and decrease in swelling. No side effects were noted and the improvement lasted for about one month post treatment. The glucosamine seemed to partially restore articular function.[12]

In one study intra-articular dimethyl sulfoxide (DMSO) injections by itself showed no positive benefits in terms of joint repair or connective tissue production.[13] In another study a 40% DMSO solution mixed with Ringer's lactate injected in to the carpal bones of horse showed a marked increase in endogenous hyaluronic acid production.[14]

Intra-articular hyaluronic acid has demonstrated to be superior to intra-articular ozone treatments for knee osteoarthritis in terms of pain relief and improved range of motion. A six-month randomized controlled trial of 174 patients who either received either hyaluronic acid injections or 10 milliliters of 30 microgram/milliliter of ozone. Both ozone and hyaluronic acid treatments showed benefits.[15] An analysis of four randomized controlled studies of 289 patients showed that hyaluronic acid was superior to ozone treatments after six months post therapy.[16]

Intra-articular injection of corticosteroids appears to be more effective on pain relief in the short term, less than one month, than intra-articular injections of HA. HA showed to be more effective in the long, for up to six months. Both medications appeared to be relatively safe and well tolerated; HA injections showed slightly more adverse effects than the corticosteroids.[17] In another study 40 milligrams of methylpredisonolone and 0.5 milliliters of 2.0% xylocaine was compared to 0.5 milliliters of a 20% dextrose solution plus 0.5% xylocaine. Intra-articular shots were repeated once per month for three months in 60 patients with hand osteoarthritis. Follow up after six months showed that the dextrose injections were slightly more effective in decreasing pain and improving range of motion than the cortisone injections.[18]

Intra-articular injections of local anesthetics can relieve joint pain. In one study the intra-articular injection of 5.0 milliliters of 0.25% bupivacaine significantly reduced the pain in the affected joint.[19] However, the use of intra-articular local anesthetics should be used with much caution. Bupivacaine, lidocaine and ropivacaine are chondro-toxic to human articular cartilage. The toxicity increases proportionally to the time exposed to the anesthetic. Even a single injection of an anesthetic can damage the cartilage matrix and promote chondrocyte cell death.[20]

Intra-articular injections of the most common anesthetics, including bupivacaine and lidocaine, are toxic to cartilage. Data from 289 studies was evaluated. Continuous intra-articular infusions of anesthetics following joint surgery are much more toxic than a single injection. The addition of norepinephrine to decrease post-surgical bleeding was also shown to be toxic to chondrocytes. Anesthetics were shown to cause chondrolysis and decrease cell density up to 50% for up to six months months after injection. Lidocaine was further shown to cause mitochondrial damage in chondrocytes leading to cartilage cell apoptosis. Some studies showed that the addition of magnesium sulphate and normal saline with the anesthetic did not significantly reduce cell viability.[21] Procaine appears to be less toxic to articular cartilage. Twenty rats were injected with intra-articular procaine anesthetic or saline and then evaluated histologically. No difference was noted between the procaine and saline groups. Further studies to evaluate the safety of procaine were suggested.[22]

I have experimented with different substances and prefer to use gentler, non-irritating solutions such as dextrose, hyaluronic acid, and PRP. Sometimes I use only one proliferant mixed with a small amount of local anesthetic such as lidocaine or procaine. Other times I mix all three of these substances with a small amount of local anesthetic. For knee osteoarthritis I typically inject one or two 3.0 cc syringes with

a 25-gauge needle from the medial and lateral sides of the infra-patellar tendon that gives access to the intra-articular joint space. All substances appear to be about equally effective for pain relief and improvement in joint range of motion. One patient may prefer hyaluronic acid while another patient may prefer dextrose or PRP injections. The combination of these ingredients seems to be moderately better than an individual single ingredient. The addition of a small amount of local anesthetic helps to reduce pain almost immediately and make the patient feel better. I prefer to use ester anesthetic procaine in small doses as it appears to be safer to cartilage tissue than amide anesthetics. With chronic cases I usually repeat the treatment in three- or four-week intervals with time for healing in between. Other patients I see when they feel they need another treatment, which can last as long as six months to a year. A few patients find no relief or benefit. Most patients find some relief and benefit. Some patients find tremendous relief and improvement.

