Fibromyalgia | Chemical Sensitivity | Pain Management

TOWNSENDLETTER.COM

Townsend Letter

The Examiner of Alternative Medicine

November 2020
Issue #448
$10.99

Testing for Fibromyalgia

Nutrients for Immune Support

How Chronic Stress Produces Pain

Jacob and Laurie Teitelbaum
Shining the Light on Fibromyalgia and Chronic Fatigue

Stacking the Deck Against Bioidentical Hormones

JUMP TO TABLE OF CONTENTS

Thank you for purchasing this issue of *TOWNSEND LETTER*

On the cover (previous page) you will find a button that will take you directly to the table of contents. Once there, you can click page numbers that take you directly to articles. Click on "return to table of contents" at the bottom of each page to take you back to the TOC.

Most web and email addresses are clickable within the articles and in the calendar. We do not guarantee the accuracy of each address/URL, or that it is clickable.

Please don't overlook our advertisers, without their support *Townsend Letter* would not exist. Take the time to discover companies you might not be familiar with, many of whom offer special pricing for *Townsend Letter* subscribers. An advertiser list is printed on page 74 with clickable page numbers that will take you directly to their ad(s).

Subscription Rates and Options

Prices valid through 2/1/2021

Name _____ Email/Phone _____

Address _____

City/State/Zip _____

Payment accepted in US funds, payable by check / money order / credit card / or billed via PayPal

Payment by: Visa/MC/AMEX/Discover # _____ Expiration date: _____

Signature _____

Click here to subscribe online

	Description	Print Version	E-Edition	Combined
US Addresses (except WA state)	1-year Domestic US	$76.99	$66.99	$91.99
	2-year Domestic US	136.99	116.99	166.99
	6-month Domestic US	45.99	41.99	–
	1-year Student Domestic US	56.99	41.99	66.99
Washington State Residents	1-year Washington state (w/tax)	86.99	74.99	99.99
	2-year Washington state (w/tax)	146.99	127.99	183.99
	6-month Washington state (w/tax)	33.99	46.99	–
	1-year Washington Student (w/tax)	56.99	46.99	66.99
1st Class	1-year First Class Domestic US	96.99	66.99	111.99
	2-year First Class Domestic US	176.99	116.99	206.99
International Rates	1-year International (US$)	105.99	66.99	120.99
	2-year International (US$)	202.99	116.99	232.99
	6-month International (US$)	63.99	41.99	–
	1-year International student (US$)	76.99	41.99	93.99

SPECIAL RECEPTION ROOM OFFER: Purchase a 2nd subscription for your waiting room

$57.99 US addresses – $87.99 International
Offer valid with current existing subscription

E-Edition Single Issue: $15.00

E-Edition Single Issue WA State (includes tax): $16.00

Single Print Issues: cover cost (for each issue), plus shipping charges, applicable taxes, and $3 per-order handling fee.

Townsend Letter
911 Tyler Street | Port Townsend WA 98368
info@townsendletter.com
360.385.6021 | 360.385.0699 (fax)
www.townsendletter.com

How Do You Detox?

Step 1: Tri-Fortify®

Open Detox Pathways*

Tri-Fortify's published research confirms intracellular absorption, natural killer and oxidative stress support, all essential for healthy detoxification.*

Step 2: ToxinPul™

Bind, Excrete & Support Liver*

ToxinPul™ utilizes four mechanisms of action to bind toxins in multiple locations throughout the body plus support and protect the critical detoxification pathways and organs such as the liver and the kidneys.*

Learn More At: ResearchedNutritionals.com/HowDoYouDetox

Researched Nutritionals
solutions for life

Tel: 800.755.3402 • Fax: 805.693.1806 • CustomerService@ResearchedNutritionals.com
www.ResearchedNutritionals.com | Available only through healthcare professionals.

Promote Healthy Immune Balance*

Transfer Factor Multi-Immune™,

the focus of multiple clinical research studies, was formulated to promote a healthy and balanced immune response. Our formulation team studied decades worth of published ingredient research, resulting in the selection of twelve specialized nutrients designed to provide a synergistic approach to immune support.

EACH SERVING CONTAINS:

- NK Maximizer BioPlex™ - Super blend of colostrum, transfer factor, larch arabinogalactan, IP-6, shiitake & maitake mushrooms
- Macrophage & T-Cell Pro Blend™ each serving contains Beta glucan, astragalus
- Health Cell GTP™ - Green tea & pomegranate extracts
- Mineral Blend - Zinc & selenium

A balanced immune system response is crucial for optimal health. Because Researched Nutritionals® is known for the quality of its products and excellent formulations, I am thrilled to have Transfer Factor Multi-Immune™ to recommend for my patients.

Joseph Burrascano Jr., MD

CLINICALLY RESEARCHED

Researched Nutritionals® solutions for life

Tel: 800.755.3402 • Fax: 805.693.1806 • CustomerService@ResearchedNutritionals.com
www.ResearchedNutritionals.com | Available only through healthcare professionals.

A4M MMI

REDEFINING MEDICINE®

Join Us!

28TH ANNUAL WORLD CONGRESS

MEDICINE LIKE YOU'VE NEVER EXPERIENCED IT...

DECEMBER 11-13, 2020

VIRTUAL
educational experience

THE LARGEST EVENT IN ANTI-AGING MEDICINE

100% ONLINE

REGISTER NOW!

SAVE $100

Use Promo Code: Townsend100

www.a4m.com

From the Publisher

Long Haulers

The COVID-19 pandemic has led to a huge uptick in folks moving from New York City. While some are remaining in suburbs and exurbs within the metropolitan area, not a few are doing big moves out of state. When I first heard the term "long hauler," I immediately envisioned truckers who habituate the interstate freeways and take breaks at truck stops that are strange little worlds unto themselves; life at the truck stop ranges far beyond gassing up and greasy spoon dining, some of which typifies the illicit business seen at any busy port. It was a little bit of a surprise to discover that those individuals who have survived a bout with SARS-CoV-2 but remain symptomatic on a prolonged basis are calling themselves "long haulers," evidently because they are dealing with the virus over the long haul; still I can't get the big trucks out of my mind.

➤

Letter from the Publisher

➤

On the August 22 NPR *Weekend Edition*, a Texan epidemiologist described her own experiences as a COVID-19 long hauler.[1] Many of the symptoms are not different from those that patients with chronic fatigue, fibromyalgia, chemical sensitivity, and Lyme disease experience: fatigue, exhaustion, muscle aching, muscle weakness, brain fog, lack of concentration, loss of endurance, depression, loss of sex drive, inability to carry out job duties and home chores, hypersensitivity, anxiety, hopelessness, and more. Dr. Margot Gage was not initially diagnosed with COVID-19 because she did not have a fever nor did she have a cough. She was healthy and physically fit before become symptomatic. Beyond the fatigue and brain fog, she experiences hot flashes that require keeping her home very cool, extreme sensitivity like an allergy when outside in the sun, loss of smell and taste, and any prolonged bout of work activity will result in exhaustion requiring bedrest. She connects with long haulers who experience other unusual symptoms, including weird skin rashes, visual difficulties, ringing in the ears, and nails growing very long while losing hair. Gage thinks that like other viral illnesses COVID-19 has a post-viral syndrome that relates to chronic fatigue syndrome.

Unfortunately, long haulers are being waitlisted to get care.[2] While Mount Sinai Hospital in NYC opened its Center for Post-COVID Care in May, many hospitals and clinics across the country do not have such specialized centers. The online patient advocacy group, Survivor Corps, is seeking to change this absence urging for opening of many more specialty centers (survivorcorps.com). Long-haulers are no longer having symptoms of acute illness and presumably have negative rt-PCR tests so they are not contagious. But that does post a dilemma – when is the right time to treat a COVID-19 patient in the clinic setting to ensure staff and other patients are not exposed to the virus? A Yale University immunologist, Akiko Iwasaki, PhD, thinks that the long-hauler may still have active COVID-19 virus causing the prolonged symptoms. But Iwasaki also hypothesizes that “non-infectious virus in some cells trigger an immune response” responsible for chronic symptomatology.

If COVID-19 post-viral syndrome behaves similarly to other viral conditions, one would expect that IgM antibody testing would be negative, IgG testing would be positive, and other inflammatory and immune system markers would be abnormal. However, such testing has not yet been adequately defined.

1. https://www.npr.org/2020/08/22/905015250/after-recovering-from-COVID-19-many-still-have-painful-symptoms
2. https://www.wsj.com/articles/as-COVID-19-symptoms-linger-demand-for-specialized-clinics-surges-11597925200

continued on page 6 ➤

STAY ENERGIZED WITH SUPPORT FOR MUSCLE AND JOINT HEALTH*

Molecular H2 Raspberry

Effervescent Hydrogen Tablets

Promotes healthy metabolic function, and balances the immune system and stress response in human studies.*

Creates a high level of hydrogen (H_2) when added to non-carbonated water. H_2 readily passes through cellular membranes and the blood-brain barrier, delivering antioxidant benefits.*

Also available as unflavored.

Taurox™ 4X

Nanotech Nutrients®

Homeopathic immune optimizer that modulates the immune system, decreases fatigue, modulates cytokines, and is nonadrenergic.*

Clinically tested and non-toxic. Clinical trials have shown that up to 90% of subjects experienced an improvement in energy levels after taking Taurox™.*

Also available in high potency pellets.

InflaMed

Connective Tissue and Joint Health*

Synergistic blend of herbs, nutrients, and proteolytic enzymes that provide nutritional support for connective and joint tissues.*

Supports the body's regulation within normal levels of COX I and II enzymes, arachidonic acid, lipoxygenase, and leukotrienes.*

POWERED BY hrw

*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

INNOVATIVE, LEADING-EDGE SUPPLEMENTS **SOURCED FROM THE PUREST RAW MATERIALS SINCE 1979**

AllergyResearchGroup® Innovative Nutrition

NSF GMP Registered

emerson QUALITY PROGRAM

emerson ecologics | wellevate

natural partners | Fullscript

Call or order online today.

www.allergyresearchgroup.com

800.545.9960

Letter from the Publisher

➤ *continued from page 4*

RLC Labs Recalls Nature-Throid and WP Thyroid Hormone Products

On August 25, RLC Labs of Phoenix, Arizona, emailed a voluntary recall notice of its Nature-Throid and WP thyroid hormone products. The lab specified more than 20 individual lot numbers for 1/2, 1, and 2 grain products; it would appear that this list included all thyroid products sold by RLC during the past year. The recall notice "has been initiated because testing has found that the product may be sub-potent (i.e. less than 90% of the labeled amount of liothyronine or levothyroxine)…To date, there have been no reports of adverse events related to the recall." Although this is a "voluntary" recall, RLC Labs specified to "immediately cease further distribution of the product and quarantine all quantities of unexpired product(s) within your possession. In addition, if you distributed product subject to this recall, please work to identify as soon as possible those customers to whom you delivered product(s) and notify them of this action."

It is understandable when a drug company manufactures an adulterated product that a recall is necessary. What is not understandable is how all thyroid products manufactured by RLC Labs were "found to be sub-potent." Does this mean that RLC Labs does not conduct quality control testing of individual lots to determine potency? It would make sense that a lot of thyroid hormone was not manufactured properly, but all lots were deemed questionable?

For the past decade there has been difficulty with thyroid hormone manufacturing, including proprietary Synthroid as well as Armour Thyroid. RLC Labs faced manufacturing difficulties a number of times resulting in no thyroid hormone availability. Why the lab was unable to manufacture thyroid hormone during these time periods has never been disclosed. In the past year RLC Labs managed to fulfill warehouse supplies in all potencies. Hence, it was quite shocking that the lab was obliged to recall its products now.

The putative reason for the recall was that inadequate thyroid hormone potency would result in failure to adequately treat thyroid deficiency based on the product's listed strength. However, it is unclear what quality control measures were employed during the manufacturing process. Beyond thyroid hormone recall, integrative doctors should question the integrity of the unregulated vitamin/nutraceutical supplement industry. The possibility that a supplement does not contain the stated quantity of nutrients/herbs is very concerning. Professional grade supplement manufacturers claim to do routine quality control; products manufactured for direct consumer sale may not be doing quality control. However, as the thyroid recall process suggests, quality control testing may be sub-par. It would be appropriate for supplement manufacturers to be forthcoming on their quality control testing and agreeable to share such reports with health professionals.

Fibromyalgia

Our theme and cover story this issue focuses on fibromyalgia. As Leslie Axelrod, ND, discusses, fibromyalgia diagnosis is undiagnosed in more than 20% of patients while 10% of patients are mistakenly diagnosed with the condition. While physicians and patients think of fibromyalgia primarily as a condition of pain and weakness, symptomatically patients experience cognitive dysfunction, malaise, insomnia, orthostatic hypotension, hormonal imbalance, and susceptibility to infection. Axelrod notes that standard testing for inflammation such as Sed Rate and C-reactive protein are frequently normal. Recent research showed that studying cytokine activity of white blood cells following protein induction of cell division (mitogen activation) was dramatically reduced in fibromyalgia patients compared to normal controls. Fibromyalgia patients frequently demonstrate elevated IgG antibodies to viruses, including Parvo19, HHV-6, HHV-7, EBV, and enterovirus as well as bacteria, including *H. pylori*. Not infrequently, patients concurrently have parasites, mold mycotoxin, candidiasis, and Lyme disease.

Alan McDaniel, MD, frames fibromyalgia as the body's inability to adapt to chronic stress. The hypothalamic-pituitary-adrenal axis (HPA-axis) upregulated by stress will initially overproduce cortisol but eventually depletes the adrenal reserve, leading to lower cortisol levels. Despite the fact that adrenal fatigue is a disputed diagnosis, reduced cortisol levels require nutrient and botanical support – if not cortisol replacement. Thyroid hormone testing generally limited to TSH frequently misses hypothyroidism. Although we generally think of insulin resistance's role in diabetes and metabolic syndrome, McDaniel notes that it is essential to the stress response seen in fibromyalgia. IgG-mediated food allergies are more easily detected once hormone and metabolic dysfunctioning is addressed. McDaniel emphasizes that DHEA, cortisol, and pregnenolone may all need to be implemented to correct HPA-axis dysfunction.

Carolyn McMakin, DC, makes the case that vagus nerve dysfunction plays a critical role in causing and perpetuating fibromyalgia. When we sustain an infection, injury, toxic exposure, or major stress, the vagus nerve maintains the integrity of our heart, lungs, digestive tract, immune and endocrine systems. Nevertheless, just like the brain, the vagus nerve will incur some level of dysfunction following trauma and chronic stress. McMakin proposes that treatment with microcurrent not only mitigates pain of fibromyalgia but also improves vagal nerve functioning.

Jacob Teitelbaum, MD, the author of our cover story, has devoted much of his medical career to understanding and treating fibromyalgia and chronic fatigue syndrome.

continued on page 8 ➤

Holistic Brain Support*

Lion's Mane Amyloban® - a unique formulation containing the active constituents of Lion's Mane mushroom, standardized for consistency and grounded in research.

- All-around brain and nerve support*
- Supports healthy cognitive function*
- Memory, mood, clarity, and focus support*
- Traditional tonic for digestion & overall health*

MUSHROOM WISDOM

Mushrooms As Nature Intended

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

Letter from the Publisher

➤ *continued from page 6*

Teitelbaum likens fibromyalgia treatment to playing a game of chess: "You can learn to play it in a few hours. And it takes a lifetime to master." Of course, chess has a winner and a loser; hopefully, the physician and patient are both winners.

Unlike the high-tech aspect of some integrative clinics, Teitelbaum's approach employs organized methodology readily available for practitioners and patients to use. He titles his treatment strategy, SHINE: Sleep and Sensitivities, Hormones and Hypotension, Infections, Nutritional Support, and Exercise. Teitelbaum has created a symptom questionnaire and treatment protocol available from him by emailing FatigueDoc@gmail.com. For the patient he has developed a questionnaire that sorts out the likely reasons for fatigue and pain and then delineates treatment recommendations from the SHINE Protocol: www.EnergyAnalysisProgram.com.

Teitelbaum is not unwilling to use pharmaceuticals in conjunction with nutrients, botanicals, and hormones. He has seen that patients respond to lower doses of multiple modalities, including drugs, rather than higher doses of fewer treatments. For sleep, his goal is eight hours of sleep and if that requires the use of drugs, then it requires the use of drugs. It is simply not acceptable to refuse prescribing drugs if all the natural remedies fail to achieve the refreshing level of sleep.

Of course, replacing and balancing hormones is critical for treatment of fibromyalgia. If the patient experiences orthostatic hypotension, increasing salt and water consumption, administering adrenal treatment, and compression stockings are recommended. Teitelbaum does treat infections but he does not make it his business to necessarily do numerous lab studies. Candidiasis diagnosis and treatment is determined by symptom history. Individuals with chronic sinusitis and/or irritable bowel syndrome require botanical and pharmaceutical treatment. He notes that patients with Lyme disease treated with antibiotics will require treatment for yeast. Patients who claim an allergy to an antibiotic should be reconsidered as having had a Herxheimer reaction rather than a true allergy.

Nutrient and nutraceutical support is essential for recovery. Teitelbaum offers recommendations of what has worked best with his patients. Special strategies are suggested for hypersensitivity and pain support. He reminds us mind/body/spirit approaches are also key to good health!

Jonathan Collin, MD
Publisher

Shorts

briefed by Jule Klotter
jule@townsendletter.com

Electrohypersensitivity Diagnosis and Treatment

In March 2020, Dominique Belpomme and Philippe Irigaray, who are affiliated with the European Cancer and Environment Research Institute, published a review article about electrohypersensitivity. The article is based on a registered database that they have maintained since 2009, which contains clinical information on over 2000 patients with electrohypersensitivity (EHS) and multiple chemical sensitivity (MCS). The World Health Organization's 2005 fact sheet 296, "Electromagnetic fields and public health," says that "EHS is characterized by a variety of non-specific symptoms…. [and] resembles MCS, another disorder associated with low-level environmental exposure to chemicals…." WHO does not recognize EHS as an illness that can be diagnosed and treated medically. Belpomme and Irigaray want WHO to add EHS to the international classification of diseases (ICD).