Side effects of hyaluronic acid injections include pain and joint swelling at the site of injection, redness, and inflammation. Some local pain after an injection may be normal and is best managed with conservative therapies such as topical ice and oral acetaminophen. Non-steroidal anti-inflammatory medication are not recommended because they can interfere with chondrocyte and fibroblast function and the healing process. In rare cases, bacterial or fungal infection has occurred. Improper aseptic technique and/or cross contamination of injectable products are to blame. Intra-articular infection is usually difficult to treat and may also require surgical intervention. *I can't over emphasize that need for proper, safe and clean technique, especially when doing joint injections*. Appropriate training courses are available for health professionals.

Hyaluronic acid injections are not recommended for pregnant and nursing patients, pediatric patients and patients with active infection, especially around the joint to be injected. Also some animal studies show that production of hyaluronic acid is over-expressed in many types of cancer cells. The clinical significance of this is not fully understood yet.[23]

My dad was a strong, powerful man who was a skilled mechanic and master craftsman. He would often be working on a car or an engine in the middle of winter in a poorly heated garage. Later in life he was riddled with degenerative arthritis and was in chronic pain. I remember receiving a letter from him one time while I was away at school. He ended the letter with a prophetic piece of advice to me whose meaning I would only understand in later years. He said, "Son, whatever you do remember to take care of your knees." I am now heeding his warning with a combination of common sense, nutritional supplementation, and injection therapy. Gentle prolotherapy with hyaluronic acid can be a great adjunct to help prevent arthritic degeneration. With time we will see how this episode plays out.

Knee Injections

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Curmudgeon's Corner

by Jacob Schor, ND, FABNO
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Acorns

Of late, my best days are those spent collecting and planting acorns. Some days, other projects, things one might call chores, take precedence, cutting and splitting firewood, as one example. Acorn planting fits into a special category, one that is more satisfying. There are few better excuses than acorn planting to spend a day wandering through the forest. Sometimes I count ten paces between plantings, sometimes I forget to. I intend to work my way in straight lines but often wander off course drawn to openings that are calling for an oak tree. The compass that might keep me on track is forgotten. The acorns go into the ground in pairs because I use a two-pronged lawn aerator to punch holes into the soil. If I had my druthers (a phrase I've never had the opportunity to put in print before), I would purchase a Squirrel Acorn Planter made by Lowell Larson and sold by Forestry Suppliers; but between its price and the cost of shipping, the lawn aerator works well enough. It pokes a pair of three-inch-deep holes about a foot apart. In theory an acorn should only be planted about 1 ½ inches deep. Concerned that the acorns end up deeper than they like, I pause after covering them and wish the little things, 'best of luck'. My dear wife and I have adopted different methods of getting the acorns into the ground. Rena, a former kibbutznik, prefers a simple hoe rather than the aerator. I think the hoe may require more skill, though she makes it look equally efficient.

If I was to really do this right, I would be planting in the fall, not now in the spring. That's when the YouTube videos say you should. But I'm here, now, last year's acorns are lying on the ground at the bottom of our neighbor Priscilla's driveway and are just starting to sprout. So why not now? There are worse things to waste one's time and energy on. Acorns on the verge of sprouting remind me of chicken eggs about to hatch. Cracks form in the nut's shell and as these cracks widen, one can spy a bit of pink interior, the naked tiny growing plant embryo about to send its root stalk down into the world. They appear to my anthropomorphic eyes as naked baby things. How can I not pick them up, collect them in shopping bags and take them into the forest hoping to find them good homes? Theoretically while it might work better to collect acorns in the fall, stratify them over the winter, and plant them the following fall, as I mentioned, I'm here, now. If lucky, I'll have trees growing by next fall.

My fixation on acorns and oak trees was inspired by a book called *The Nature of Oaks.* The author, Douglas Tallamy, is an entomology professor at the University of Delaware and has written a marvelous book. It is the sort of 'nature book' that one reads slowly and savors. The book follows the annual cycle of oak trees and the animals they interact with over the course of a year, starting in November and advancing through winter, spring, summer, and fall; each month gets a chapter.

Entomology of course is the study of insects, not trees; but years back Dr. Tallamy became fascinated by the keystone role oak trees play in a forest. It was insects, in particular caterpillars, that drew him to oak trees. Caterpillars are the fuel that powers the food webs that feed most inhabitants in a forest. They are the currency that the economy of the forest relies upon.

I am among the many who falsely believed that if you want to help birds survive the winter you feed them birdseed. This is the direct influence of my fourth-grade teacher, who imposed a 'bird tax' on each of her students that went toward purchasing bird seed; we 'volunteers' tramped out in coats and galoshes to replenish her bird feeder outside her classroom window with this seed. Tallamy writes that only a rare few bird species can survive on seeds. Most songbirds in North America depend primarily on insects for food; seeds and berries only occasionally supplement their diets. Many species cannot digest seeds at all.

Insects and the birds they support are at a crucial juncture. "We have removed more than half of the forests on earth and, not surprisingly, insect populations have declined globally by at least 45% since 1979. And again, it should be no surprise

that with insect declines come bird declines. There are now 3 billion fewer birds in North America than there were just 50 years ago…." As a result, 430 bird species are now considered at risk of extinction. There are large differences between plants in their capacity to support insects both in variety and quantity. The biggest difference is between native and non-native plants.

Plants make chemicals that dissuade insects from eating them, phytotoxins to insects (phytonutrients often enough to people). Insects over time evolved tolerance to these chemicals and can feed on one or two native plant species. Tallamy writes, "Most insects have become very good at eating a few plants but are completely unable to eat most plants." There are often no insects capable of feeding on non-native plants, so those plants supply no nutrition into the food web. A few of our native plants are known as keystone plants because they supply the majority of the food that enters the web. Just a few plant genera supply about 75% of the insect food required by birds. For most areas the list of keystone plants in order of variety of insects fed goes like this: oaks, cherries, willows, birches, hickories, pines and maples. It's those first three, the oaks, cherries, and willows that support the most life.

In the United States there are 897 caterpillar species that depend on oak trees. Maples, supporting 295 species, come in second place in the caterpillar competition. Humans value maple trees because we love maple syrup; on the other hand oak trees produce acorns, an estimated three million acorns over an oak tree's lifespan, which in turn feed other animals. Oak leaves also win the contest when it comes to feeding the micro-organisms of the forest floor. Oak leaves are slow to decay and provide a lasting mulch long after other leaves have disintegrated. Oak trees enhance the biodiversity of a locale more than any other plant.

If we value having birds in our world, we want oak trees growing near us to supply the insects for birds to eat. Similar arguments can be made for clean water. Oak leaves dropped on the forest floor do better at filtering water, preventing soil erosion, and preventing flooding than leaves from other trees. I could go on; Tallamy certainly does for a full year's worth of chapters. The book is fascinating reading and a pleasant departure for me from reading about cancer and other diseases. Tallamy's approach to life seems to be to take careful note of things he doesn't understand, mysteries as he calls them, and to observe carefully in order to explain them. It is his ability to see the world so closely that comes across in reading his writing and that leaves the reader envious, hoping to mimic this way of seeing. It may be what you would expect from a professor of entomology, but it's an uncommon trait to marvel at the world these days, one we would all do well to try and copy.

I used the term marvelous earlier in describing this book because I can think of no better word to describe how this book leaves me pondering than to say marvel. Take for example, the wasps that deposit their eggs in the maturing buds of oak trees. The maturing wasp eggs release growth hormones that convince the tree to form a protective shell around each egg forming what is called an oak gall, sheltering and feeding the infant insect. The phenotype, that is the outward appearance of some of these wasps, alternates between generations. The appearance of the descendants of the wasp that lays the eggs, when matured to adulthood, will look like a different insect than their parents; only their grandchildren will look like the grandmother. I use the singular as some generations do not require a male to fertilize the eggs. This would be like cats and dogs alternating through the generations, as in "my dog Ruby just had kittens." Marvel is a better word than 'think' when pondering this phenomenon.

Reading Tallamy's book on oak trees has me convinced that one can alter a forest for the better by planting acorns. Anything really worth doing should alter the world for the better. This idea of giving nature a helping hand isn't how we usually relate to nature. In the US, we believe that left totally to its own, Nature will make the best choices. We prize wilderness areas, places where Nature is left wholly alone to restore and maintain her biosystems. That belief isn't held everywhere. Years ago, Michael Pollan, in his first book that was called, *Second Nature,* examined this particularly American hands-off-approach to Nature. Pollan compared our attitudes to the European-style approach, which involves a far more active stewardship. *Second Nature* may be my favorite Pollan book as it challenged the way I see the world more than his other works.

Tallamy's oak book has done more than change the way I see things. Tallamy has me actively trudging through the forest and taking pleasure in doing so. If a good book changes the way we see the world, a great book changes what we do in the world.