The review authors conducted a prospective study, using questionnaire-based interviews and clinical physical examinations of the first 727 consecutive cases included in the database: 521 (71.7%) self-reported EHS only; 52 (7.1%) reported MCS only; and 154 (21.2%) reported EHS and MCS. Two-thirds of the EHS-only and MCS-only groups were women, and women accounted for three-fourths of the combine EHS/MCS group.

Like MCS, those with EHS report diverse symptoms – many of which are neurological – including the following: headache (88%), dysesthesia (pain, itchy, or burning sensations; 82%), ear heat/otalgia (70%), dizziness (70%), tinnitus (60%), concentration/attention deficiency (76%), immediate memory loss (70%), fatigue (88%), insomnia (74%), and tendency for depression (60%). The EHS patients report that the symptoms arise or increase with exposure to electromagnetic field sources. While the incidence of some clinical symptoms (eg, headache, balance disorder, concentration/attention deficiency) was statistically similar in those with EHS only and MCS only, other symptoms appeared more often in those with EHS, including dysesthesia, ear heat/otalgia, tinnitus, hyperacusis (sound sensitivity), dizziness, immediate memory loss, insomnia, and fatigue. Patients with both EHS and MCS tended to be more ill. The EHS/MCS group also was more likely to be inflicted with skin lesions (45%), found mostly on the hands – "particularly on the hand which held the mobile phone."

Belpomme and Irigaray sought biomarkers that characterize EHS and/or MCS. They found increased histamine in both EHS and MCS patients (30-40%), "suggesting a low-grade inflammatory process is involved…." Also, about twenty percent of the 727 patients had autoantibodies against O-myelin. About 80% of EHS patients had increased levels of one or more of the measured oxidative/nitrosative stress-related biomarkers: thiobarbituric acid reactive substances (TBARS), oxidized glutathione, and nitrotyrosine. Patients with EHS also had abnormal neurotransmitter profiles.

In addition to blood and urine biomarkers, the doctors used radiological tests to find clues about these conditions. They report that brain imagery, including CT scans, MRIs, and angioscans, "are usually normal" in both EHS and MCS patients. Transcranial Doppler ultrasound, however, shows decreases in mean pulsatility index in cerebral arteries, particularly in those with both EHS and MCS, resulting in decreased blood flow velocity. Ultrasonic cerebral tomosphygmography (UCTS) shows that people with EHS and/or MCS tend to have decreased capillary blood flow to the limbic system and the thalamus in the brain: "Although these abnormalities are not specific, since they may be similar to those found in Alzheimer's disease and other neurodegenerative disorders, we recently confirmed that UCTS could presently be one of the most accurate imaging techniques to be used to diagnose EHS and/or MCS and to follow objectively treated patients."

Because EHS and MCS symptoms are diverse and non-specific, Belpomme and Irigaray suggest ruling out known pathologies that could account for the symptoms first. A repeatable association between EMF exposure and changes in clinical symptoms, as well as the presence of chemical sensitivities (which is associated with EMF), indicate the possibility of electrohypersensitivity. Increased histamine (in absence of allergy) and/or increased oxidative/nitrosative stress-related biomarkers are found in about 70% of patients with EHS. By adding ultrasonic imaging, Belpomme and Irigaray were reportedly able "to objectively diagnose EHS in about 90% of EHS self-reported patients."

The authors report that many EHS patients have "a profound deficit in vitamins and trace minerals, especially in vitamin D and zinc, which should be corrected." They have also used fermented papaya preparation and *Ginkgo biloba* to restore brain pulsatility. Treatment also includes glutathione, antioxidants, anti-histaminics (if histamine levels are high), and anti-nitrosative medications. Avoidance of electromagnetic radiation and chemical stressors

➤

➤

and use of protective measures are also important. In the authors' experience, symptoms may decrease and even disappear with treatment and protection, but "hypersensitivity to EMF and/or MCS-related chemical sensitivity never disappears…EHS and MCS appear to be associated with some irreversible neurological pathological state, requiring strong and persistent prevention."

Electrohypersensitivity affects 3% to 5% of the population in many countries, according to current estimates. As environmental exposure to man-made electromagnetic radiation continues to increase, the incidence is likely to grow. Belpomme and Irigaray organized an international scientific consensus meeting on EHS and MCS in 2015 (Brussels) during which "scientists unanimously asked WHO to urgently assume its responsibilities, by classifying EHS and MCS as separate codes in the ICD, so as to increase scientific awareness of these two pathological entities in the medical community and the general public, and to foster research…." WHO has not yet responded.

Belpomme D, Irigaray P. Electrohypersensitivity as a Newly Identified and Characterized Neurologic Pathological Disorder How to Diagnose, Treat, and Prevent It. *Int J Mol Sci.* 2020;21:1915.

Altered Microbiome and Fibromyalgia

Can the composition of the GI microbiome become an objective diagnostic measure for fibromyalgia? A group of Canadian researchers conducted a controlled study that compared the microbiomes of 77 women with fibromyalgia (FM) to 79 control volunteers.

The control group consisted of first-degree female relatives of the patients (genetic control; n=11), male and female household members of the patients (environmental controls; n=20), and unrelated healthy women (n=48). Dietary analysis found no significant differences between the FM group and controls.

Using 16S rRNA and metagenome methods, the researchers validated the presence of 196 species in 156 stool samples from the participants. (Another 80 species were not in the database used to make identification.) Species diversity between the FM group and control groups differed nonsignificantly, but there was a significant difference in abundance: "…species found in higher abundance in FM patients clustered together, whereas those found in higher abundance in controls clustered separately." Most notably, the women with FM had less butyrate metabolism-related bacteria, such as *F. prausnitzii* and *B. uniformis,* but an increase in others (ie, *F. plautii*, *I butyriciproducens*). The researchers also found an association between the abundance of several organism groups and FM-related symptoms (ie, pain intensity and distribution, fatigue, sleep disturbances, and cognitive issues).

After identifying composition differences, the Canadians used machine-learning algorithms to define the types of organisms most associated with FM and used this analysis to determine which patients were controls and which were diagnosed with FM. Using microbiome composition alone, they were able to differentiate patients from controls (receiver operating characteristic area under the curve 87.8%). The authors say, "…these results suggest that the composition of the microbiome could be indicative of the diagnosis of FM."

More research, of course, is needed. This study population was small and consisted primarily of Caucasians; GI microbiome

Townsend Letter
ISSN 1940-5434

Subscriptions • Editorial • Advertising

360/385-6021
24 Hr. Fax – 360/385-0699

911 Tyler Street
Pt. Townsend, Washington 98368-6541 USA
http://www.townsendletter.com | info@townsendletter.com

Editor-in-Chief	Jonathan Collin, MD
Publisher	Jonathan Collin, MD
Editor	Jule Klotter
Contributing Medical Editor	Alan Gaby, MD
Managing Editor	Barbara Smith
Circulation Manager	Joy Reuther-Costa
Managing Assistants	Julie Reuther; Jill Tomasi
Advertising Projects & Accounts	Barbara Smith Joy Reuther-Costa Jonathan Collin

Columnists & Writers
Majid Ali, MD
Eleonore Blaurock-Busch, PhD
Jim Cross, ND, LAc
Nancy Faass, MSW, MPH
Peter A. Fields, MD, DC
Alan R. Gaby, MD
Michael Gerber, MD, HMD
Robert Goldman, MD, PhD, DO, FAASP
Ira Goodman, MD
Tori Hudson, ND
Ronald Klatz, MD, DO
Ingrid Kohlstadt, MD, MPH, FACN
Sarah A. LoBisco, ND
Marianne Marchese, ND
Alan B. McDaniel, MD
Ralph W. Moss, PhD
Judyth Reichenberg-Ullman, ND
Jacob Schor, ND, FABNO
Pamela Smith, MD
Jacob Teitelbaum, MD
Jade Teta, ND
Keoni Teta, ND
John Trowbridge, MD
Robert Ullman, ND
Rose Marie Williams, MA
Elaine Zablocki

Contributing Writers
Katherine Duff
Bob Frost
Gary Null, PhD

Layout & Design
Barbara Smith/Sign Me Up! Inc.

Design Team
Jonathan Collin
Joy Reuther-Costa
Barbara Smith

Cover Photo Credit
Robin Bourne Photography

Printing
Dartmouth Printing Company

Website Design & Maintenance
Joy Reuther-Costa

Published by
Townsend Letter for Doctors & Patients, Inc.
Jonathan Collin, President
Deborah Nissen-Collin, Vice-President

Disclosure: The *Townsend Letter* publishes information about alternative medicine written by researchers, health practitioners, and patients. As a forum for the entire alternative medicine community, we present information discussing a wide variety of alternative and integrative medicine practices. In addition to publishing original research and literature abstracts and reviews, we encourage case studies and anecdotal reports. Detailed anecdotal reports are not viewed as proof but as possibilities that need further investigation. All authors are requested to submit their reports to other professionals for review.

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.

composition varies with geographic location, diet, lifestyle, and ethnicity. But the study does open the possibility of an objective way to diagnosis fibromyalgia. The authors note that this study was not designed to show a cause-effect relationship between altered microbiome and fibromyalgia.

Minerbi A, et al. Altered microbiome composition in individuals with fibromyalgia. *Pain.* November 2019;160(11):2589-2602.

Fragrances and Chemical Sensitivity

Australian Anne Steinemann, an internationally recognized authority on indoor air quality and fragranced consumer product emissions, recently looked at the incidence of chemical sensitivity in four countries. Chemical sensitivity usually arises from exposure to commonly used petrochemical products and pollutants (eg, pesticides, building materials, solvents, new carpet and paint, and consumer products). Steinemann used population samples that mirrored the age, gender, and region of the general population: United States (US; n=1137), Australia (AU; n=1098), Sweden (SE; n=1100), and the United Kingdom (UK; n=1100). Her epidemiological study also looked at chemical sensitivity's co-prevalence with fragrance sensitivity (health problems from fragranced products), medically diagnosed multiple chemical sensitivities (MCS), asthma/asthma-like conditions, and autism/autism spectrum disorders.

Chemical sensitivity affects 19.9% of the general population across the four countries (US 25.9%, AU 18.9%, SE 16.3%, UK 18.5%). More people in the general population reported sensitivity to fragrances: (US 34.7%, AU 33.0%, SE 27.8%, UK 33.1%). Not unexpectedly, the incidence of fragrance sensitivity is even higher among people with chemical sensitivity: (US 81.0%, AU 82.6%, SE 77.7%, UK 86.8%). In addition, the incidences of asthma/asthma-like conditions and of autism spectrum disorders were higher among those with chemical sensitivity.

Steinemann says that fragranced consumer products – such as air fresheners/deodorizers, laundry products, cleaning products, personal care products (eg, soap, hair products), and perfumes – "can be a primary trigger of health problems." Fragrances are particularly problematic for people with chemical sensitivity and can trigger several symptoms, including respiratory problems (50.2%), mucosal symptoms (39.4%), migraine headaches (36.9%), skin problems (29.9%), asthma attacks (25.2%), and neurological problems (17.7%). Nine percent of the general population reported losing workdays or a job in the previous year because of sickness from fragranced product exposure in the workplace.

The most highly rated treatment for chemical sensitivity, according to a 2003 survey of 917 people with self-reported multiple chemical sensitivity, is avoidance; 56.5% of the 875 people who tried it found chemical avoidance very helpful and 38.0% found it somewhat helpful. Yet, avoiding fragrances and troublesome chemicals is challenging. As Steinemann explains in an article on fragrance-free policies, no country monitors the health effects of the 4000 documented fragrance ingredients. Most product labels do not report fragrance ingredients. Even "fragrance-free" products may not be devoid of fragrance chemicals; "products called 'unscented' may in fact be a fragranced product with the addition of a masking fragrance to cover the scent." Steinemann also reports that products reportedly "green," "natural," "organic," or made with essential oils also emit many of the same potentially hazardous chemicals as regular fragranced products. One option for finding fragrance-free products is to use the US Environmental Protection Agency's search engine (https://www.epa.gov/saferchoice/products).

Gibson PR, Elms A N-M, Ruding LA. Perceived Treatment Efficacy for Conventional and Alternative Therapies Reported by Persons with Multiple Chemical Sensitivity. *Environmental Health Perspectives.* September 2003; 111(12);1498-1504.

Steinemann a. Ten questions concerning fragrance-free policies and indoor environments. *Building and Environment.* 2019;159

Steinemann A. International prevalences of chemical sensitivity, co-prevalences with asthma and autism, and effects from fragranced consumer products. *Air Quality, Atmosphere & Health.* 2019;12:519-527.

Medicinal Cannabis and Opioid Use

Can the use of medicinal cannabis (MC) by patients with chronic pain decrease their use of opioids? Several studies based on patient surveys and/or interviews indicate that people are using MC, when available, as an alternative or as a complement to pain medication that allows them to use fewer addictive opioids – or taper off the drugs altogether. Patients report that medical cannabis acts more quickly, has fewer side effects than opioid medications, and increases their quality of life. As Bia Carlini, PhD, explained in a 2018 article, pre-clinical research studies have verified that exogenous cannabinoids (like those in the marijuana plant) provide pain relief by binding to the body's endocannabinoid receptors. Randomized clinical trials have shown that cannabinoid agents "are effective analgesics for chronic pain," but most of the studies involved pharmaceutical products like Nabiximols (a botanical extract not available in the US) or Nabilone, a synthetic THC. These studies cannot verify that medical marijuana use, in which the plant is usually smoked or consumed, has the same effects.

Although the US government restricts the use of marijuana, which is listed as a Schedule 1 drug (no medicinal value and high potential for abuse), some states now permit its medicinal use. As a result, real-world evidence is showing that MC use appears to be useful in treating pain with less adverse effects. For example, Medicare prescriptions for pain have decreased in states with legal MC, and a 2014 *JAMA Internal Medicine* study showed that states with legal MC had significantly lower death rates from opioid overdose (1999-2010) than those that did not. Still, at this point, no randomized controlled trials have compared the effectiveness of opioids to MC in relieving pain.

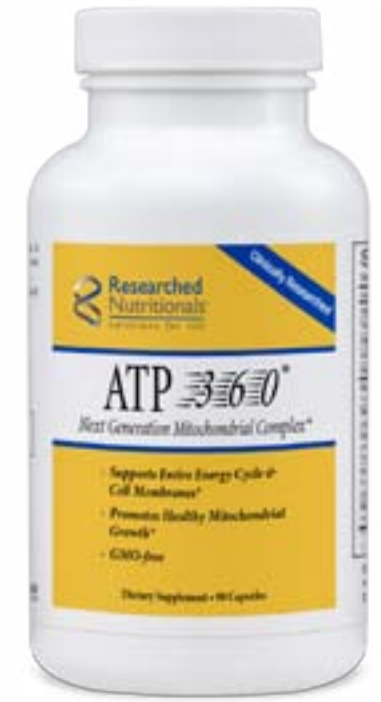
The federal government has not supported MC research until recently. The National Institutes of Health has awarded a grant to researchers at Albert Einstein College of Medicine and Montefiore Health System for a prospective cohort study that will follow 250 patients with recent MC certification, severe chronic pain, and opioid use for 18 months (NCT03268551). Its estimated date of completion is June 30, 2022. States that permit MC also are conducting research. Using tax money from marijuana sales, the Colorado Public Health Department has funded a double-blind crossover study with 100 participants that assesses how cannabis compares to oxycodone and to a placebo in reducing neck and back pain (NCT 02892591). This study is scheduled to conclude in January 2021. Studies like these may provide more evidence that medical cannabis can be as effective and less harmful than opioid drugs in treating chronic pain.

Carlini B. Role of Medicinal Cannabis as Substitute for Opioids in Control of Chronic Pain: Separating Popular Myth from Science and Medicine. University of Washington Alcohol and Drug Abuse Institute. February 2018.

◆

Invigorate *Your* Mitochondria

ATP 360™ is a complete mitochondrial complex, clinically researched to provide targeted support for…



Mitochondrial Function

- Proprietary phospholipid blend promotes a healthy membrane*
- Antioxidants to support against oxidative stress*
- Healthy membrane is essential for vigorous ATP production*

Krebs Cycle

- Key nutrients to optimize Krebs energy production*

Mitogenesis & Membrane Potential

- Provides nutrients for optimizing the electron transport chain*
- PQQ to promote healthy mitochondrial mass*
- Promote healthy mitochondrial formation*

Visit www.ResearchedNutritionals.com/atp-360 for a full list of ingredients

Researched Nutritionals
solutions for life

Tel: 800.755.3402 • Fax: 805.693.1806 • CustomerService@ResearchedNutritionals.com
www.ResearchedNutritionals.com | Available only through healthcare professionals.

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

In this Issue

November 2020 | #448

ON THE COVER: Jacob and Laurie Teitelbaum (pg. 16); How Chronic Stress Produces Pain (pgs. 31, 54); Testing for Fibromyalgia (pgs. 9, 28); Nutrients for Immune Support (pg. 61); Stacking the Deck Against Bioidentical Hormones (pg. 66)

A Medical Maverick
Dr. Nicholas Gonzalez
coming in our December issue

ImmunMax™

PEPTIDE IMMUNOTHERAPY

Protection for the Whole Family

SECOND WAVE

WINTER ILLS & CHILLS

INFLUENZA SEASON

SAD SYNDROME

BACK-TO SCHOOL

STRESS

- Maintain a Balanced Immune System
- Promote Healthy Cytokine Production

(Available in Powder, Capsules or Spray)

For more information, call 480.553.7768
or email us at Info@ProSovLabs.com

Sovereign Laboratories

Foundational Nutrition for Immune and Gut Health

The Great Plains Laboratory, Inc

GPL Academy

Practitioner Workshops

CME AVAILABLE!

DAY 1 WORKSHOP
ORGANIC ACIDS TESTING

- How to use this comprehensive test (76 markers) in your practice to help your patients
- How the OAT helps you discover underlying causes of many chronic conditions
- What kinds of treatments have been most effective

DAY 2 WORKSHOP
ENVIRONMENTAL TOXIN TESTING

- About the epidemic of environmental toxin exposure
- About common environmental pollutants tested by our GPL-TOX Profile (173 markers)
- How these chemicals affect our health and what steps can be taken to help detoxify the body
- About multiple types of mold mycotoxins tested for in our new MycoTOX Profile
- About the chronic health conditions mycotoxin exposure can cause and treatment options

Live Online!
January 29-30, 2021

USE PROMO CODE **TOWN10** FOR 10% OFF!

Practitioners attending all three days receive one **free** Organic Acids Test!

Evan Brand, CFMP, FNTP

Suzanne Gazda, MD

Shanhong Lu, MD, PhD

William Shaw, PhD

Kurt Woeller, DO

For all workshop details and to register, please visit **www.GPLWorkshops.com**

The Great Plains Laboratory, Inc.

CME AVAILABLE!
Learn more at GPLWorkshops.com
913.341.8949 | marketing@gpl4u.com

On the cover

Effective Treatment of CFS and Fibromyalgia *Can* Be Easy

by Jacob Teitelbaum, MD

Treating chronic fatigue syndrome and fibromyalgia (CFS/FMS) is a bit like playing chess. You can learn to play it in a few hours. And it takes a lifetime to master. Unfortunately, most physicians aren't even at checkers yet – not even trained to treat day-to-day fatigue, let alone these devastating syndromes. Unless they are holistic.

In this article, we will give an overview and free tools that will dramatically simplify treatment. I will also organize how to approach the illness and discuss my most recently completed study of a simple treatment, called Recovery Factors (www.recoveryfactors.com) that resulted in 60% of people improving, with an average 69% improvement in energy and quality of life.

For those who would like a very in-depth and organized understanding of the dizzying array of processes going on in these conditions, and how to treat them, the fourth edition of my book *From Fatigued to Fantastic!* (Penguin; September 2020) just came out. And it is, well, fantastic! Here is a quick overview.

Free Treatment Tools Make It Easy

Gathering and assessing the information can take you hours. Or about 10 minutes. For those who prefer the latter, I have created several free tools:

1. We have an extensive questionnaire and treatment protocol, both of which are organized by condition (e.g. – sleep, thyroid, etc.). Simply scanning the questionnaire to see which areas have a lot of check offs can tell you what key issues are going on. Meanwhile, instead of (illegibly) writing out the same directions over and over and over, you can simply check off the recommended treatments on the treatment checklist. This is available in a free word document, so you can tailor it to your practice. Simply email me at FatigueDoc@gmail.com and ask for the free treatment tools, and I will be happy to send them to you.
2. Want to make it even easier? I hold the US patent for a computerized physician. I designed this to make effective treatment available for everyone. We have modified this into an Energy Analysis Program. People with any degree of fatigue can simply go to www.EnergyAnalysisProgram.com and fill out the free quiz (including optionally adding their pertinent lab test results). They will get a printout of what their likely energy drains are, and a detailed management program applying the SHINE Protocol. Simply have them bring you the report.

This is all part of our making effective treatment available for everyone!

Organizing Your Treatment Approach

There are literally over 100 different factors contributing to CFS/FMS. This can easily make it overwhelming if you don't organize your approach. The key is to figure out which mix is present in each individual. Begin by using the SHINE algorithm:

- **S** – Sleep and Sensitivities
- **H** – Hormones and Hypotension (orthostatic intolerance)
- **I** – Infections
- **N** – Nutritional Support
- **E** – Exercise as able (low key, to prevent excessive deconditioning)

Then treat the mind/body/spirit components and reset the circuit breakers in their limbic system.

S – Addressing Sleep

CFS/FMS represents an energy crisis where people have essentially tripped a circuit breaker in their brain, called the hypothalamus. The circuit controls sleep, along with hormonal and autonomic function. Severe insomnia is the norm. So aggressive support to optimize sleep is needed. Here are a few of many helpful treatments.

I give people whatever combination of the below is needed to get seven to eight hours of solid sleep a night. For medications, people do far better with a low dose of several of these in combination, than a high dose of just one.

Begin with natural remedies:

1. Hemp Oil caps (EuroMedica), three to five capsules at bedtime work wonderfully for many resistant cases, helping sleep and pain. I find the whole hemp oil to be much preferable to simply CBD for both sleep and pain, as it has at least 10 synergistically active cannabinoids.
2. Revitalizing Sleep Formula (Enzymatic Therapy), two to four at bedtime. A mix of six herbs and nutrients
3. Terrific ZZZZ (EuroMedica), one to two at bedtime. A mix of essential oils.
4. Melatonin, 5 mg, Dual Spectrum (Nature's Bounty)

Then I add low doses of several medications as needed to get eight hours sleep without hangover. Low doses of several things work better than a high dose of one. I begin with:

1. Zolpidem, 5-10 mg. It has its issues but is the most effective treatment I've found for initiating sleep in this population.
2. Trazodone, 25-50 mg
3. Gabapentin, 100-600 mg
4. Cyclobenzaprine, 2.5-5 mg

All of the above can be combined if needed to get 8 hours restorative sleep.

H – Hormones and Hypotension (Orthostatic Intolerance)

As the hypothalamic pituitary axis controls most of our hormonal system, and the hypothalamus also controls autonomic function, hormones and orthostatic intolerance need to be addressed. The key points are summarized below.

Hormones. Optimizing is essential – even if the blood tests are normal. In fact, the majority of people who benefit from hormonal support in general are in the "normal range." It helps to understand that the normal ranges, in most cases, are simply based on two standard deviations.

continued on page 19 ➤

Fast relief for **DRY MOUTH**

Safe. Effective. Convenient.

Improved Formula with **XYLITOL**

- Naturally increases saliva production
- Fresh citrus taste
- Helps Prevent Tooth Decay
- No interaction with medications
- Safe for diabetics
- Available in convenient flip-top container

Available from major distributors such as *Threshold, Emerson Ecologics, McKesson Corp., and Super Natural*.

Ingredients:
• Xylitol • Citric Acid • Apple Acid • Sodium Citrate Dihydrate
• Sodium Carboxy Methyl Cellulose • Dibasic Calcium Phosphate
• Silica Colloidal • Magnesium Stearate • Stearate Acid.

Scandinavian Formulas

Sellersville, PA 18960 • P: 215-453-2507 800-688-2276 • F: 215-257-9781 • scandinavianformulas.com

➤ *continued from page 17*

This means they check 100 healthy people, and the 95% in the middle are defined as normal. To put this in perspective, the normal range for shoe sizes would be 6 – 13. This does not mean that any shoe size in that range fits everyone. Diagnosis is based on symptoms predominantly, and only secondarily on lab testing. So here are the symptoms to look for:

1. Thyroid. Tired, achy, weight gain, constipation, cold intolerance, or infertility. I consider a trial of desiccated thyroid if the person has even two of these. *The dose is adjusted to what feels best to the person*. At optimal dosing, most people find the TSH will be low (because of the hypothalamic/pituitary dysfunction). I do follow the free T4, making sure that it is not in the top 20th percentile of the normal range or higher. It is not uncommon for the free T4 to be low on the optimal dose of desiccated thyroid, because it may be suppressed by the T3 component. A subset of people will need high doses of triiodothyronine (T3) instead.
2. Adrenal. Simply asking the person if they get irritable when hungry ("hangry") or if they have symptoms of low blood sugar will indicate whether adrenal support is needed. Low blood pressure, orthostatic intolerance (see below), and frequent or prolonged respiratory infections and sore throats are also suggestive.

   In most people, except women with elevated DHEA-S or testosterone, where I suspect polycystic ovarian syndrome (PCOS), I treat with Adrenaplex (by EuroMedica). If needed, I add low doses of hydrocortisone (5 – 12.5 mg a day split between morning and lunchtime dosing). Doses up to 20 mg a day tend to be quite safe for most people. For more information, I recommend a book called *Safe Uses of Cortisone* by Prof. William Jefferies.
3. Reproductive hormones. In women over 40 whose fibromyalgia symptoms are worse around their menses, I generally recommend compounded BiEst (4:1 ratio estriol to estradiol) 2.5 mg plus progesterone 30 mg and testosterone 1.5 mg vaginally. In menopausal women, an FSH or LH over 70, or onset of symptoms around perimenopause, leave me to consider a therapeutic trial.

Hypotension/Orthostatic Intolerance (POTS/NMH). If one thinks about it, humans are largely a big bag of water.

continued on page 21 ➤

RAISE CORE TEMPERATURE!

Relax® Far Infrared Sauna

"An infrared sauna at 140 degrees for 30 minutes, that REALLY TAKES CARE of viruses in the body, including the Corona virus!" ~ Dr. Gary Null

"No Sweat? Know Sweat!" Author Recommends Relax Sauna

The Relax Sauna is Highly recommended by thousands of Medical professionals, doctors and therapists. Dr. Bill Akpinar, Best Cancer Doctor NYC, says. "The Relax Sauna creates more Chi than any other Sauna."

WHY IS THE RELAX SAUNA PREFERRED BY MEDICAL PROFESSIONALS?

for unbiased reports on the Relax Sauna comparing to other saunas, go to: relaxsaunas.com/superior

- Warms instantly! 20 seconds versus 30 or more minutes to heat up.
- Short, yet sufficient and effective sessions.
- Uses less electricity and takes less time with great results.
- Fast acting! Relief of symptoms happen quickly!
- You can breathe! Head outside the tent makes a huge difference in comfort and endurance.
- Effective even with clothes on for 5-10 minute treatments!
- Amazing, deep river sweats in 15-20 minutes or even less! (not 30-60 minutes or not at all!)
- It is safe, simple, strong, pure, portable, medical grade and very affordable!

EFFECTIVE, SAFE, DURABLE & CONVENIENT TO USE

Very low EMF with a patented technology with ceramic semi-conductors

Many environmental doctors working with EMF-sensitive or multi-chemical-sensitive people use the Relax Sauna in their homes and clinics and highly recommend it to their patients.

There is NO EMF above the Knees in the Relax Sauna. The EMF by the radiators is low in EMF in comparison to the 21 most common household appliances. The microwave energies from your cell phone and wi-fi is about 100 times more dangerous than the EMF of any household appliance or sauna. One well respected Doctor, one of the foremost authorities on the dangers of EMF, confirms this, and is working with us in helping to promote the Relax Sauna.

Raving Relax Sauna Users: **EXCELLENT & HIGHLY EFFECTIVE FOR TREATING FIBROMYALGIA**

*"I bought a Relax Sauna 2 years ago. ALL the muscle aches and pains and everything that I had from Fibromyalgia - IF I USE IT EVERY OTHER DAY - there are NONE. I am also hyperthyroid, at 96 * temperature. I am always at 98.6 when I get out of the Relax Sauna." Humorously, she adds: "If the motor ever died, I would eat peanut butter for a month just to but another one. It is THAT AMAZING. I come out with ENERGY." - No Name*

"I have suffered from fibromyalgia for the last 10 years. I did 15 minutes in the Relax Sauna and it was wonderful because the pain went away. I am so relieved. Yes, and I'm very happy!" - Amelia S.

"A friend of mine recommended I try the sauna for my fibromyalgia. i did not believe this would actually help but after 7-8 minutes my My pain level was about an 8, and now it is a 0 or 1. the pain is pretty much gone!" - -Amanda

Relax SAUNA
THE SUPERIOR SAUNA

phil@relaxsaunas.com CALL 626.200.8454 relaxsaunas.com/townsend

See Over 800 Testimonials: relaxsaunas.com/youtube

Go to: relaxsaunas.com and use code town11 to get $125 OFF the cost of a Relax Sauna until NOV 30, 2020

➤ *continued from page 19*

When we stand up, gravity routinely sends our blood down into our legs. If the autonomic system is functioning poorly, circulation to the brain and muscles suffers. Research shows this to be routinely occurring in CFS/FMS.

I do not bother with tilt table testing. For a one minute orthostatic intolerance screening quiz (validated in the Mayo Clinic journal), a quick 10-minute pulse test, and a summary of helpful treatments, email me at FatigueDoc@gmail.com. If you requested the free treatment tools (see Sidebar, page 16), this will be included.

I begin with adrenal support, increasing salt and water intake, using medium pressure (20-30 mm) compression stockings when up and around, and midodrine (ProAmatine). Numerous other treatments can be helpful.

Infections

Immune dysfunction and opportunistic infections are a routine part of this illness.

I do not do much immune system testing as the results do not impact my treatment choices. Rather, these are made clinically based on symptoms and history. Here are the key infections that I address:

1. *Candida.* I do no testing for this. The free questionnaire that I mentioned above includes a simple screening quiz that I find to be more helpful. Especially helpful? The majority of people who have either chronic sinusitis/nasal congestion or symptoms of irritable bowel syndrome find that these resolve with candida treatment. Along with many other fibromyalgia symptoms. Treatment can be done with Caprylex (Douglas Labs) and/or Lufeneron (www.shop4lufe.com), a good probiotic, plus Diflucan (fluconazole) 200 mg daily for six to eight weeks. In addition, I routinely include the sinusitis nose spray (ITC Compounding Pharmacy 888-349-5453) one spray in each nostril twice a day for one to two months. If I suspect mold toxins (see below) I give the sinusitis spray for six months.

   You'll be amazed at how many people find both their irritable bowel syndrome and sinusitis resolve with this approach.
2. *Antibiotic – sensitive infections.* Lyme has been discussed at length elsewhere, so I will not include that discussion here. But I will note that simply giving antibiotics results in initial improvement, followed by worsening as the candida is aggravated from the antibiotics. Although the antibiotics can be essential, the person must also be covered for candida during the antibiotic treatment to prevent overgrowth. And the rest of the SHINE Protocol is essential to optimizing recovery.

   Numerous other antibiotic-sensitive infections may be present, but I find blood testing to not be reliable and prefer to treat based on symptoms and clinical response to the antibiotic. In any patient who gives a history of their fibromyalgia improving (even transiently) on antibiotics, I routinely will give the antibiotic that helped for extended periods. Also suspect antibiotic-sensitive infections (there is a wide array) in those who are allergic to several different antibiotics and nothing else. These are unlikely to be allergies but rather represent Herxheimer reactions. Also consider antibiotic trials for those with chronic lung congestion, elevated white blood cell counts, or chronic scalp scabs.
3. *Small Intestinal Bacterial Overgrowth* (SIBO) is also common. Suspect when the person has a lot of foul-smelling gas. Ask them if their gas smells like the "silent but deadlies" most kids in grade school are familiar with. This reflects increased sulfur in the gas from the SIBO. I treat with Ultra MFP Forte (Douglas Labs) for one month, repeating as needed. Optimizing thyroid function is critical to preventing recurrence. If symptoms are severe, I consider the antibiotic rifaximin 550 mg three times a day for 10 days. But rifaximin is now obscenely expensive. ➤

New Research Offers Dramatic Hope

I recently submitted a study using a serum polypeptide extract called **Recovery Factors** (www.RecoveryFactors.com). The results were remarkable, and usually seen within one month (one bottle).

In the 60.5% of subjects who improved, significant improvement was seen in all categories:

1. 69.4% average increase in energy ($p<.001$)
2. 69.2% average increase in overall well-being ($p<.001$)
3. 53.8% average improvement in sleep ($p<.001$)
4. 60.5% average improvement in mental clarity ($p<.001$)
5. 37.9% average decrease in pain ($p<.013$)
6. 57.5% average composite improvement in the above five domains ($p<.001$)
7. 34.8% average decrease in anxiety ($p<.001$)
8. 54.6% average improvement in digestive symptoms ($p<.001$)
9. FIQR decreased from 59.2 to 39.3. (33.5%) ($p<.001$)

In the six people who also had pre- and post-IgG antibody levels, total IgG increased by 13.8% on average, with similar improvements seen in the IgG 1-4 subsets.

I have people follow the dosing instructions on the website. For a copy of the study report that I submitted for publication, you can email me at FatigueDoc@gmail.com. A second study with over 200 people is currently underway.

➤

4. *Viral infections.* Suspect this if the person's CFS/FMS began with a viral infection or they have chronic flulike feelings. I will check HSV-1, CMV, HHV-6, and EBV IgG (not IgM) antibodies if I am suspicious. These are only minimally helpful, however, as over 95% of the healthy population will also show positive on these. But for HSV-1, CMV, and HHV-6, I have an increased index of suspicion if the IgG is greater than four or greater than 1: 320.

CFS and fibromyalgia can now be very effectively treated!

Generally, if I am suspicious of chronic viral reactivation, I will begin with Famvir 500 to 750 mg TID plus Celebrex 200 mg BID for six months. It takes four months to see if it will start helping. In rare cases, I will go with Valcyte if the Famvir is ineffective and the CMV or HHV-6 antibodies are elevated. If the illness began with marked GI symptoms, I consider a trial of Equilibrant (Equilibrenthealth.com) for possible enterovirus. Directions for use are on their website. A small percentage of very refractory cases have responded to this.

5. *Parasites.* If significant gut symptoms persist despite candida and/or SIBO, or travel history is suggestive, I will consider parasite testing at Genova, DiagnosTechs, and/or the Parasitology Center. In CFS/FMS, all parasites should be treated.

Nutritional Support

I start everyone on the following:

1. Energy Revitalization System vitamin powder (Enzymatic Therapy)
2. Smart Energy System (www.EndFatigue.com). This is a mix of ribose, ashwagandha, rhodiola, schisandra, green tea extract, and licorice. The effect on energy can be remarkable.
3. CoQ10, 100 mg (I use the orange chewable from EuroMedica – one tablet gives the absorption of 800 mg coenzyme Q 10)
4. EurOmega-3 (EuroMedica) one daily. Equal to seven normal fish oil pills.

The above supplies the equivalent of 80 pills in one drink and four capsules/tablets daily. While giving outstanding and overall comprehensive nutritional support. It is very important to keep the pulldown count when possible. I find this mix helpful for everyone who wants to increase energy and vitality.

Also add nutritional support with the Recovery Factors (www.recoveryfactors.com), having them follow the dosing instructions on the website. One bottle will tell them if it will help (see Sidebar, page 21).

Exercise

Simply have the person walk to the degree where they feel good tired after and better the next day. This is to prevent deconditioning. Simply giving an overaggressive exercise program is likely to make the person worse. Have them walk so they feel good tired after and better the next day. If they feel wiped out the next day, they did too much. After eight weeks on the protocol above, their ability to condition will usually markedly increase.