I find planting acorns deeply pleasing. Doing so touches on that 'purpose driven life' business that Viktor Frankl wrote about in *Man's Search for Meaning*. Being actively engaged in doing something one views as beneficial is certain to foster a sensation of purpose and meaning. Feeding the forest ecosystem, helping the forest mature into long living hardwoods, creating greater diversity and complexity, believing that something one has done will endure into the future and leave the world even a tinge better, what more can one ask for after this last year we've endured? This entire acorn business is giving me such satisfaction that I'm pondering the logistics of giving away acorns to patients with instructions how to "make the world a better place."

Like any new convert to a cause, I've been sharing my oak tree enthusiasms with friends and colleagues. Our colleague Kurt Beil, ND, wrote back:

> Trees provide many of the things we need for optimal health. Beside the physical benefits of oxygen and temperature regulation (shade), just looking at a tree lowers our blood pressure, heart rate, and cortisol. The airborne chemicals produced by many trees (including oaks) stimulate our immune system and help improve our sleep. Just the presence of a mighty tree can be a source of measurable comfort and support, especially reconnecting with a favorite childhood spot as if it were an old friend.

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Acorns

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Speaking of old friends, one dear friend, who I've kept in touch with since high school and who ended up a horticulturist of some note, wrote back that she too has been planting sprouted acorns, and much to my relief gotten good results: "… so you should have made great progress of repairing the world. *tikun olam*, one tree at a time."

That phrase, *tikun olam*, is Hebrew for "World Repair." It's a term that originated in the 16th century in the writing of the kabbalist Isaac Luria. It encapsulates Luria's complex conception of Jewish mysticism, which I will forego detailing here.[1] Suffice to say that followers of Luria's tradition mean by repair, the restoration of the light of the divine to its proper place. In modern usage, *tikkun olam* describes working to improve the conditions of this world, usually with a focus on social justice or environmental action.

Given what Tallamy has written about oak trees, planting acorns is practicing *tikkun olam*, or as close to it as I'm going to get.

This dear friend also pointed out that, "There is great genetic variation in oaks, even within a species. So, pick a tree you like especially well. A venerable tree…" This concept that distinct genetic variation exists between individual oak trees is probably what we've alluded to when we say that 'an acorn doesn't fall far from the tree.'

The term "Venerable Trees" is actually the title of a book by Tom Kimmerer about his efforts to save the American chestnut tree from extinction, a book that I've added to my reading list.

Up until now I've been planting acorns from our neighbors' trees; sheer convenience determined which acorns I planted. This idea of searching out specific, venerable trees and selecting their acorns purposefully may need to be marveled over before I make the extra effort.

Tallamy's book is a pleasant read, one that may change the way you walk through the world and even put you on the lookout for venerable trees. If you're affected like me by this book, you'll soon find yourself carrying acorns in your pocket.

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1. According to Luria, God contracted the divine self to make room for creation. Light of the divine coalesced into vessels called kelim, some of which shattered and scattered. Most of the light returned to its divine source, but some light attached to the broken shards of the kelim and these shards became the basis of the material world and the evil contained in it. By repairing the world, followers of the Luria's tradition mean restoring the light of the divine to its proper place. Sadly, Luria's image of creation as shattered pottery has merged in my mind with the story about Humpty Dumpty; all the King's horses and all the King's men has been converted to All of the old rabbis and all of the old sages, couldn't…but perhaps better if I don't go there.

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CALENDAR

OCTOBER 1: LDN 2022 VIRTUAL ON-DEMAND CONFERENCE BEGINS online. Available for 12 months. CONTACT: https://ldnresearchtrust.org/ldn-2022-conference

OCTOBER 27-29: A4M/MMI IV/CHELATION THERAPY in Charleston, South Carolina. CONTACT: https://www.a4m.com/iv-chelation-therapy-symposium-a4m-october-2022.html

OCTOBER 27-29: A4M/MMI PELLET THERAPY in Charleston, South Carolina. CONTACT: https://www.a4m.com/pellet-therapy-a4m-october-2022.html

OCTOBER 27-29: A4M/MMI LONGEVITY MEDICINE AND BIO-HACKING: OPTIMIZING LIFESPAN in Charleston, South Carolina. CONTACT: https://www.a4m.com/module-viii-a4m-october-2022.html

OCTOBER 28-29: INTERNATIONAL CONFERENCE ON PREVENTIVE MEDICINE AND INTEGRATIVE MEDICINE in Los Angeles, California. CONTACT: https://waset.org/preventive-medicine-and-integrative-medicine-conference-in-october-2022-in-los-angeles