Mind-Body Spirit

This is covered in depth in *From Fatigued to Fantastic*. But here is the very short version:

1. Teach people to say no to things that *feel* bad – with no justification needed. This is important for authenticity and protecting one's energy boundaries.
2. Reset the "tripped circuit breakers" in the limbic system by doing the Dynamic Neural Retraining System (retrainingthebrain.com). This DVD training series is remarkably effective at helping the overall process without any pills. Benefits are usually seen after about 8 to 10 weeks of one hour a day. They can be extraordinary.
3. Release emotional trauma with techniques such as the Emotional Freedom Technique.
4. Release muscle memory of trauma by using the trembling technique described in Peter Levine's simple book *Waking the Tiger*.

Sensitive to Everything?

If sensitivity is routinely to the same foods, using the Nambudripad Allergy Elimination Technique (www.NAET.com) can be very helpful.

If they have sensitivity reactions to multiple different things, but what they react to varies from day-to-day, suspect *mast cell activation.* The regimen below can help:

1. Quercetin (500-1000 mg), 2–4 times daily.
2. Montelukast (Singulair), 10 mg at bedtime.
3. Loratadine (Claritin), 10 mg in the morning. If this medication helps, consider diphenhydramine (Benadryl) 12.5 – 50 mg bedtime.
4. Some people will get additional benefits by adding famotidine (Pepcid), 20 mg twice a day. Do not use the other acid blocking medications (called PPIs). They will not help here and are quite toxic long-term.
5. Cromolyn (Rx – gastrocom) ampules (100 mg in 5 mL) one before each meal can be quite effective for histamine reactions from food but is often not insurance covered. But with the Good Rx app, they are about a $1.60 per ampule.
6. In persistent severe cases, consider a low histamine diet (these can be found online).

For those fibromyalgia cases that are refractory, especially associated with severe environmental and treatment sensitivities, or anxiety and depression, consider urine **mycotoxin** testing (Great Plains Labs) and treatment. I highly recommend the book *Toxic* by Dr. Neil Nathan, who simplified the complex work of Ritchie Shoemaker. I have simplified it even further in *From Fatigued to Fantastic*. Unfortunately, this area is complex enough that space does not allow me to do it justice here.

Pain Relief

When you treat the root causes of the pain using the protocols above, our research shows that much of the pain goes away. But in the interim, I find the following to be especially helpful for pain management:

1. Low Dose Naltrexone (3-4.5 milligrams a night). It takes two months to start working.
2. Curaphen (EuroMedica). This has been a pain relief miracle for many people.
3. Hemp Oil (EuroMedica) (3 – 5 caps, twice a day as needed for pain). I am very picky about the forms of hemp oil I use and have found this to be the most effective.
4. Tramadol, gabapentin, and other medications can also be helpful.

I find that virtually everybody can get good solid pain relief, usually without narcotics, by treating the root causes of the pain using the protocol above and other (often) natural treatment options.

*The good news? CFS and fibromyalgia can now be very effectively treated***!**

Jacob Teitelbaum, MD, is one of the most frequently quoted integrative, pain and fibromyalgia medical authorities in the world. He is the author of the best-selling From *Fatigued to Fantastic!*, *Pain Free, 1,2,3!,* the *Complete Guide to Beating Sugar Addiction*, *Real Cause Real Cure*, *The Fatigue and Fibromyalgia Solution*, *Diabetes Is Optional*, and the popular free Smart Phone app *Cures A-Z*. He is the lead author of five 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 and www.EndFatigue.com.

◆

Literature Review & Commentary

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

Magnesium for Postoperative Pain

Eighty young Croatian adults (mean age, 24 years) who were scheduled for surgical removal of both lower third molars were enrolled in this trial. The molars were removed one at a time, 14 days apart. For the first procedure, the participants were randomly assigned to receive, in double-blind fashion, 400 mg per day of magnesium or placebo for four days, beginning on the day of surgery. The participants then received the other treatment (magnesium or placebo) for the second procedure. Mean pain severity was significantly lower at 24, 48, and 72 hours postoperatively in the magnesium group than in the placebo group. Mean severity of trismus (as determined by the degree to which the mouth could be opened) was also significantly lower at 24, 48, and 72 hours postoperatively in the magnesium group than in the placebo group.

Comment: Pain and trismus (spasm of the jaw muscles) are the most common postoperative complications following surgical removal of a lower third molar. Magnesium has demonstrated analgesic effects and may also decrease muscle spasm. The results of this study suggest that short-term magnesium supplementation can decrease postoperative pain and trismus in young adults undergoing removal of a lower third molar.

Jerkovic D, et al. Effect of orally administered magnesium on postoperative pain level and trismus after surgical removal of the lower third molars: a randomized, double-blind, placebo-controlled trial. *Clin Oral Investig*. 2020 May 20 [Online ahead of print].

Glucosamine and Diabetes

The association between habitual use of glucosamine and incidence of type 2 diabetes was examined in a prospective cohort study of 404,508 individuals in the United Kingdom who were participants in the UK Biobank study and who were free of diabetes, cancer, and cardiovascular disease at baseline. During a median follow-up period of 8.1 years, 7,228 new cases of type 2 diabetes were documented. After adjustment for age, sex, body mass index, race, lifestyle factors, and other potential confounding variables, glucosamine use was associated with a significant 17% lower risk of type 2 diabetes.

Comment: Glucosamine (as glucosamine sulfate or glucosamine hydrochloride) is widely used to treat osteoarthritis. Concern has been raised that glucosamine might cause insulin resistance,[1] because continuous intravenous infusions of glucosamine sulfate have induced insulin resistance in normoglycemic (but not hyperglycemic) rats.[2] However, the intravenous doses of glucosamine sulfate that induced insulin resistance in rats are said to produce higher blood levels of glucosamine than those achievable with therapeutic oral doses.[3] In two studies lasting three years each that included a total of more than 200 patients treated with 1,500 mg per day of glucosamine sulfate, there was no evidence that the treatment interfered with glucose metabolism.[4,5] Based on the results of the present study and previous research, it does not appear that glucosamine, when given in doses typically used to treat osteoarthritis, increases the risk of developing diabetes or other abnormalities of glucose metabolism.

Ma H, et al. Glucosamine use, inflammation, and genetic susceptibility, and incidence of type 2 diabetes: a prospective study in UK Biobank. *Diabetes Care*. 2020;43:719-725.

High-Dose Vitamin D and Critical Illness

Some 1,078 critically ill patients who were at high risk for death, and who had a serum 25-hydroxyvitamin D (25[OH]D) level below 20 ng/ml (mean, 11.1 ng/ml) were randomly assigned to receive, in double-blind fashion, a single oral dose of 540,000 IU of vitamin D3 or placebo within 12 hours of the decision to admit the patient to an intensive care unit. The primary endpoint was 90-day all-cause mortality. The mean 25(OH)D level on day 3 was 46.9 ng/ml in the vitamin D group and 11.4 ng/ml in the placebo group. Ninety-day mortality was 23.5% in the vitamin D group and 20.6% in the placebo group ($p = 0.26$). The effect of vitamin D on mortality did not differ according to the baseline level of 25(OH)D.

Comment: Serum 25(OH)D levels are frequently very low in patients with critical illness. However, 25(OH)D is an acute-phase reactant that falls in response to inflammation, so it is debatable whether these low 25(OH)D levels indicate true vitamin D

deficiency. In the present study, rapid normalization of low 25(OH) levels by administering a single large dose of vitamin D did not decrease mortality in critically ill patients. To the contrary, there was a nonsignificant trend toward a slight increase in mortality among those treated with high-dose vitamin D. Additional research is needed to determine whether lower, more frequent doses of vitamin D would be beneficial for this patient population.

National Heart, Lung, and Blood Institute PETAL Clinical Trials Network, et al. Early high-dose vitamin D_3 for critically ill, vitamin D-deficient patients. *N Engl J Med*. 2019;381:2529-2540.

Low FODMAPs Diet for Quiescent Inflammatory Bowel Disease

Fifty-two adults with quiescent (inactive) Crohn's disease or ulcerative colitis who had persistent gastrointestinal symptoms consistent with irritable bowel syndrome (IBS) were randomly assigned to consume a low-FODMAPs diet or a sham diet for four weeks. The sham diet was an exclusion diet of similar intensity and burden as the low-FODMAPs diet. Both diets contained similar amounts of nutrients and fiber. The proportion of patients who reported adequate relief of gastrointestinal symptoms was significantly higher in the low-FODMAPs group than in the sham group (52% vs. 16%; $p = 0.007$). The mean IBS Symptom Severity Score improved by 30% in the low-FODMAPs group and by 15% in the sham group ($p < 0.08$ for the difference in the change between groups). At the end of the treatment period, the mean Health-Related Quality of Life score was significantly higher (better) in the low-FODMAPs group than in the sham group ($p < 0.05$).

Comment: "FODMAPs" is an acronym for fermentable oligosaccharides, disaccharides, monosaccharides, and polyols. FODMAPs include fructose, lactose, sorbitol, fructo-oligosaccharides (fructans, including inulin), and galacto-oligosaccharides (such as raffinose). Foods restricted on a low-FODMAPs diet include fruits that contain fructose in excess of glucose (e.g., apples, pears), fructan-containing foods (e.g., wheat, onions, leeks, artichokes), sorbitol-containing foods (e.g., stone fruits), raffinose-containing foods (e.g., legumes, lentils, cabbage, and Brussels sprouts), and lactose- and fructose-containing foods, if lactose and fructose malabsorption, respectively, are demonstrated.

Patients with inactive ulcerative colitis or inactive Crohn's disease frequently have IBS-like symptoms such as bloating, abdominal pain, and flatulence. Several studies have shown that consuming a low-FODMAPs diet can relieve gastrointestinal symptoms in patients suffering from IBS. The present study demonstrated that a low-FODMAPs diet can also relieve IBS-like symptoms in patients with inactive inflammatory bowel disease.

Cox SR, et al. Effects of low FODMAP diet on symptoms, fecal microbiome, and markers of inflammation in patients with quiescent inflammatory bowel disease in a randomized trial. *Gastroenterology*. 2020;158:176-188.e7.

Alpha-Lipoic Acid for Cystine Kidney Stones

Two girls (ages 6 and 15 years) with recurrent cystine kidney stones due to cystinuria were treated with alpha-lipoic acid (ALA). The dosage was 300 mg per day (increased to 300 mg twice a day) for the younger girl and 600 mg twice a day for the older girl. Both patients had been receiving potassium citrate, which was continued. In both cases, the solubility of cystine in urine increased markedly. The frequency of symptomatic and asymptomatic kidney stones decreased, and in one patient an existing stone disappeared after two months. No change was seen in urinary cystine excretion or urine pH.

Comment: Cystinuria is an autosomal recessive disorder characterized by excessive urinary excretion of cystine, resulting in recurrent cystine kidney stones. It affects about 1 in 7,000 to 1 in 10,000 people in the United States. Treatment options include increased fluid intake, reduced sodium intake, and supplementation with potassium citrate to reduce cystine excretion and/or increase cystine solubility. ALA was found to be effective for preventing and treating kidney stones in a mouse model of cystinuria. The present case reports suggest that ALA can increase the solubility of cystine in urine and possibly prevent stone formation in patients with cystinuria.

Cil O, Perwad F. Alpha-lipoic acid (ALA) improves cystine solubility in cystinuria: report of 2 cases. *Pediatrics*. 2020;145:e20192951.

Probiotic for Depression, Oxidative Stress, and Inflammation, or More Iranian Research Fraud?

Forty-four Iranian patients who had undergone a successful percutaneous coronary intervention after an acute myocardial infarction were randomly assigned to receive, in double-blind fashion, a daily probiotic or placebo for 12 weeks. Compared with placebo, significant improvements were seen in the probiotic group in depressive symptoms (as measured by the Beck Depression Inventory), serum malondialdehyde (a measure of oxidative stress), and C-reactive protein (a measure of inflammation).

Comment: Readers of the *Townsend Letter* know I suspect that a large proportion of the research coming from Iran is fraudulent. Several aspects of the present study cause me to question its validity. Before reviewing these concerns, I will mention that three different papers have been generated from the study described above. One is the paper cited at the end of this discussion (from *Psychosomatic Medicine*), which was reviewed above. I will refer to it as the "depression paper." A second paper presented data on cardiac remodeling in the patients who participated in this trial.[6] I will refer to this paper as the "cardiac remodeling" paper. The third paper provided a description of the methods and protocols that were employed in the depression paper and the cardiac remodeling paper.[7] I will refer to it as the "protocol paper."

1. Issue regarding inclusion criteria: To be eligible for the trial, patients had to be 30 to 60 years of age. At baseline the mean age of participants was 56.7 ± 9.1 years in the probiotic group and 57.1 ± 7.8 years in the placebo group. With those means and standard deviations, if one assumes there was a Gaussian distribution of ages, then approximately 16% of the study participants would have been over 65 years of age. Even with a non-Gaussian distribution, it seems highly unlikely that all of the participants could have been 60 years old or younger.
2. Issue regarding exclusion criteria: The protocol paper stated that participants who fail to take at least 90% of their assigned capsules will be excluded from the study. The depression paper stated that 40 of the 44 participants completed the trial, but it also stated that the compliance rate was only 85% in the probiotic group and 80% in the placebo group. Thus, it would seem that a large proportion of participants (probably more than half) took less than 90% of their capsules, so it is difficult to understand why so few participants were excluded. The cardiac remodeling paper did not mention anything about excluding patients because of noncompliance.

➤

➤

3. Issues related to recruitment dates: The depression paper, which was submitted to the journal on November 20, 2018, stated that the study was conducted from April to October of 2018 (a period of 6 or 7 months). However, the protocol paper, which was submitted to the journal on January 5, 2019, stated that the study "Will be conducted over a period of 1 year, from April 2018." Since the protocol paper was submitted after the study had been completed, the researchers should have known that the study was not conducted over a period of one year. In addition, the document on the Iranian Registry of Clinical Trials (IRCT) website stated that the study was "registered while recruiting," but it also stated that recruitment was complete. Both of those statements cannot be true. The IRCT document stated that the expected recruitment start date was June 10, 2018. However, at the time the study was registered (June 27, 2018), the researchers should have known that recruitment had begun in April 2018.
4. Ethical issue: According to the IRCT registration document, the study was approved by the ethics committee on May 21, 2018. Thus, the study was started before it was approved by the ethics committee.
5. Discrepancy related to the placebo: The depression paper, the protocol paper, and the IRCT document listed the placebo as maltodextrin. The cardiac remodeling paper listed the placebo as inulin. While both of these compounds are used as encapsulating agents, they are completely different molecules.

Moludi J, et al. The effect of probiotic supplementation on depressive symptoms and quality of life in patients after myocardial infarction: results of a preliminary double-blind clinical trial. *Psychosom Med*. 2019;81:770-777.

Can Dietary Fiber Prevent Diverticular Disease?

A meta-analysis was conducted on five prospective cohort studies (including a total of 865,829 participants) that examined the association between dietary fiber intake and risk of diverticular disease. In the pooled analysis, the relative risk was 0.74 (95% confidence interval [CI], 0.71-0.78) for each 10 g per day increase in fiber intake. As compared with 7.5 g per day of fiber, there was a 23%, 41% and 58% reduction in risk for an intake of 20, 30, and 40 g per day, respectively. The relative risk for each 10 g per day increase was 0.74 (95% CI, 0.67-0.81) for cereal fiber, 0.56 (95% CI, 0.37-0.84) for fruit fiber, and 0.80 (95% CI, 0.45-1.44) for vegetable fiber.

Comment: In the 1970s, Denis Burkitt (the physician for whom Burkitt's lymphoma was named) developed the hypothesis that modern-day refining of foods, which removes a substantial proportion of dietary fiber, is the main cause of diverticular disease.[8,9] The meta-analysis of observational studies described above supports that hypothesis.

One possible mechanism by which high fiber intake might prevent the development of diverticula is related to colonic intraluminal pressure. The presence of fiber in the stool increases the water-holding capacity of the stool, making it relatively bulky, soft, and easy to pass at relatively low intraluminal pressure. In contrast, the stools of people who consume a low-fiber diet tend to be smaller and harder, and require higher intraluminal pressure to pass. Chronically elevated intraluminal pressure could weaken portions of the colonic wall, rendering them more susceptible to the development of diverticula.[10]

Another possible explanation for the apparent protective effect of a high-fiber diet is that many high-fiber foods (e.g., fruits, vegetables, and some whole grains) are good sources of flavonoids. Because flavonoids enhance tissue integrity, consuming a high-flavonoid diet might help fortify colonic tissues against the effects of high intraluminal pressure. If components of a high-fiber diet other than the fiber contribute to its protective effect, then eating whole foods high in fiber would be more effective for preventing diverticular disease than would adding purified fiber supplements (such as psyllium or cellulose) to a low-fiber diet.

Aune D, et al. Dietary fibre intake and the risk of diverticular disease: a systematic review and meta-analysis of prospective studies. *Eur J Nutr*. 2020;59:421-432.

***Lactobacillus rhamnosus* GG for Infantile Colic**

Forty-five breastfed infants with colic were randomly assigned to receive *Lactobacillus rhamnosus* GG (*L*. GG; 5 x 10^9 colony-forming units per day) or placebo for four weeks. All mothers were advised to remove dairy products from their diet. At the end of the treatment period, mean crying time was significantly less in the probiotic group than in the placebo group (105 vs. 240 minutes per day; $p < 0.001$). In addition, the mean concentration of fecal calprotectin (an indicator of intestinal inflammation) decreased significantly in the probiotic group but did not change in the placebo group (it was not stated whether the difference in the change between groups was significant).

Comment: Colic occurs in an estimated 10-30% of otherwise healthy infants. It is characterized by extended periods of inconsolable crying for no apparent reason, frequently accompanied by the passage of flatus. The condition typically begins in the first few weeks of life and resolves or improves considerably by three months of age.

The intestinal flora of infants with colic differs from that of infants without colic (*L. brevis* and *L. lactis lactis* were found only in the former, whereas *L. acidophilus* was found only in the latter). *L. brevis* and *L. lactis lactis* ferment glucose to produce ethanol and carbon dioxide, which might trigger various intestinal symptoms.[11] The present study demonstrated that *L.* GG, a widely available probiotic preparation, is effective for treating colic in breastfed infants. Another commercially available probiotic that has been reported to be effective for preventing[12] and treating[13] colic is *L. reuteri* DSM 17938.

Savino F, et al. Lactobacillus rhamnosus GG (ATCC 53103) for the management of infantile colic: a randomized controlled trial. *Nutrients*. 2020;12:E1693.

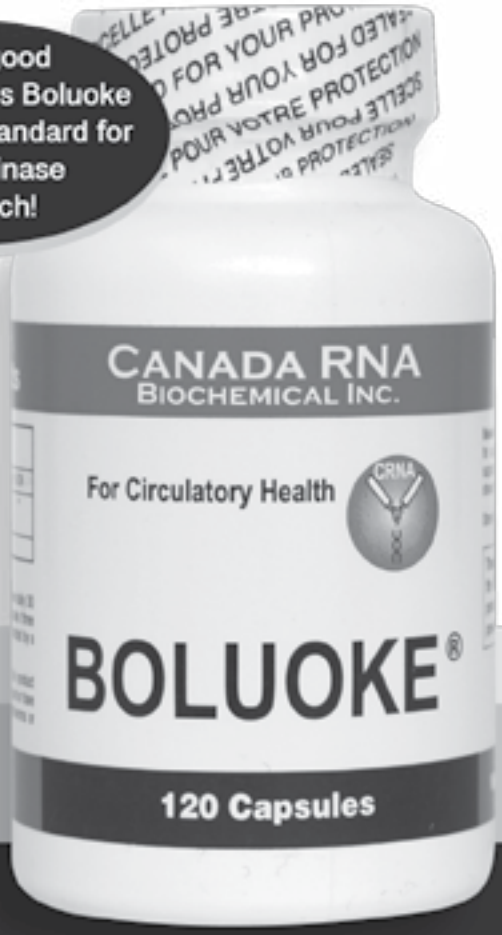
References

1. Adams ME. Hype about glucosamine. *Lancet*. 1999;354:353-354.
2. Rossetti L, et al. In vivo glucosamine infusion induces insulin resistance in normoglycemic but not in hyperglycemic conscious rats. *J Clin Invest*. 1995;96:132-140.
3. Rovati LC, et al. Glucosamine in osteoarthritis. *Lancet*. 1999;354:1640.
4. Pavelka K, et al. Glucosamine sulfate use and delay of progression of knee osteoarthritis: a 3-year, randomized, placebo-controlled, double-blind study. *Arch Intern Med*. 2002;162:2113-2123.
5. Reginster JY, et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. *Lancet*. 2001;357:251-256.
6. Moludi J, et al. Probiotics supplementation on cardiac remodeling following myocardial infarction: a single-center double-blind clinical study. *J Cardiovasc Transl Res*. 2020 Jul 17 [Online ahead of print].
7. Moludi J, et al. The efficacy and safety of probiotics intervention in attenuating cardiac remodeling following myocardial infraction: Literature review and study protocol for a randomized, double-blinded, placebo controlled trial. *Contemp Clin Trials Commun*. 2019;15:100364.
8. Burkitt DP, et al. Dietary fiber and disease. *JAMA*. 1974;229:1068-74.
9. Burkitt DP. Hiatus hernia: is it preventable? *Am J Clin Nutr*. 1981;34:428-31.
10. Findlay JM, et al. Effects of unprocessed bran on colon function in normal subjects and in diverticular disease. *Lancet*. 1974;1:146-9.
11. Savino F, et al. Bacterial counts of intestinal Lactobacillus species in infants with colic. *Pediatr Allergy Immunol*. 2005;16:72-5.
12. Indrio F, et al. Prophylactic use of a probiotic in the prevention of colic, regurgitation, and functional constipation: a randomized clinical trial. *JAMA Pediatr*. 2014;168:228-33.
13. Szajewska H, et al. Lactobacillus reuteri DSM 17938 for the management of infantile colic in breastfed infants: a randomized, double-blind, placebo-controlled trial. *J Pediatr*. 2013;162:257-62.

◆

HYPERCOAGULATION

It's so good that FDA uses Boluoke as the gold standard for lumbrokinase research!



A central issue in:

- conditions with a poor circulation
- growth and spread of malignant cells
- chronic infections with biofilm
- poor tissue healing due to hypoxia

Boluoke (lumbrokinase), simply the best in:

- Enzymatic strength
- Research data
- Quality, safety, and efficacy

Your Patients. Your Reputation.

TRUST NOTHING LESS!

Boluoke is also available through

Researched Nutritionals
solutions for life

BIORESOURCE

antiaging-systems.com

return 2 health

MP
Mountain States Health Products, Inc.

Pro Health Network

NaturoDoc

Dragon's Medical Bulletin
www.dragonsmedicalbulletin.com
Your Quick Stop for Integrated Clinical Research Updates

CRNA

1-866-287-4986

www.canadaRNA.com

Considering the Evidence for Treating Fibromyalgia as an Inflammatory Disease

by Leslie Axelrod, ND, LAc

Fibromyalgia (FM) is a chronic pain syndrome that is multisystem and extends far beyond having tender points and muscular involvement. Multiple etiologies have been theorized including inflammatory, infectious, mitochondrial dysfunction, environmental, and genetic factors. It essentially affects all systems of the body, including but not limited to the neuroendocrine, neurotransmitter, immune, autonomic nervous systems, as well as at a cellular level.

Diagnosis has been challenging and the present criteria utilized focuses on subjective reporting of regions of pain, referred to as the widespread pain index. The most current 2016 criteria now include a symptom severity score, including fatigue, waking unrefreshed, and cognitive changes, which are all interrelated. These criteria do not include objective findings such as physical exam or laboratory findings.[1] A study of almost 500 patients found that 11% of patients were diagnosed with FM and did not meet criteria, while 24% were not diagnosed with FM despite meeting present criteria. Women were more commonly misdiagnosed in favor of FM.[2]

Until recently, there have not been laboratory tests to confirm the diagnosis. The inflammatory markers ESR (erythrocyte sedimentation rate) and CRP (C-reactive protein) are commonly used to assess for other conditions that may mimic FM. The serum test FM/a, yet to be FDA approved, is starting to gain favor among some practitioners. It is covered by some insurance plans, including Medicare, according to the company EpiGenetics. The FM/a tests the WBC (white blood cell) chemokine and cytokine profile and gives a score of 1-100, with a positive at or above 50. The test is based on the cytokine response to mitogenic activation of plasma and peripheral blood mononuclear cells. Studies indicate cytokine response in samples tested in this way was significantly reduced in FM patients compared to healthy individuals, indicating an altered cell-mediated immunity unique to these patients.[3,4] "The sensitivity, specificity, positive predictive and negative predictive value for having FM using this measure compared to controls was 93, 89, 92, and 91%, respectively," as reported in a study of 477 patients, including rheumatoid arthritis, systemic lupus erythematosus, fibromyalgia patients, and 119 controls.[4]

Other diagnostic testing that was on the market for a period of time was based on research regarding investigation into microRNA (miRNA) profiles, small non-coding RNA molecules that translocate into mitochondria and act to downregulate gene expression and control cellular processes, among many other functions. Particular patterns of miRNA's are being used as biomarkers for a variety of conditions. There are five particular miRNAs that are considered a "signature of FM" and have a high sensitivity and specificity for the condition.[5-7] These miRNAs are varied in their function and appear to play an important role in the presentation of symptoms. For instance, one of the five miRNAs found, miR-143, contributes to neuropathic pain.[8] Another miR-145 that was elevated in blood and cerebrospinal fluid of FM patients correlated with the pain and fatigue consistent with FM.[5,9] Studies revealed abnormal levels of FM-related miRNAs affected sleep quality, pain threshold, and overall pain.[6,9] Continuing research on miRNA is being performed to assist in the diagnosis and ultimately treatment of an array of different medical conditions.

The cytokine and mitochondrial alterations present in FM patients influence the onset and course of the disease. Cytokines have been shown to communicate between the immune and nervous system. Cytokines become activated in infections and act to modulate or stimulate the immune system. In many cases, the symptoms of infection and fibromyalgia may resemble each other, with lethargy, myalgias and changes in social behavior. FM patients have elevated circulating cytokines, such IL-8, TNFa, and IL-10 compared to controls.[10,11] These cytokines can induce the symptom picture of FM: IL-8 promotes sympathetic pain, TNFa affects brain cell function, fatigue and anorexia.[11] IL-10 appears to play an anti-inflammatory role.[12]

The role of infection has been investigated regarding an etiology of FM, particularly in those with acute onset. There have been a number of

studies revealing elevated IgM or IgG levels, indicating a possible triggering event or concomitant infection. Associations have been made with Parvo19, HHV-6, HHV-7, *H. pylori*, EBV, as well as other infections for FM or FM-like syndromes.[13-16] However, titers do not consistently correlate to the symptoms.[13] A small study comparing viral antibodies in patients with acute onset FM revealed 50% of the patients had IgM antibodies against enterovirus compared to 15% of controls.[17] Another study investigated the skeletal muscle of patients with chronic inflammatory muscle disease and FM, finding enterovirus viral RNA in 20% and 13% respectively, compared to none in the controls.[18] Other studies showed higher frequency of persistent HHV-6, HHV-7 infection and *H. pylori* IgG antibody compared to controls.[14,15] In addition to an infectious etiology, there are a multitude of other etiologies that may account for or contribute to abnormal cytokine profiles, including exposure to mold, environmental factors and autoimmune diseases, all of which might be considered when treating FM.[19,20] These pro-inflammatory cytokines, combined with oxidative stress and mitochondrial dysfunction, contribute to the symptom picture of hyperalgesia, fatigue, depression, and cognitive changes.[4]

Low dose naltrexone (LDN) is being used by clinicians with some promising results, possibly due to its effect on cytokines, as well as pain receptors. In a small single-blind crossover pilot trial, eight women were given low dose naltrexone, 4.5 mg, one hour before bed for eight weeks. The results found LDN statistically reduced plasma concentrations of multiple interleukins, including but not limited to IL-1B, IL1Ra, IL6, IL10, and TNFa compared to baseline. Concomitantly, a 15% reduction of FM-related pain and 18% overall symptoms were found.[21] The limitations of the study included the small sample size, duration, and absence of a placebo or control group. Another pilot study, placebo-controlled single-blind crossover with a washout period, revealed a reduction of symptoms compared to placebo by greater than 30%.[22] Although erythrocyte sedimentation rate is not typically considered an indicator of FM, multiple studies found that patients with higher ESR's had more severe symptoms. LDN was more effective in the high ESR groups with the greatest reduction of symptoms.[21,22]

Cytokine testing may be a consideration for FM patients, especially those unresponsive to treatment.

In addition to addressing cytokine aberrations, therapeutic protocols directed at mitochondrial dysfunction have shown efficacy for FM. CoQ10 is involved in mitochondrial ATP production, regulation of oxidative stress, and cellular respiration. Deficiency has been associated with increased inflammation. Supplementation with CoQ10, 300 mg in divided dosages, was found to stimulate mitochondrial biogenesis and antioxidant activity, along with improving pain, number of tender points, and fatigue in FM patients.[23] CoQ10 significantly reduced cytokines, including TNFa.[24,25] Acetyl-L-Carnitine (ALC) assists in the transfer of acetyl groups into the mitochondrial inner membrane. The function of acetylated proteins in the mitochondria is to influence energy metabolism of the cell. A double-blind placebo-controlled study of 102 FM patients, taking 500 mg TID, resulted in statistically significant improvement in musculoskeletal pain, reduction of tender points and depression at 10 weeks, with improvement beginning at six weeks, compared to placebo.[26] ALC was also found to modulate cytokine production in human peripheral mononuclear cells, particularly IL-6, IL1B, and TNFa.[27] S-Adenosylmethionine, a methyl donor and precursor to glutathione, also decreases symptoms of FM, including tender point score, pain. and depression at a dose of 800 mg orally.[28] It has also been found to decrease TNFa expression and increase IL10 an anti-inflammatory cytokine.[29]

There are multiple supplements that are utilized for FM, but one cannot discount the role of diet as well. There is an association between FM and higher BMI scores, which are relative to symptom severity.[30] Obesity has been related to elevated TNFa in adipose tissue.[31] A study in which mice with acid-saline injection-induced FM were fed a high fat diet "exhibited robustly increased levels of TNFa in plasma, muscles and spinal cord after acid saline injections compared with low fat-diet treated mice." Hyperalgesia was significantly worsened after 24 weeks of the high fat diet. Mice lacking a specific TNFa receptor were resistant to the FM-like pain behavior when injections were given, indicating an association between TNFa activation and hyperalgesia.[32] Other studies revealed a positive influence for dietary changes in FM patients. Findings from a food intake assessment study of women with FM revealed a high protein intake was related to improved pain threshold.[33] A 2019 metanalysis of a variety of diets for FM stated raw vegetarian, low FODMAP, and hypocaloric diets showed promising results for symptom improvement and reduction of inflammatory markers. However, the authors' assessment of the metanalysis was that overall the dietary intervention studies for FM are "scarce and low quality" and do "not allow conclusions to be drawn."[34]

Cytokine testing may be a consideration for FM patients, especially those unresponsive to treatment. A finding of elevated cytokines may help confirm the inflammatory nature of the condition but should also prompt further investigations to rule out possible autoimmune disease or other causes. Cytokine biomarkers can be used to determine the level of inflammation, monitor progress as well as individualize a patient's treatment plan. Accuracy of testing may vary depending on multiple factors: stage of the disease, timing of the test (cytokine release is episodic), location of inflammation, etc.

➤

➤

For example, TNFa has a peak plasma concentration of two hours with a half-life of 18.2 minutes after exposure to an initiating substance and IL-6 levels are biphasic with peaks at 6 and 74 hours.[35] Also, cytokine levels may differ between body fluids, i.e. some patients with neuropsychiatric disorders have higher cytokine levels in CSF vs. serum, depending on the integrity of the blood brain barrier.[36] Still, there is value in testing, especially when evaluating the broader picture of multiple biomarkers. Cytokine panels are offered by a variety of labs, including Arup Lab (13 cytokine panel) and Life Extension (4 cytokine panel) while Labcorp and Sonora Quest only offer individual tests for each specific cytokine.

In practice, dietary intervention is a core therapeutic approach for all my autoimmune and FM patients. I find that it is very difficult to address complicated patients without dietary changes, particularly eliminating food sensitivities and increasing vegetable intake. Typically, IgG food sensitivity testing is performed, or I recommend a strict elimination diet of nine days, followed by a re-introduction phase of a new food every three days eaten repeatedly. If any reaction occurs, the offending food is removed immediately, and a new food is not re-introduced for two-to-three days or until symptoms resolve. A modified Whole 30 or Paleo diet can be beneficial as an alternate plan. Patients are instructed to avoid pork and red meat and are told to systematically introduce eggs and almonds, common reactive foods, after avoidance for 10 days.

Depending on the patient, other investigations that may be considered include testing and treatment for adrenal function, gut dysbiosis, environmental toxicity, infections or cytokines, as indicated. Common prescriptions include a modified IV Myer's cocktail weekly for four weeks (includes ascorbic acid 12.5 grams and MgCl 3-5 cc) or an IV magnesium push (MgCl 3 cc, 7 cc sterile H20) as an alternative. Sleep is a key issue and must be addressed. SAMe at a dosage of 400 mg twice daily can be very effective for pain reduction, sleep, as well as improve depression.[28] Otherwise, I may recommend melatonin 3 mg or 5-HTP 100 mg, which improves both sleep and symptoms of FM.[37, 38] Low dose naltrexone may be prescribed at bedtime, 1.5 mg and titrated up every two weeks to 4.5 mg. While it can be very helpful for the pain, intense dreams can occur initially, and compliance may become an issue.

Fibromyalgia is a complex condition with multiple causative factors. The approach should depend on each individual patient, their signs and symptoms, as well as history. The dysfunction may occur at many different levels including, but not limited to, cellular, neuroendocrine, and immune. Diagnostic testing may be helpful but has limitations. Inflammation appears to play an important role in the presentation and severity of FM and should be one of the considerations in designing an effective therapeutic plan.