OCTOBER 28-30: ACADEMY OF INTEGRATIVE HEALTH & MEDICINE CONFERENCE – People. Planet. Purpose in San Diego, California. CONTACT: https://www.aihm.org/conference/

OCTOBER 28-30: AzNMA NATUROPATHIC MEDICINE EDUCATION CONFERENCE in Scottsdale, Arizona. CONTACT: https://www.aznma.org/

NOVEMBER 3-5: FRONTIERS 6 CONFERENCE – The Cancer Revolution and Ozone's Role in Scottsdale, Arizona. CONTACT: https://www.ozonetherapiesgroup.com/

NOVEMBER 4-5: NEW HAMPSHIRE ASSOCIATION OF NATUROPATHIC DOCTORS CONFERENCE in Newcastle, New Hampshire. CONTACT: https://www.nhand.org/

NOVEMBER 5-6: OREGON ASSOCIATION OF NATUROPATHIC PHYSICIANS ANNUAL CONFERENCE in Portland, Oregon. CONTACT: https://www.oanp.org/page/AnnualConference

NOVEMBER 10-13: AMERICAN COLLEGE FOR ADVANCEMENT IN MEDICINE ANNUAL MEETING in Las Vegas, Nevada. CONTACT: https://na.eventscloud.com/website/42444/

NOVEMBER 12: THE WELL WOMAN CONFERENCE - Integrative and Functional Strategies for Optimizing Women's Mental Health and Vitality online. CONTACT: https://www.psychiatryredefined.org/

NOVEMBER 12-13: HEARTQUEST GLOBAL INTERACTIVE CONFERENCE on the Renaissance of New Healing Solutions in Scottsdale, Arizona. CONTACT: https://www.heartquestglobalsolutions.com/nov-2022-conference

NOVEMBER 13-16: AMERICAN COLLEGE OF LIFESTYLE MEDICINE CONFERENCE in Orlando, Florida. CONTACT: https://lmconference.org/

DECEMBER 9-10: INTERNATIONAL CONFERENCE ON PREVENTIVE AND INTEGRATIVE MEDICINE in New York City, New York. CONTACT: https://waset.org/preventive-medicine-and-integrative-medicine-conference-in-december-2022-in-new-york

DECEMBER 9-11: A4M presents LONGEVITY FEST 2022 in Las Vegas, Nevada. CONTACT: https://www.a4m.com/longevity-fest-2022.html

DECEMBER 9-11: A4M/MMI PEPTIDE THERAPY CERTIFICATION in Las Vegas, Nevada. CONTACT: https://www.a4m.com/peptides-ii-a4m-december-2022.html

DECEMBER 9-11: A4M/MMI ADVANCED ENDOCRINOLOGY: THE HORMONAL SYMPHONY (Module 1) in Las Vegas, Nevada. CONTACT: https://www.a4m.com/module-i-a4m-december-2022.html

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JANUARY 28-29, 2023: INTERNATIONAL CONFERENCE ON TRADITIONAL MEDICINE AND HERBS in New York City, New York. CONTACT: https://waset.org/traditional-medicine-and-herbs-conference-in-january-2023-in-new-york

FEBRUARY 23-25: INTEGRATIVE HEALTHCARE SYMPSOIUM in New York City, New York. CONTACT: https://www.ihsymposium.com/

FEBRUARY 28-MARCH 2: INTEGRATIVE MEDICINE AND HEALTH SYMPOSIUM in Chicago, Illinois. CONTACT: **https://www.consortiummeeting.org/#home**

MARCH 3-5: EXPLORING COMPLEX, CHRONIC ILLNESS THROUGH THE LENS OF TRUE HEALING online. CONTACT: https://forumforintegrativemedicine.org/

MARCH 24-26: JOINT AMERICAN HOMEOPATHY CONFERENCE in San Antonio, Texas. CONTACT: https://www.jahc.info/

APRIL 22-23: INTERNATIONAL CONFERENCE ON INTEGRATIVE MEDICINE AND NUTRITION in New York City, New York. CONTACT: https://waset.org/integrative-medicine-and-nutrition-conference-in-april-2023-in-new-york

JUNE 2-4: SASKATCHEWAN ASSOCIATION OF NATUROPATHIC DOCTORS HEALING SKIES CONFERENCE in Saskatoon, Saskatchewan, Canada. CONTACT: http://www.sasknds.com/healing-skies-conference.html