References

1. Wolfe F, et. al. Revisions to the 2010/2011 Fibromyalgia Diagnostic Criteria. *Arthritis Rheum*. 2016;68 (supp 10)
2. Wolfe F, Schmulkler J, Castrejon I. Diagnosis of Fibromyalgia: Disagreement Between Fibromyalgia Criteria and Clinician-Based Fibromyalgia Diagnosis in a University Clinic. *Arthritis Care Research*. 2019 Mar;71(3):343-351
3. Behm FG, et. al. Unique immunologic patterns in fibromyalgia. *BMC Clin Path.* 2012, Dec 17;12:25
4. Wallace DJ, et. al, Cytokine and chemokine profiles in fibromyalgia, rheumatoid arthritis and systemic lupus erythematosus: a potentially useful tool in differential diagnosis. *Rheumatol Int*. 2015, 35:991–996
5. Cerdá-Olmedo G, et.al. Identification of a microRNA signature for the diagnosis of fibromyalgia. *PLoS ONE*. 2015, 10(3)
6. Bjersing JL, Bokarewa MI, Mannerkorpi K. Profile of circulating microRNAs in fibromyalgia and their relation to symptom severity: An exploratory study. *Rheumatol Int*. 2015, 35, 635–642
7. Masotti A, et. al. Circulating microRNA Profiles as Liquid Biopsies for the Characterization and Diagnosis of Fibromyalgia Syndrome. *Mol Neurobiol*. 2017;54: 7129–7136.
8. Dai A, et. al. The Regulatory Mechanisms and Therapeutic Potential of MicroRNAs: From Chronic Pain to Morphine Tolerance. *Neurosci*. 2018; 11: 80.
9. Bjersing JL, et. al. Profile of cerebrospinal microRNAs in fibromyalgia. *PLoS One*. 2013 Oct 25;8(10)
10. Fatima G, et. al. Lack of circadian pattern of serum TNF-alpha and IL-6 in patients with fibromyalgia syndrome. *Indian J Clin Biochem*. 2012;27:340–343.
11. Wallace DJ, et.al., Cytokines Play an Aetiopathogenetic Role in Fibromyalgia: A Hypothesis and Pilot Study. *Rheumatology* (Oxford). 2001 Jul;40(7):743-9.
12. Bazzichi L, et al. Cytokine patterns in fibromyalgia and their correlation with clinical manifestations. *Clin Exp Rheumatology*. 2007: 25;225–30
13. Buyukkose M, et. al. Seroprevalence of parvovirus B19 in fibromyalgia syndrome. *Clin Rheum*. 2009 Mar;28(3):305-9
14. Krumina A, et al. The role of HHV-6 and HHV-7 infections in the development of fibromyalgia. *J Neurovirol*. 2019 Aug;25(4):617
15. Akkaya N, Akkaya S, Polat, Y. Helicobacter Pylori Seropositivity in Fibromyalgia Syndrome. *Clin Rheumatol.* 2011 Jan;30(1):43-9.
16. Willams M, et. al. Epstein-Barr Virus dUTPase Induces Neuroinflammatory Mediators: Implications for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Clin Ther*. 2019 May;41(5):848-863.
17. Wittrup IH, et. al. Comparison of viral antibodies in 2 groups of patients with fibromyalgia. .*J Rheumatol*. 2001 Mar;28(3):601-3.
18. Douche-Aourik F, et al. Detection of enterovirus in human skeletal muscle from patients with chronic inflammatory muscle disease or fibromyalgia and healthy subjects. *J Med Virol*. 2003 Dec;71(4):540-7.
19. Lichtenstein JHR, et. al., Environmental Mold and Mycotoxin Exposures Elicit Specific Cytokine and Chemokine Response. *PLoS One*. 2015; 10(5)
20. Gruzieva O, et. al. Exposure to Traffic-Related Air Pollution and Serum Inflammatory Cytokines in Children. *Environ Health Perspect*. 2017 Jun; 125(6): 067007.
21. Parkitny L, Younger J. Reduced Pro-Inflammatory Cytokines after Eight Weeks of Low-Dose Naltrexone for Fibromyalgia, Biomedicines. 2017 Apr 18;5(2):16
22. Younger, J, Mackey S, Fibromyalgia Symptoms Are Reduced by Low-Dose Naltrexone: A Pilot Study. *Pain Medicine*. May 2009;10(4): 663–672.
23. Cordero M, et al. Can Coenzyme q10 Improve Clinical and Molecular Parameters in Fibromyalgia? *Antioxid Redox Signal*. 2013 Oct 20;19(12):1356-61.
24. Abodollahzad H, et al. Effects of Coenzyme Q_{10} Supplementation on Inflammatory Cytokines (TNF-α, IL-6) and Oxidative Stress in Rheumatoid Arthritis Patients: A Randomized Controlled Trial. *Archives of Medical Research*. October 2015:46(7): 527-533
25. Fan Li, et. al. Effects of Coenzyme Q10 Supplementation on Inflammatory Markers: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Pharmacol Res*. 2017 May;119:128-136
26. Rossini M, et. al. Double-blind multicenter trial comparing acetyl l-carnitine with placebo in the treatment of fibromyalgia patients. *Clin Exp Rheumatol*. 2007 Mar-Apr;25(2):182-8.
27. Kouttab NM, Simone C. Modulation of cytokine production by carnitine. Mediators Inflamm. *PLoS One*. 1993; 2(7): S25–S28.
28. Jacobsen S, Danneskiold-Samsøe B, Andersen RB. Oral s-adenosylmethionine in primary fibromyalgia. Double-blind clinical evaluation. *Scand J Rheumatol*. 1991;20:294–302.
29. Pfalzer AC, et. al. PS-adenosylmethionine mediates inhibition of inflammatory response and changes in DNA methylation in human macrophages. *Physiologic Genomics*.Sept 2014; 46(17)
30. Correa-Rodriguez M, et. al. The Association of Body Mass Index and Body Composition with Pain, Disease Activity, Fatigue, Sleep and Anxiety in Women with Fibromyalgia. *Nutrients*. 2019 May; 11(5): 1193.
31. KirchgessnerTG, et. al. Tumor Necrosis Factor-a Contributes to Obesity-related Hyperleptinemia by Regulating Leptin Release from Adipocytes. *J Clin Invest*. 1997 Dec 1; 100(11): 2777–2782.
32. Tian D, et. al., High Fat Diet Sensitizes Fibromyalgia-Like Pain Behaviors in Mice via Tumor Necrosis Factor Alpha. *PLoS One*. 2018 Feb; 14;13(2)
33. Dias Batista ED, et. al. Food intake assessment and quality of life in women with fibromyalgia. *Rev Bras Reum Engl Ed*. 2016;56: 105–110
34. Silva AR, et. al. Dietary interventions in fibromyalgia: a systematic review. *Annals of Medicine*. 2019;51(sup1):2-14.
35. Brocco M, et. al. A study of interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α) serum levels in rats subjected to fecal peritonitis and treated with intraperitoneal ropivacaine. *Acta Cir Bras*. July 2012;27 (7).
36. Lepennetier G, et. al. Cytokine and immune cell profiling in the cerebrospinal fluid of patients with neuro-inflammatory diseases. *J Neuroinflammation*. Nov 2019.
37. Hemati K, et. al. Melatonin in the treatment of fibromyalgia symptoms: A systematic review. *Complement Ther Clin Practice*. February 3, 2020.
38. Caruso I, et al. Double-blind study of 5 hydroxytryptophan versus placebo in the treatment of primary fibromyalgia syndrome. *Int Med Res*. 1990 May-Jun;18(3):201-9

Dr. Axelrod has been in practice for over 30 years as a naturopathic physician and acupuncturist. She worked in an integrative rheumatology practice for 18 of those 30 years. She is a published author both nationally and internationally on topics including osteoarthritis, fibromyalgia, rheumatoid arthritis, and treating autoimmunity with natural medicine. She also lectures nationally on these topics. Dr. Axelrod is a full time professor at SCNM and has been teaching for 24 years.

◆

An Approach to Managing Fibromyalgia and Chronic Pain

by Alan B. McDaniel, MD

References are posted online at www.townsendletter.com.

Preface

Twenty years ago, a middle-aged man came to see Doc for chronic fatigue. He also endured severe pain from spinal degeneration, many times-operated with hardware implanted. After ordering labs, Doc gave him two recommendations: To see an excellent pain specialist and to adjust his diet for his apparent insulin resistance. The consultant's report four weeks later was memorable: While the patient was waiting for his appointment, the new diet had completely relieved his chronic pain.

Stress, in medical usage, is a challenge to the body's homeostasis.[1] Pain activates a complex stress-response,[2,3] and chronic pain can maladaptively perpetuate it.[2,4-7] Fibromyalgia and chronic pain conditions promote stress-related endocrine, metabolic, immunological, and psychological consequences that cause a "feed-forward" downward-spiral. This article reviews methods by which these detrimental responses can be identified and the cycle of dysfunction interrupted, then reversed.

Clinically Relevant Stress Responses

The acute stress response is adaptive when triggered by injury or illness: It ensures energy precursors are available, curtails unnecessary expenditures of energy,[8-10] and heightens protective immunity. Sometimes, its perpetuation is beneficial, as during starvation – but maladaptive chronic stress is well-documented on intensive care-units.[11-13] Such problems are also identified in chronically stressed patients who are not critically ill but ambulatory.[14,15] They walk into our offices.

The Practitioner's Role

People can become ensnared in dysfunction: "…the (stressed patient's) system may be incapable of returning to its normal operating regime and instead may assume a new alternate resting state."[16] Unfortunately, the standard American diet and lifestyle – and perhaps a healthcare model focused upon acute interventions – are ill-suited for overcoming these problems. Successful practitioners address the patient's physical needs, emphasizing diet and lifestyle, nutrition, and restoring endocrine balance; *and* they facilitate patients' psychological rehabilitation, as their choice of coping strategies significantly influences outcome.[17-21]

Stress-induced autonomic dystonia is strongly associated with chronic pain conditions.

Diagnosing Dysfunctional Adaptation to Chronic Stress

Many patients with these disorders will not have been properly diagnosed. Take a personal and family history, which with physical findings will indicate the appropriate laboratory tests.

History. Symptoms related to chronic stress have been summarized[22] and health issues associated with PTSD are reported.[23] It is useful to employ a long questionnaire, including questions about intrauterine life and birth trauma,[24-26] family of origin, abuse, early memories, and childhood personality traits.[27-31] The author's form (*free on request*) also collects the review-of-systems, asking prospective patients to score symptom severity on a 0-4 scale. Carefully review their medication and phytopharmaceutical use – many can interfere with the H-P axis and thyroid hormone metabolism.

Affect and behavior. Stress-induced autonomic dystonia is strongly associated with chronic pain conditions, including fibromyalgia.[32] Sympathetic over-drive is expressed somatically in well-known ways and psychologically, as "vigilance" becomes *hyper*-vigilance,[22] depression, anxiety, and catastrophizing.[33] These in turn worsen the perception of pain, further increasing stress.[34-36]

Laboratory Diagnosis

The Adrenals. The hypothalamic-pituitary-adrenal (HPA)-axis is up-regulated by stress. When the stimulus becomes chronic, this can continue with elevated cortisol production – or it may become suppressed.[37] When elevated cortisol is suspected, check a 24-hour, urinary, free cortisol or a late-night salivary cortisol,[38,39] of which a value >5.24 ng/mL is significantly high.[40] The increased HP-A axis activity of chronic stress is not Cushing's syndrome.[16,41-43] True Cushing's is verified with a dexamethasone suppression test.

Low adrenal function is more difficult to evaluate, for *both* HP-A axis responses to chronic stress can cause it. Hypothalamic-pituitary suppression produces secondary adrenal

➤

➤

insufficiency.[44] However, a persistently up-regulated HP-A axis and prolonged over-drive can eventually deplete the adrenals, which Selye termed "the exhaustion state."[45] Although "adrenal fatigue" is not an accepted medical diagnosis,[46] Selye's observation is reinforced by subsequent work.[47,48] Routine blood tests can offer clues suggesting adrenal insufficiency. These include hyponatremia (in 85-90% of Addison's); hyperkalemia; low blood bicarbonate; elevated BUN and ESR; mild anemia with eosinophilia and even mildly elevated TSH.[49]

If "adrenal fatigue" exists, how is it diagnosed? In physiology, "fatigue" is decreased output due to factors related to use (or over-use).[50] On the continuum of adrenal dysfunction,[51] fatigued adrenals are simply in the *process* of decline. Thus, the condition cannot be detected by the insensitive ACTH-stimulation test, which identifies only end-stage glands.[52] There is no gold-standard biomarker to identify the controversial adrenal fatigue.[53] Physicians whose clinical observations are consistent with Selye's statements can find the following options useful.

Adrenal hormones can be tested to predict "burnout."[54] Many variations of saliva cortisol testing have been used in studies, particularly by psychologists.[55]

Some patients with *normal* cortisol-response one hour after ACTH-stimulation report worsening adrenal symptoms, starting a few hours post-injection and lasting a day or more.[56,57] Jonathan Wright stated this indicates the lack of adrenal reserve: The ACTH bolus forces-out "the last drop" of cortisol and nothing is left to make more. Because this late collapse is missed by testing only a one hour-cortisol, Wright recommended collecting 24 hour-urine specimens before and after ACTH-injection, expecting the stimulated cortisol output *normally* to double.

The 24-hour urine adrenal steroid profile (and possibly its variant, the DUTCH test) offers increased sensitivity: As cortisol is the last steroid hormone to become low in adrenal insufficiency,[51] applying "metabolomics" – the study of precursors and waste-products – offers greater sensitivity than testing cortisol alone. "Wastes" are the first to show high or low adrenal stimulation and production. Precursor quantities reveal reduced LH and the loss of "back-up" capacity. The cortisol/cortisone ratio is also used to assess adrenal reserve.[58-60]

Gonadal Hormones. Stress down-regulates the HP-gonadal axis, thus prioritizing precursors to make cortisol.[61] However, steroid sex hormones are also made by the adrenals, the status of which influences their levels. Thus, sex hormones can be measured as proxies for the adrenals,[62] sparing expense and inconvenience. Men and menopausal women, whose hormone levels fluctuate only in a diurnal pattern, are easily tested. Younger women often have unpredictably irregular cycles due to HP-G axis suppression and reduced insulin sensitivity.[61,63] For consistency, check their hormones in early-follicular, on cycle day #4.

Thyroid Hormones. Autoimmunity is common – even more so due to the immunological effects of chronic stress,[64] so patients with palpably indurated thyroid glands are appropriately tested for thyroid autoantibodies (TPO-Ab & Tg-Ab), as also may be those with a compelling history or other physical findings. When clinically indicated, TSH-receptor antibody (TR-Ab) is added as an indicator of autonomous function or atrophic Hashimoto's.

Blood tests are *proven* to accurately reflect *tissue* levels of thyroid hormones.[65] Five tests are ordered: TSH, freeT4 (fT4), freeT3 (fT3), totalT3 (tT3) and ReverseT3 (RT3). Measuring TSH alone is insufficient, due to hypothalamic suppression and other issues.[66,67] When the deiodination of T4 to reverse T3 rather than to T3 is perpetuated, a state of functional hypothyroidism can occur (euthyroid sick-syndrome *or* non-thyroidal illness).[68] The value of analyzing these multiple parameters has been supported.[69]

The active thyroid hormone is T3 (T4 is a *pre*-hormone). Much evidence validates the concept that RT3 is an inhibitory hormone; it is yin to the yang of T3.[70] Thus, the critical measure of thyroid hormone effect at the cellular level is the **ratio** of T3 to RT3.[71,72] Because RT3 is available only as a *total* measure, *total* T3 is used to derive this ratio.[71,72] The desirable tT3/RT3 value lies between 10 and 14 (probably a bit higher for teenagers). The thyroid gland releases T3 and RT3 in a 10:1 ratio[73,74] and tissues normally produce relatively more T3 by T4-deoidination. Studies have determined healthy controls have tT3/RT3 between 11-13.[75-77] **Note**: The ratio compares the TOTAL values for both T3 and RT3.

Insulin Resistance (IR). Insulin resistance is integral to the stress-response; it occurs at a nearly six-times-increased frequency in pain patients.[78] Glycemic control is achieved through greater insulin production – and the many effects of insulin to which there is **no** resistance are *exaggerated*, causing harm.[79] Simply testing fasting blood insulin can be informative[80] but this alone is not adequate. Insulin resistance is diagnosed by determining the amount of insulin needed to maintain glycemic control. Like tests for thyroid metabolism, a comparison is necessary – that of glucose to insulin.

Evaluate the relationship of *fasting* glucose and insulin with any of several methods: A simple ratio,[81] or calculations like the HOMA-IR or QUICKI-index.[82,83] However, these efforts are insensitive and fail to identify about 40% of cases.[84]

At the first visit, patients can begin to correct two "core" problems, adrenal fatigue, and insulin resistance.

A dynamic test is needed and there are several.

Insulin "clamp" tests are considered the "gold-standard" but are not unavailable to clinicians.[85] Thus, the practitioner's most accurate test (*and* increasingly used in research) is a four-hour, 75 gram oral glucose tolerance test, measuring both glucose *and* **insulin**. The diagnosis is made by comparing the areas under the curves, which become distorted with resistance.[86] Emphatically, blood must be sampled also at 30 minutes – this is not routine on the standard OGTT, but is essential to assess the reflexive first-phase of insulin release.[87,88]

Other tests give helpful clues about IR and are useful to monitor treatment: Elevated triglycerides and low HDL cholesterol suggest hyperinsulinemia.[79] Elevated transaminases do too, as nonalcoholic steatohepatitis is strongly associated with IR. High insulin reduces hepatic SHBG production, with consequently low totalTestosterone to freeTestosterone balance in women. Increased aromatase due to IR reduces men's totalTestosterone to estradiol ratio.[89] Insulin-induced 5-alpha-reductase results in low totalTestosterone vs. DHT in women.[90]

Test Immune Hypersensitivity. The immune system is activated by stress: The acute, cellular type-1 response shifts in chronicity to humoral, type-2 dominance (which favors atopy and autoimmunity).[64] In both, cytokines are released and elevated cytokines are associated with neuro-inflammation,[91] fibromyalgia[92,93] and neuropathic pain.[94] A fundamental doctrine of treating immune hypersensitivity is to reduce its "total load." Thus, proponents advocate antigen-specific testing and treatment by avoidance and hyposensitization.

While IgE-mediated immunity is observed to effect mentation and behavior (the "allergic tension-fatigue syndrome"),[95] it seems non-IgE mediated-immune responses are highly correlated with fibromyalgia and related conditions.[96] After the nutritional, endocrine, and metabolic needs of the patient have been addressed, their skin will more reliably respond to allergy tests – in which measuring late and delayed reactions is crucial.[97,98] Until then, simple elimination/challenge tests can be performed at home for any highly-suspicious food or allergen. In-vitro tests for antigen-specific IgG can be useful but must be interpreted with a degree of skepticism.

Ancillary Tests. Practitioners cherish particular tests that have borne fruit for previous patients. The author frequently tests for nutritional deficits associated with chronic pain, including vitamin 25(OH)-D3,[99] iron/ ferritin,[100] potassium, RBC magnesium and zinc and, by hair elements analysis, lithium.[101]

Treatment

The protocol is simple: Test for what you suspect; fix what you find – then evaluate the remaining symptoms and repeat as needed. The complexity of maladaptive chronic stress requires an orderly process, though – to the extent of your patient's abilities. At the first visit, patients can begin to correct two "core" problems, adrenal fatigue, and insulin resistance.

Adrenal. Sufficient cortisol is essential to sustain virtually every metabolic function. The persistent lack of cortisol in chronically stressed-individuals promotes vulnerability for the development of post-traumatic or stress-related bodily disorders.[102] Also, the stability of the thyroid, gonads, and

➤

➤

even neurosteroids depends upon the foundation of healthy adrenals. So, we start by supporting the adrenals – while the patient considers diet and lifestyle choices.

Hydrocortisone (cortisol) is the preferred treatment for *complete* adrenal gland failure, about 20 mg/day (10-12 mg/m^2 body surface area) in three divided doses/daily, mimicking normal diurnal variation.[44,49] Although the use of low-dose supplemental hydrocortisone (HC) 5-10 mg/day has been validated by Cleare *et al*,[103,104] he later cautioned against it: Low dose-HC will suppress the already dysfunctional HPA-axis and further depress the sex hormones.[105]

There are good alternatives – over-the-counter nutrition and precursors – to prescribing HC. Nutrition – from desiccated neonatal bovine adrenal cortex (a "glandular") – can give significant and enduring improvement, apparently by replenishing co-factors for the enzymes of the steroid-synthetic pathways. This benefits all steroid-synthesizing tissues: The adrenals, gonads and apparently also the brain, which importantly synthesizes neurosteroids. While adrenal cortical tissue retains negligible cortisol,[106] and the glandular is theoretically hormone-free, some brands contain nanogram-doses of cortisol and even T3.[107]

As with hydrocortisone, the timing of glandular doses is important – with a vital difference: HC is taken when the body needs cortisol, *but* nutrition needed for its synthesis must be available when the body starts to make cortisol. Cortisol production mainly occurs overnight, when levels rise from their nadir at bedtime to the daily peak at waking. Thus, the single best time to take the glandular is at bedtime. Because "re-feeding" symptoms can occur – with wakefulness, enormous energy and vivid dreams – have patients start one tablet (or less!) in the AM and gradually build their dose – *as tolerated* –to waking, midday-meal and lastly, at bedtime.

Bypass the "roadblocks" with precursors. The HPA-axis may be depressed, meaning insufficient ACTH production – which controls the rate-limiting step of steroid production, the conversion of cholesterol to pregnenolone.[108] This roadblock in the synthetic pathway is easily circumvented by giving pregnenolone – the product – which is over-the-counter safe, inexpensive, and effective.[109,110]

As the precursor of **all** adrenal, gonadal and neuro-steroids, pregnenolone replenishes steroid pathways, starting with progesterone,[111] exerts a mild GABA-ergic effect[112] and can reduce pain/stress responses.[113] Safety is ensured by feedback inhibition[114] and "downstream" enzyme regulation, which prohibit overproduction of cortisol due to any excess of precursors.[115,116]

Start pregnenolone after your patient achieves the full dose of adrenal glandular, *without which* this precursor may be of little avail. Women start with 10 mg daily, usually at bedtime and often need 20 mg daily, which per preference can be divided AM and bedtime. Cycling women often double the dose on cycle days 14-24. Limit a man's dose to 5 mg daily, best at bedtime.

Side effects can occur when *starting* pregnenolone treatment – because it works, allowing patients to make formerly suboptimal hormones: Cortisol production can give excess energy and perhaps wakefulness *early* in the AM. Aldosterone adds a few pounds of water weight as salt is retained. Increased progesterone can enlarge breasts ½ cup-size (concerning in men) with heightened nipple sensitivity. These effects remit in about a month, when the body has adapted to its restored hormone production. Finally, neurosteroids calm people, sometimes quite surprisingly, and menstrual cycling can resume with increased fertility (*caution* – accidents cause people!).

Stress disrupts luteinizing hormone (LH) production, which regulates steroid sex hormone synthesis two ways: LH activates gonadal production of pregnenolone, the step regulated in the adrenal by ACTH. Importantly also, both in adrenals and gonads, LH activates 17-20 desmolase (lyase) to move precursors of cortisol to the sex-hormone pathways, producing DHEA and androstenedione. Chronically stressed patients (CFS, chronic inflammation) have reduced DHEA.[117,118] Supplementing DHEA bypasses the reduced 17-20 desmolase activity.

Prospective studies show DHEA supplementation benefits women with Addison's,[119-121] hypogonadal men,[122-124] soldiers in survival training,[125] and CFS patients.[126] DHEA has OTC safety: "Downstream" enzymes are regulated to prevent over-production of testosterone.[115] However, androgen-excess can follow excessively high DHEA doses *via* conversion in tissues, particularly in the skin (acne, hair loss or hirsutism). Because DHEA is a weak androgen, there is also concern it may compete with testosterone for androgen-receptor binding sites and inhibit its effects.

Men's best DHEA doses are usually 25 mg-daily, *occasionally* 50 mg[122]; women rarely need more than 10 mg (added to pregnenolone). Regardless of dose, oral DHEA usually results in elevated blood DHEA-S, apparently from conjugation during the hepatic first-pass – so, monitor therapy by testing unconjugated DHEA, testosterone, or urine adrenal steroid profile.

Stimulate the depressed HPA-axis. Naltrexone is considered a safe drug[127] and the standard dose is known to stimulate the HPA axis, significantly raising ACTH and cortisol in humans.[128] In low doses (LDN), it has been used successfully to treat the related disorders of chronic fatigue syndrome/myalgic encephalomyelitis,[129] fibromyalgia[130] and complex regional pain syndrome,[131] with benefits including the reduction of pro-inflammatory cytokines[129] (one effect of cortisol) and protection of the microglia.[132]

Insulin resistance (IR). Treatment for suspected IR can begin at the first office visit, sometimes with spectacular results. Diet recommendations are simple: Eat no sugar, no starch, no fruit, nothing sweet (even stevia) and take "vitamins." Technically, the diet is described as low glycemic-index; low insulinemic-index and supplying slowly accessible glucose.[79] Many acceptable versions exist, from Atkins to "*Candida*" to ketogenic.

The lack of sleep worsens insulin resistance.[133,134] Recommend between eight and nine hours of sleep daily and if present, *promptly* address sleep

apnea syndrome. Exercise improves insulin sensitivity in muscles, which consume 75 to 80% of post-prandial glucose-load.[135,136] So, recommend physical activity, at least walking, for 30 minutes every day – understanding that chronically ill-people may need a long time to reach that goal.

Diet and lifestyle measures are more effective than medications.[137] Of these, metformin may best address the fundamental cause of IR – defective insulin-stimulated translocation of glucose-transporter isoform 4 in muscle (and adipose) cells.[138] Berberine has similar effects. Lack of space prohibits discussion of which to choose and how to give them, but it should be noted that both seem to block GI absorption of simple sugars – so they must be taken with a good diet, else lower GI symptoms resembling lactose-intolerance will occur.

The uses of chromium as a nutrient and vanadyl sulfate as a nutraceutical are surprisingly well supported in the medical literature. An excellent effect of these supplements is to curtail cravings for sugar and starch.

Thyroid hormones. The stress-related inhibition of T4-activation is metabolically comparable to driving in first-gear with the parking brake on. Remember: It is adaptive when people are unstable. Therefore, we start thyroid treatment *only* after the patient's adrenals are supported with a "glandular," perhaps a precursor and when they are eating a healthier diet.

The "key" to thyroid hormone dysfunction is this postulate: ReverseT3 (RT3) inhibits the action of T3. The assertion is controversial but as stated above, there is good evidence for it. When the tT3/ RT3 ratio is persistently low, successful treatment is based on a simple fact: Approximately 95% of circulating RT3 is made from T4.[139] To restore a desirable tT3/ RT3 ratio and "release the parking brake," prescribe T3, which will bypass another stress-induced blockade: Dysfunctional T4-deiodination.

Therapeutic T3 acts on the HP-T axis to reduce T4 production, thereby decreasing circulating RT3 and restoring a good T3/RT3 ratio – and cellular thyroid function.[140] When given for chronic conditions (*not* acute), T3 treatment has been reported to be beneficial in a wide variety of laboratory and clinical settings.

Several points must be remembered: The half-life of T3 is brief, so the dose must be divided at least every 12 hours[141] and sometimes every eight. If your patient is hypothyroid and taking T4, divide the T4 dose, then replace some of it cautiously, using a rough equivalency of 5 mcg T4 = 1 mcg T3. Remember, *everyone* needs some T4 – but not 100% T4. Euthyroid-sick patients need to take only T3: They will make their own T4 unless TSH is badly suppressed.

The risks of prescribing biologically identical T3 (*after* adrenals and diet are addressed) are simple: We might give too much – or too little. Therapeutic blood levels should be tested according to peak/trough fluctuations, preferably at mid-dose: Again, the ratio of tT3/ ➤

➤

RT3 is the most accurate measure of the actual thyroid hormone function at the cellular level.

Two therapeutic interactions require attention: First, the stimulatory effects of caffeine relieve some symptoms of ambulatory ESS but that dose can become intolerable once tT3/ RT3 is normalized. Taper-off and stop all caffeine as T3 is cautiously escalated. Secondly, T3 and estradiol have complicated interactions and T3 treatment can "unmask" estradiol deficiency: Sleepless nights and hot flashes may resume *and* T3 will be blamed – but it is not the real problem.

Gonadal hormones. The stress-induced loss of gonadal hormones can have significantly adverse results.[142-145] The trophic effects of steroid sex hormones on the body and brain (they are precursors of neurosteroids) emphasize the importance of treating chronically stressed patients.[146,147]

Strategies for supplementing DHEA and pregnenolone are described above. Their ability to increase sex hormone production was cited – and effectiveness in pain management has been demonstrated in humans.[145,146] Menopausal women can produce normal follicular levels of progesterone and testosterone from pregnenolone and DHEA supplementation – but not estradiol.

Low estrogen levels are significantly correlated with the perception of pain in women worldwide and replacement should be *considered*.[148-152] Certainly, the risk vs. benefit of hormone-replacement therapy must be calculated for each person individually. When a menopausal woman receives the *proper* dose of estradiol (caution: There is a "J-shaped" curve),[153] its CNS-protective effects[154-157] are most reliably achieved with modestly-dosed transdermal delivery. Importantly, although progesterone is beneficial, progestins (not bio-identical) are not – they *worsen* pain and fail to protect the brain.[158]

Sex hormone imbalances are related to insulin resistance. Men excessively convert testosterone to estradiol by insulin-induced aromatase.[159] Natural (chrysin) and prescription (anastrozole or letrozole, in small doses) aromatase inhibitors can restore a desirable testosterone/estradiol balance. Clomiphene, used to overcome hypothalamic hypogonadism (low testosterone) in men,[89] also inhibits aromatase.

Women's 5-alpha-reductase (5α-R) is up-regulated by insulin.[90] This causes unbalanced neurosteroids and is related to PMDD/PMS, dysmenorrhea, menstrual migraines, and even catamenial seizures. A variety of natural 5α-R inhibitors can help (saw palmetto; chaste tree/vitex; turmeric/curcumin; reishi and St. John's wort). These are most effective after the insulin resistance has been addressed by diet, lifestyle, and supplementation as indicated.

Allergy/Hypersensitivity. Successful hyposensitization immunotherapy improves many symptoms associated with fibromyalgia and this treatment is encouraged after proper testing. Alternatively, low-dose allergen immunotherapy (LDA; also enzyme-potentiated desensitization) can succeed[160,161] – sometimes dramatically.

The success of immunotherapy suggests not only that fibromyalgia is associated with non-IgE immune hypersensitivity but that fibromyalgia may have more manifestations than is commonly appreciated. The concept of "central nociceptive hypersensitivity" is generally accepted for somatic nerves (muscle pain, joint pain [TMJ], and trigger points)[162] and reports suggest *visceral* nerves are also involved, causing irritable bowel, pelvic pain, and interstitial cystitis. Does FM also induce cranial nerve hypersensitivity? Cephalgia, olfactory, vestibulo-cochlear and even ophthalmological symptoms can respond to immunotherapy, implying this may be the case.

Psychotherapy. This vital service has earned high esteem: It alone is often successful.[163,164] It is plausible that restoring a patient's body facilitates this work – and referrals from therapists endorse this idea. When we mitigate sympathetic over-drive; correct HP-adrenal problems; relieve dysfunctional thyroid deiodination; restore and balance gonadal hormones; quench hypersensitive immune release of inflammatory cytokines and correct other nutritional and medical issues… how could this fail to improve patients' ability to respond to psychotherapy?

Summary

Persuasive evidence indicates that fibromyalgia and chronic pain conditions often have neuro-psychological origins or amplification, triggering and being maintained by the stress response. Because the central nervous system both regulates and responds to the immune and endocrine systems and the metabolism, the dysfunction becomes a "vicious cycle" in which patients become trapped. The successful practitioner understands mechanisms of this problem – and methodically treats the underlying causes, employing the resources of allied specialists as needed. ◆

References are posted online at www.townsendletter.com.

Alan McDaniel, MD, is a 1977 Tulane medical graduate. He trained in general surgery and emergency medicine before becoming Board-certified in otolaryngology with sub-specialties in neurotology and allergy. He has practiced privately since a two-year faculty appointment at the University of Louisville.

He has presented at various national meetings in the US (AAO-HNS, AAOA, ANS, AAEM, IFM, PAAS) and Mexico. Topics of his lectures and publications have included general surgery and otolaryngology; otology and neurotology; allergy; chronic fatigue and endocrinology. He has been a faculty member for the American Academy of Otolaryngic Allergy Basic and Advanced Courses and for the American Academy of Environmental Medicine. His two-day course "New Endocrinology" has been presented at the AAEM and elsewhere since 2005, to physicians from five continents. Work with dizziness and allergy in the 1980s led him to seek solutions for chronic fatigue syndrome. In turn, these investigations extended to the endocrine aspects of this and related conditions.

Since basic surgical training emphasizes the need to know several alternative approaches to an operation, he saw the logic of studying integrative and controversial medical methods. He has endeavored to understand these in the light of new facts from research, mindful that medical history shows innovation begins as a minority opinion.

Still the Best

A Must Have for Kidney Function Support!

CORDIMMUNE ™

The only cordyceps product that is standardized for and declares its cordycepin content

- Supports mitochondrial function and ATP production
- Modulates immune system
- Enhances athletic performance safely
- An excellent adaptogen and adrenal support
- Supports hematopoiesis
- 0.2% Cordycepin (worth over $100 per bottle)
- 0.3% Adenosine • 22% Polysaccharides

Immune Support Beyond Just Polysaccharides!

CORIO PSP ™

The most clinically researched mushroom in Japan and China

- Unmatched 38% polysaccharides
- Lessens the side effects of toxic treatments
- Raises the quality of life
- Raises the activities of NK cells and macrophages
- Increases thymus weight

The statements herein have not been evaluated by the FDA. This product is not intended to diagnose, treat, or prevent any disease.

CRNA

CANADA RNA BIOCHEMICAL INC.
Tel: (604) 273-2233 • **www.canadaRNA.com**

1-866-287-4986

Helicobacter pylori and Severity of COVID-19: Possible Connection?

by Davis W. Lamson, MS, ND

Abstract
The factors that result in mild versus severe COVID-19 infection have not been fully elucidated. Many viral infections are accompanied by bacterial co-infection. *Helicobacter pylori* infection affects more than one-half of the world population. That statistical factor alone might be a good reason to examine possibilities of *H. pylori* co-infection predisposing to more severe COVID-19 morbidity/mortality. Additionally, the pathology and symptoms of the two infections have overlap and might mutually re-enforce more severe outcomes. This possibility needs investigation by properly checking for *H. pylori* infection across various severities of COVID-19 infection.

Highlights:

- Potentially, a co-infection with COVID-19 could increase lethality.
- One, and perhaps the most extensive, infection is *Helicobacter pylori*, found in more than one-half of the world population.
- Many of the extra-gastric effects of *H. pylori* coincide with effects of COVID-19 infection and could potentially re-enforce them.
- This possibility has not been explored.

Introduction

The title encompasses the idea that severity of any infection might be more intense when accompanied by co-infection. That possibility with respect to COVID-19 is considered with respect to *Helicobacter pylori*, which may be statistically the world's most prevalent infection. There is a wide range of COVID-19 infection severity from asymptomatic to fatality.[1] Certain risk factors for severity of infection have been suspected or demonstrated, such as lower vitamin D level,[2] advanced age, or presence of other underlying illness.[1] However, these are not enough to distinguish between the young asymptomatic carriers and the young who died. Thus, it is easy to imagine that there are major undiscovered factors that might incline to increasing severity. One could be co-infection. While perhaps any co-infection might increase severity of COVID-19, there are reasons to especially consider one.

Many viral infections are known to be accompanied by bacterial co-infections.[3,4] It would seem possible that each could accentuate the pathological or symptomatic effects of the other, especially when there was overlap of the effects. In one study, only 8% of COVID-19 hospital patients were reported to have bacterial or fungal co-infection.[5] If these co-infections were determined by usual culture methods, *H. pylori* would likely not be detectable, and usual short-term anti-bacterial therapy does not eliminate *H. pylori*.

The low 8% figure is unexpected from both the point that many viral infections have high bacterial co-infection rates and as will be seen below, the proportion of persons overall with *H. pylori* infection is considerably higher than 8%.

H. pylori infection is very widespread and includes more than half of the world's population.[6] It is not detected by usual bacterial culture methods.[7] The degree of spread varies geographically, with the highest estimated at 75-80% in some countries and 37% in the United States.[6] (In the US the reported prevalence in non-Hispanic "whites" ranges from 18.4% to 26.2% and "non-whites" from 34.5% to 61.6%.[6] These numbers also correspond to differences in fatality statistics from COVID-19 in those groups.)