JUNE 16-18: 5th INTERNATIONAL HOMEOPATHY RESEARCH in London, United Kingdom. CONTACT: https://www.hri-research.org/2022/07/hri-london-2023-save-the-date/

Women's Health Update

by Tori Hudson, ND
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Fibromyalgia: A Women's Health Disorder

It will not be surprising to hear that chronic pain is a major source of disability, suffering and health care utilization affecting approximately 100 million US adults – more than one-third of the adult population.[1] Just one of those many causes of chronic pain is fibromyalgia, a potentially disabling and poorly understood rheumatic condition. Fibromyalgia is characterized by chronic widespread pain and tenderness, fatigue, cognitive difficulties, and overall functional impairment. There is no widely accepted etiology of fibromyalgia.

The prevalence of fibromyalgia in the US has been estimated to range from 2% to 8%, affecting 5-10 million adults.[2,3] What I want to call your attention to is that fibromyalgia **is most prevalent among middle-aged women, encompassing 75% – 90% of those diagnosed**.[4-6]

For many years, the diagnosis of fibromyalgia has been reliant on an evaluation of "tender points," or areas of tenderness around joints, assessed by palpation or algometer. Women tend to report more tender points than men[7] and have also been reported to feel more intense pain at these designated tender point sites.[8] This diagnostic criterion may account for the greater frequency of fibromyalgia among women.

In 2016, the American College of Rheumatology revised their diagnostic criteria which now includes the following:

- Widespread Pain Index (WPI) ≥7 **and** Symptom Severity Scale (SSS) score ≥5 **or** WPI between 4–6 and SSS score ≥9.
- Generalized pain, in at least 4 of 5 regions, is present.
- Symptoms present at a similar level for at least 3 months.
- A diagnosis of FM is valid irrespective of other diagnoses. A diagnosis of FM does NOT exclude the presence of other illnesses.

It is possible that with these new diagnostic criteria, the gender difference is smaller than previously estimated. Another problem with determining the magnitude of gender difference is that there are very few men in most of the studies.

Despite efforts to develop diagnostic efforts and consistency in diagnosing fibromyalgia, not all clinicians and clinical settings apply these guidelines; and at this point, there seems to be no "gold standard" for a clinical diagnosis of fibromyalgia. What makes it especially challenging is that there is no lab or imaging test to make such a diagnosis.

Fibromyalgia is commonly associated with psychiatric disorders,[3] and international research has shown high rates of depression, anxiety disorders, bipolar disorder, obsessive-compulsive disorder, personality disorders, and posttraumatic stress disorder (PTSD) in patients with fibromyalgia.

As I mentioned earlier, the underlying cause(s) of fibromyalgia remain unknown, although there is evolving insight with findings that it is associated with dysregulated dopamine in the brain.[10,11] Without the tender point criteria, the diagnosis now relies exclusively on self-report data. That makes things more ambiguous and highlights the influence of anxiety and/or depression on the experience of the pain. While I'm not comfortable with it, this diagnostic ambiguity leaves many to view fibromyalgia as a somatoform psychiatric disorder. As a result of this diagnostic ambiguity and substantial psychiatric comorbidity, fibromyalgia is frequently, and controversially, viewed as a somatoform psychiatric disorder.[12,13]

A somatoform disorder also known as somatic symptom disorder (SDD) or psychosomatic disorder, is a mental health condition that causes an individual to experience physical bodily symptoms in response to psychological distress. I'm concerned that characterizing fibromyalgia as a psychosomatic disorder is just too reminiscent of the disregard, disrespect, and discounting of women and their health issues that have existed in medicine and our culture for decades and that still exist today.

Another comment on gender differences in fibromyalgia brings to mind a recent study that examined gender differences

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in the demographics and clinical correlates of musculoskeletal disorders among veterans. Fibromyalgia was included among 14 groups of musculoskeletal disorders and was not examined separately.[14] As of the writing of my column today, I'm not aware of any study that has systematically compared sociodemographic characteristics, patterns of comorbidity, health care utilization, and psychotropic medication prescriptions use among patients with fibromyalgia in comparison to patients with other pain syndrome diagnoses, or between males and females diagnosed with fibromyalgia.

A new diagnostic proposal has been proposed by the Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks (ACTTION), a public–private partnership with the US Food and Drug Administration (FDA) and the American Pain Society (APS). Their attempt is to try to develop a clinically useful and consistent diagnostic system for chronic pain disorders, including FMS.

What I appreciate of this new diagnostic proposal is that they conceptualize FMS as a dimensional syndrome which includes five dimensions: (1) Core Diagnostic Criteria, defined as the presence of pain in six or more body sites from a total of nine possible localizations, sleep disturbance, and fatigue; (2) Common Features, like tenderness, dyscognition (e.g., trouble concentrating, forgetfulness, and disorganized or slow thinking), musculoskeletal stiffness, and environmental sensitivity or hypervigilance; (3) Common Medical and Psychiatric Comorbidities like chronic fatigue syndrome, irritable bowel syndrome, chronic pelvic pain, interstitial cystitis, orofacial conditions, chronic headaches, depression, anxiety disorders, central sleep apnea, restless leg syndrome, etc.; (4) Neurobiological, Psychosocial and Functional Consequences, which includes general outcome, functional disability, social and medical cost of FMS, morbidity, and mortality; and (5) Putative Neurobiological and Psychosocial Mechanisms, Risk Factors, and Protective Factors that focus on risk factors, comorbidities, and pathophysiology aspects. This proposal is much more inclusive of the risk factors, course, prognosis, and pathophysiology of FMS. We need to wait for validation of this criteria with data about accuracy of diagnosis.

If we end up using these criteria, it is likely that the diagnosis of FMS would significantly increase, but also likely the false positives.

Rheumatology experts think that FMS is not a distinct rheumatological diagnosis and assert the correct rheumatological diagnosis has just not been made. While I cannot yet agree with this assertion, I do use that perspective to motivate me to be more studious and diligent in the ability to diagnosis disorders that I might have missed, including rheumatoid arthritis, ankylosing spondylitis, and systemic lupus but might include more challenging diagnostic situations such as small fiber neuropathy and Ehlers Danlos syndrome.

I will assume that other articles in this *TL* issue have brought attention to strategies in treating FMS, including addressing and reducing stress triggers, lifestyle factors such as sleep habits and sleep quality, regulating cortisol, identifying and addressing co-existing and/or underlying disorders or influences such as vitamin D insufficiency/deficiency, low iron stores, hormonal factors, toxin exposures and other chronic viruses and/or bacteria. In addition, tools of the trade might include magnesium, tryptophan, L-tyrosine, vitamin D, omega-3 fatty acids, saffron, palmitoylethanolamide (PEA), malic acid, ribose, SAMe, curcumin, California poppy, and other traditional plants.

I look forward to reading the other articles in this issue to gain insight and consider other ideas and knowledge about addressing this very complex and challenging disorder.

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iron supplementation frequently reduced or eliminated the symptoms of RLS.[7,8]

Magnesium

One of the manifestations of magnesium deficiency is neuromuscular and central nervous system irritability, which could contribute to the development of RLS. Suboptimal magnesium intake and low or suboptimal magnesium status are common in Western societies.[9] Certain factors that tend to deplete magnesium, such as pregnancy, stress, alcohol consumption, and caffeine intake, are also associated with an increased risk of RLS. In an uncontrolled trial, six patients suffering from insomnia related to mild-to-moderate RLS received 300 mg of magnesium (as magnesium oxide) each evening for four to six weeks. Five of the 6 patients reported a decrease of RLS symptoms and/or an improvement in insomnia.[10] In my experience, magnesium supplementation is frequently beneficial for people with RLS.

Vitamin E

Nine patients with a history of RLS for 1.5 to 30 years were treated with vitamin E at a dose of 300-1,600 IU per day. Seven patients experienced prompt and almost complete relief and the other two patients reported improvements of 75% and 50%, respectively. Symptoms tended to recur if vitamin E was discontinued, or if the dose was reduced below an adequate maintenance level.[11] Two patients responded to a dose of 300 IU per day, and in one case the improvement was maintained with 200 IU per day.[12] The mechanism of action of vitamin E is not known.

Folic Acid

In a small proportion of patients with RLS, the condition appears to be caused by a genetically determined folic acid dependency. One investigator described 45 patients from five families with folic acid-responsive RLS. The amount of folic acid required to control the symptoms ranged from 5 mg to 30 mg per day.[13] I have a seen a few patients with familial RLS who required high doses of folic acid to relieve their symptoms. One patient was symptom-free on 10 mg to 25 mg per day but experienced a partial return of symptoms when the dose was reduced to 5 mg per day. For comparison, a typical diet provides approximately 0.3 mg per day of folic acid. High-dose folic acid therapy should be considered for patients with RLS who have a strong family history of the disorder.

Conclusion

As is often the case with many health conditions, mainstream medicine tends to overlook safe and effective nutritional therapies and to overprescribe potentially dangerous medications, sometimes in excessive dosages. If doctors would pay closer attention to these nutritional treatments, the need for dopamine agonist therapy could probably be greatly decreased.

Alan R. Gaby, MD

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Treatment of Restless Legs Syndrome: Too Many Drugs, Not Enough Nutritional Therapy

Restless legs syndrome (RLS) is a common condition characterized by dysesthesia (such as a painful burning, prickling, or aching feeling) in the legs and an irresistible urge to move the legs. The prevalence of this condition has varied in different studies, from 4% to 29% of adults in Western countries. Symptoms often occur at night and interfere with sleep. Dopamine agonists are the most commonly prescribed drugs for RLS. Three dopamine agonists have been approved by the US Food and Drug Administration (FDA) to treat RLS: ropinirole, pramipexole, and rotigotine.

Dose-related side effects of dopamine agonists include daytime sleepiness, nausea, impulse control disorders (such as pathological gambling), and other psychiatric conditions. In addition, long-term use of dopamine agonists for RLS can lead to a situation known as augmentation, in which the duration of action of the drugs becomes shorter and the symptoms become worse and/or spread to the upper extremities. It has been estimated that augmentation occurs in 20-30% of patients treated with a dopamine agonist for RLS. Physicians often respond to the occurrence of augmentation by increasing the dosage of the medication. This dosage increase typically produces short-term improvement in RLS symptoms but eventually causes a return of augmentation (sometimes more severe than before). A vicious cycle of progressively worsening symptoms and progressively higher medication dosages can result in patients taking dopamine agonists at far higher dosages than are approved by the FDA for RLS.

A study was recently conducted to determine to what extent RLS patients in the US are receiving potentially excessive dosages of dopamine agonists.[1] The study examined data from a US prescriptions database from October 2017 through September 2018. This database included about 65% of all retail and mail-order prescriptions in the US. Of 670,404 patients diagnosed with RLS without Parkinson's disease, 58.8% were prescribed a dopamine agonist. The dosage of these drugs was categorized as "low/middle" if it was within or slightly above the FDA-approved dosage range; "high" if it was 101%-149% of the maximum approved dosage; and "very high" if it was 150% or more of the maximum approved dose. Overall, 19.1% of RLS patients were receiving a dosage above the maximum FDA-approved level, and 10.4% of the patients were receiving a "very high" dosage. The frequency of high/very high-dose prescribing increased with increasing age of the patients and was highest for those aged 70-79 years. Extrapolating the findings from this study to the entire US population, approximately 115,000 people with RLS are receiving dopamine agonists in dosages above FDA guidelines. The author of this report concluded that progressively increasing the dosage of dopamine agonists in the face of progressively worsening symptoms is widespread but inappropriate, "akin to putting out a fire with gasoline."

Nutritional Therapy for RLS

A number of nutritional treatments have been reported to be effective for patients with RLS. Most of these treatments are not well known to the conventional medical community, although many doctors are aware of the importance of identifying and treating iron deficiency.

Dietary Factors

In one study, of 131 patients with reactive hypoglycemia, 59 (45%) had RLS. The symptoms usually improved on a diet designed to improve blood glucose control.[2] Such a diet typically includes avoidance of refined sugar, other refined carbohydrates, caffeine, and alcohol; consuming abundant amounts of protein and complex carbohydrates; and eating small, frequent meals.

Iron

In several studies, iron deficiency was found in around 25% of RLS patients.[3-6] Among patients who were iron-deficient,

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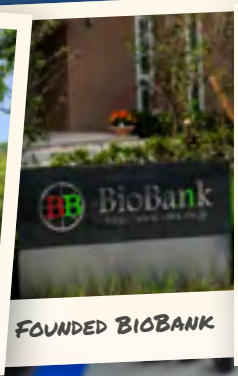

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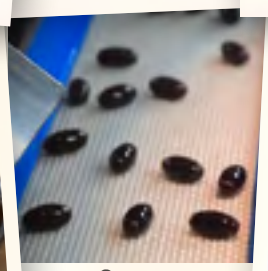

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