H. pylori was first noted in 1983 as the principle cause of gastritis and gastric ulcer.[6] Later it was realized that difficulty from the infection was not limited to the stomach and can be relatively silent in numerous other organ systems. Reviews were published on "extra-gastric manifestations" of *H. pylori* along with many articles on specific manifestations.[8-12]

There are so many coincidental overlaps in the effects of *H. pylori* infection and those of COVID-19 that it raises curiosity about possible connection. Data are presented here to support the reason for research on the title question. A partial list of overlapping pathology or symptoms follows:

- Fever – While considerable publicity has been given to this symptom as a disease marker, about 50% of asymptomatic COVID-19 cases testing positive have no fever.[1] Fever has also been noted in cases of *H. pylori* infection.[13]
- Cough – Dry cough is a frequently cited COVID-19 symptom in 60%.[1] It is cited elsewhere that about one-third have a productive cough.[14] *H. pylori* can likewise produce chronic persistent cough.[15]

- Headache – *H. pylori* has been associated with headache, which resolved when treated with standard *H. pylori* therapy.[16]
- Loss of taste or smell – *H. pylori* has been associated with loss of taste or smell.[17,18]
- Sore throat – *H. pylori* has been cited as a cause of chronic pharyngitis.[19]
- Thrombocytopenia – *H. pylori* has been prominently associated with thrombocytopenia.[13]
- Diarrhea – *H. pylori* may actually protect against diarrhea,[20] but diarrhea is a common effect of immunodeficiency.[21]
- Nausea – In spite of *H. pylori* having symptoms from dyspepsia, gastritis, and nausea of pregnancy, no references to solitary nausea were found.
- Shortness of breath or difficulty breathing – *H. pylori* is associated with chronic bronchitis.[22]

More serious conditions cited for COVID-19 infection (see below) have also been found in patients with *H. pylori*:

- Cardiac arrhythmia[23] – In one large meta-analysis, 33% of *H. pylori* patients were in atrial fibrillation.[24]
- Large vessel stroke[25] – *H. pylori* seropositivity was associated at a high level with large vessel disease.[26]
- Acute kidney injury[27] – *H. pylori* has been responsible for acute kidney injury.[28]
- Cytokine storm[29-31] – *H. pylori* infection creates inflammatory chemistry, particularly via NF-kB and high IL-6, considered the major driver behind the fatal cytokine storm of COVID-19.[32]

Additional Data and Illustration

As an example of bacterial co-infection with viral infection, a Japanese study of 93 persons with hepatitis C infection found 45 (48%) were positive for *H. pylori* infection and that presence of *H. pylori* correlated with the liver fibrosis score.[33]

Negative correlations between levels of vitamin D across various countries and the number of COVID-19 cases and relationship to mortality have been observed.[2] Similarly, vitamin D deficiency was associated with *H. pylori* seropositivity in children and a risk factor for eradication failure of *H. pylori* infection in adults.[34,35]

Chronic respiratory diseases are among the extra-gastric possibilities of *H. pylori*. There are studies of seroprevalence of *H. pylori* as well as meta-analyses suggesting a significant association with *H. pylori*.[36-39] There is also association of *H. pylori* with lung cancer.[40]

Summary

While a number of co-infections might cause COVID-19 infection to be more severe, most are not as "silent' as *H. pylori* can be. The data above provide a statistical basis for the most common infection in the world (*H. pylori*, 37% of persons in the US) accompanying many COVID-19 infections and being a potential reason for increased severity. If the association is found present, this is a relatively easily removed influence that might decrease severity and the various morbidities of COVID-19 infection.

References

1. Baek WK, et al. A Comprehensive Review of Severe Acute Respiratory Syndrome Coronavirus 2. *Cureus*. 2020;12(5):e7943.
2. Ilie PC, Stefanescu S, Smith L. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. *Aging Clin Exp Res*. 2020 May 6:1–4.
3. McCullers JA. The Co-Pathogenesis of Influenza Viruses With Bacteria in the Lung. *Nat Rev Microbiol*. 2014 Apr;12(4):252-62.
4. Bakaletz LO. Viral-bacterial Co-Infections in the Respiratory Tract. *Curr Opin Microbiol.* 2017 Feb;35:30-35.
5. Rawson TM , et al. Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis*. 2020 May 2;ciaa530.
6. Hooi JK, et al. Global Prevalence of Helicobacter Pylori Infection: Systematic Review and Meta-Analysis. *Gastroenterology*. 2017;153(2):420-429.
7. Crowe SE. Helicobacter pylori Infection. *NEJM*. 2019;380;1158-1165.
8. Testerman TL Morris J. Beyond the stomach: An updated view of Helicobacter pylori pathogenesis, diagnosis, and treatment. *World J Gastroenterol*. 2014 September 28; 20(36): 12781-12808.
9. Goni E, Franceschi F. Helicobacter pylori and extragastric diseases. *Helicobacter*. 2016; 21 (Suppl.1):45–48.
10. de Korwin J-D, et al. Helicobacter pylori infection and extragastric diseases in 2017. *Helicobacter*. 2017;22(Suppl. 1):e12411.
11. Ražuka-Ebela D, Giupponi B, Franceschi F. Helicobacter pylori and extragastric diseases. *Helicobacter*. 2018;23(Suppl.1):e12520.
12. Pellicano R, et al. A 2016 panorama of Helicobacter pylori infection: key messages for clinicians. *Panminerva medica*. 2016 December;58(4):304-17.
13. Chen H, et al. Serum cytokines and clinical features in patients with fever and Thrombocytopenia syndrome. *Clinica Chimica Acta*. 494 (2019) 22–30.
14. https://www.webmd.com/lung/covid-19-symptoms#1 (2020)
15. Talaat M, et al. Helicobacter Pylori Infection and Chronic, Persistent Cough: Is There an Association? *Laryngol Otol*. 2007 Oct;121(10):962-7.
16. Sav Li, et al. Is Helicobacter Pylori the Infectious Trigger for Headache?: A Review. *Infect Disord Drug Targets*. 2013 Oct;13(5):313-7.
17. Bezgin SU, et al. Association of Helicobacter Pylori Infection With Olfactory Function Using Smell Identification Screening Test. *Eur Arch Otorhinolaryngol*. 2017 Sep;274(9):3403-3405.
18. Cecchini MP, et al. Might Helicobacter Pylori Infection Be Associated With Distortion on Taste Perception? *Med Hypotheses*. 2013 Sep;81(3):496-9.
19. Zhang J-P, et al. Helicobacter Pylori Infection in the Pharynx of Patients With Chronic Pharyngitis Detected With TDI-FP and Modified Giemsa Stain. *World J Gastroenterol*. 2006 Jan 21;12(3):468-72.
20. Bode G, Rothenbacher D, Brenner H. Helicobacter Pylori Colonization and Diarrhoeal Illness: Results of a Population-Based Cross-Sectional Study in Adults. *Eur J Epidemiol*. 2001;17(9):823-7.
21. Pecoraro A, Nappi L, Crescenzi L. Chronic Diarrhea in Common Variable Immunodeficiency: A Case Series and Review of the Literature. *J Clin Immunol*. 2018 Jan;38(1):67-76.
22. Roussos A, Philippou N, Gourgoulianis KI. Helicobacter pylori infection and respiratory diseases: a review. *World J Gastroenterol*. 2003;9(1):5-8.
23. Long B, et al. Cardiovascular complications in COVID-19. *Am J Emerg Med*. 2020 Apr 18;S0735-6757(20)30277-1.
24. Tetta C, et.al. Association Between Atrial Fibrillation and Helicobacter Pylori. *Clin Res Cardiol.* 2019 Jul;108(7):730-740.
25. Oxley TJ, et al. Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young. *NEJM*. 2020 May 14;382(20):e60.
26. Markus HS, Mendall MA. Helicobacter pylori infection: a risk factor for ischaemic cerebrovascular disease and carotid atheroma. *J Neurol Neurosurg Psychiatry.* 1998 Jan;64(1):104-7.
27. Adapa S, et al. COVID-19 and Renal Failure: Challenges in the Delivery of Renal Replacement Therapy. *J Clin Med Res*. 2020 May;12(5):276-285.
28. Case Records of the Massachusetts General Hospital. Weekly Clinicopathological Exercises. Case 10-1999. A 53-year-old Man With Acute Renal Failure, Cortical Blindness, and Respiratory Distress. *NEJM*. 1999 Apr 8;340(14):1099-106.
29. Ye Q, Wang B, Mao J. The Pathogenesis and Treatment of the `Cytokine Storm› in COVID-19. *J Infect*. 2020 Jun;80(6):607-613.
30. Pedersen SF, Ho, YC. SARS-CoV-2: a storm is raging. *J Clin Invest*. 2020 May 1;130(5):2202-2205.
31. Sanchez CI, Levy HR. COVID-19 and cytokine storm syndrome. https://www.mlo-online.com/continuing-education/article/21138224/covid19-and-cytokine-storm-syndrome.
32. Subhash VV, Ho, B. Inflammation and proliferation- A causal event of host response to H. pylori infection. *Microbiology*. 2015 Jun;161(6):1150-60.
33. Umemura T, et al. Anti-Helicobacter pylori seropositivity: influence on severity and treatment response in patients with chronic hepatitis C. *J Viral Hepatitis*. 2007;14:48–54.
34. Gao T, et al. Association of Helicobacter pylori Infection With Vitamin D Deficiency in Infants and Toddlers. *Am J Trop Med Hyg*. 2020 Mar;102(3):541-546.
35. Yildirim O, et al. The influence of vitamin D deficiency on eradication rates of Helicobacter pylori. *Adv Clin Exp Med*. 2017 Dec;26(9):1377-1381.
36. Caselli M, et al. Helicobacter pylori and chronic bronchitis. *Scand J Gastroenterol*. 1999;34(8): 828-830.
37. Bennett D, et al. Helicobacter pylori seroprevalence in patients with idiopathic pulmonary fibrosis. *Eur Respir J.* 2014, 43(2): 635-638.
38. Wang L, et al. Association between chronic respiratory diseases and Helicobacter pylori: A *meta*-analysis. *Arch Bronconeumol*. 2015, 51(6): 273-278.
39. Wang F, et al. Association of Helicobacter pylori infection with chronic obstructive pulmonary disease and chronic bronchitis: a *meta*-analysis of 16 studies. *Infect Dis* (Lond). 2015; 47(9): 597-603.
40. Gonzalez I, Araya P, Rojas A. Helicobacter Pylori Infection and Lung Cancer: New Insights and Future Challenges. *Zhongguo Fei Ai Za Zhi*. 2018 Sep 20;21(9):658-662.

◆

Davis W. Lamson, MS, ND, practices at Tahoma Clinic in Tukwila, Washington, with chief interests in autoimmunity and cancer. He has published over thirty-five research and review papers, including the subjects of hepatitis C, controlling MRSA, stimulating immune function, emphysema, autism, diabetes, gastroesophageal reflux, kidney failure, autoimmunity, and various cancer-related topics.

The Stressed Brain – A Clinician's Perspective Part 2

by Jonathan E. Prousky, ND, MSc, MA, RP(Qualifying)
Professor, Chief Naturopathic Medical Officer
Canadian College of Naturopathic Medicine

Full article (Parts 1 and 2) and the references are posted online at www.townsendletter.com.

Prenatal and Postnatal Early Life Experiences Alter Biology and Create Life-Long Vulnerability

Research has consistently shown that early life experiences promote a more vulnerable or hardy (i.e., resilient) human being. McEwen and Getz[7] reviewed animal research demonstrating that "early life experiences become biologically inscribed" (p.S22). They noted that factors before birth (e.g., prenatal stress) and those occurring postnatally (e.g., extended separation of the infant from mother) can impair normal brain development and function. By contrast, adequate maternal care and consistent caregiving benefited the offspring by creating durable patterns of reduced anxiety, more efficient stress reactivity, and better social and cognitive development. There are also transgenerational effects that have been shown to be behaviorally and genetically transmitted by mother rats to their offspring. For instance, environmental manipulations that alter maternal rat behavior will impart nongenomic differences in stress reactivity across generations of female offspring.[21] Similarly, environmental manipulations that increase maternal stress during pregnancy resulted in genetically transmitted alterations in hypothalamic-pituitary-adrenal (HPA) axis reactivity to stress and anxiety-like behaviors among second generation male rats.[22]

In humans, similar findings have shown that stress does become biologically inscribed in human fetuses and children and yields effects that endure well into adulthood. One of the more salient (and perhaps extreme) examples of this comes from an extensive systematic review done on the intergenerational (or transgenerational) effects of Holocaust survivors and the mental health of their offspring (a.k.a., ***Holocaust survivor offspring***; HSO).[23] The findings of this review yielded convincing evidence of intergenerational effects that showed associations between parental mental health, perceived parenting and attachment quality, and increased psychiatric symptoms among HSO, including high conflict and less cohesion within families of HSO. Having two survivor parents was associated with greater mental health problems among the HSO compared to having only one survivor parent. The HSO also exhibited a heightened vulnerability for stress, but this seemed to only happen when faced with genuine danger. Lastly, intergenerational effects on cortisol modulation (i.e., levels) was also evidenced among the HSO.

Heritable factors, such as genetics, also represent an avenue that exposes how stress becomes biologically inscribed. For instance, some human carriers of a particular allele – i.e., the methionine allele of the valine 66met ***brain-derived neurotrophic factor*** (BDNF) polymorphism or the Val66Met polymorphism in the BDNF gene – have inherited genetics that influence the expression of this important growth factor.[11] BDNF is a "major neurotrophic factor that plays an important role in the formation, guidance, and survival of neurons during development but also in synaptic plasticity and survival in the adult brain" (p.410).[24] Having this polymorphism can result in lower grey matter volume in the hippocampus and PFC due to alterations in the production and expression of BDNF, thus, undermining synaptic or cellular plasticity and neurogenesis in response to stress exposure.[11] This particular polymorphism is also linked to impaired episodic memory, as well as cognitive impairment in older adults more than 55 years of age.[25]

In keeping with our discussion about genetics, other alleles can impact stress regulation over the course of a person's life. Aggression from difficulties coping with stress, for example, can arise due to genetic variants that are associated with increased ***monoamine oxidase-A activity*** (i.e., results in an increased breakdown of monoamine neurotransmitters, such as dopamine, norepinephrine, and serotonin).[26,27] This speaks to the concept known as ***reactive alleles***, which refers to how some gene variants increase or decrease in response to environmental influences like stress.[7] The point is that all allelic variants are in a sense reactive, whether the heritable variants involve BDNF or those variants are associated with monoamine oxidase-A; when combined with environmental stressors, phenotypic expression changes, which may facilitate allostasis, or may result in

enduring patterns of allostatic load (AL) and/or allostatic overload (AO).

The length of ***telomeres*** is another example of how stress becomes biologically inscribed. A telomere is a region situated at each end of a chromosome, which protects the chromosome from deterioration while preserving vital genetic information.[28] Age-related health problems and diseases have been consistently associated with excessive or accelerated telomere shortening.[28] Stress, resulting in the release of glucocorticoids, has been shown to reduce the levels of antioxidant proteins, leading to increased oxidative damage to DNA, and quickened telomere shortening.[28] Cross-sectional human studies have demonstrated associations between compromised telomere integrity and high levels of psychosocial stress exposure.[29] Even factors that happen before birth, such as prenatal stress exposure, have been shown to be a significant predictor of subsequent shorter leukocyte telomere length in young adulthood. These findings are believed to represent an important biological pathway that broadly influences the "developmental origins of adult health and disease risk" (p.E513).[29]

Other, and perhaps more relevant research to the practicing clinician, involves associations between large cohorts (i.e., involving several thousand individuals or more) that experienced ***adverse childhood experiences*** (known as ACEs) and enduring problems in adulthood. ACEs have been described by the CDC as potentially traumatic experiences happening in childhood (i.e., between 0-17 years of age) that comprise a child's sense of safety, security, and bonding, and include all or some of the following: witnessing or experiencing violence in the home or community; experiencing neglect; having a family member attempt or die by suicide; and being in a household with substance misuse, mental health problems, or parental separation or members of the household being in jail or prison.[30] Increasing amounts of ACEs have been associated with adult health risk behaviors and diseases.[31] Compared to individuals without any ACEs, those exposed to four or more categories of ACEs experienced a 4- to 12-fold increase in alcoholism, drug abuse, depression, and suicide attempt. The same individuals had a 2- to 4-fold increase in smoking, poor self-rated health, 50 or more sexual intercourse partners, and sexually transmitted disease. There was also a 1.4- to 1.6-fold increase in physical inactivity and obesity. This data was sadly presumed to have underestimated the actual consequences of ACEs, and their relationship to adult risk behaviors and diseases.

Additional data has demonstrated that a graded relationship exists between ACEs and the risk of attempted suicide.[32] Merely having experienced an ACE was associated with a 2- to 5-fold increased risk of attempted suicide. Individuals without ACEs were shown to have a 1.1% prevalence of attempted suicide. Though the statistical marker known as odds ratio is somewhat different from prevalence, individuals with seven or more ACEs had an odds ratio of attempted suicide of 31.1%. Other studies evaluating the impact of ACEs demonstrated an association between elevated ACE exposures or scores and problems in adulthood that include childhood autobiographical memory disturbance,[33] alcoholism and depression,[34] depressive disorders,[35] and hallucinations.[36]

There are also consequential changes to brain structures and function, and overall physiology that result from ACEs. Several examples are provided here to demonstrate this association. A report that documented a 10-year history of children growing up with mothers having chronic depression, showed larger amygdala volumes in the childrens' brains.[37] Another report identified increased negative functional connectivity between the PFC and amygdala among adolescents exposed to physical, sexual, or emotional abuse compared to adolescents without a history of maltreatment.[38] These findings were more pronounced among adolescents that had more severe abuse, and were also associated with higher amounts of ***externalizing psychopathology*** (e.g., opposition/conduct and attention disorders) some 2 years later. Other data has shown that children raised without sufficient verbal stimulation, and in unstable home environments were more likely to develop impaired cognitive function, increased systemic inflammation, cardiovascular disease, substance abuse, anti-social behavior, and depression.[39,40]

Prenatal and postnatal stress become biologically inscribed, impacting vulnerable brain structures and altering physiology.

Above all, prenatal and postnatal stress does become biologically inscribed by adversely impacting vulnerable brain structures, altering physiology, and shaping adult development. Not surprisingly and almost in a rather banal way, a combination of these aforementioned factors disrupt allostatic mechanisms to such a great extent, practically guaranteeing AL and AO, psychopathology, physical disease, and a cascading path of enduring mental and physical problems lasting well into adulthood.

Chronic Stress and Social Isolation, Loneliness, and Socioeconomic Status

Similar to prenatal and postnatal stress, social isolation, loneliness, and socioeconomic status (SES) activate allostatic systems, and result in AL and AO due to detrimental life outcomes, pathophysiological changes, and consequential brain changes.

Social isolation and loneliness are common experiences that all of us have endured (or will endure) at certain times over the course of our lives. In a meta-analytic review on loneliness and social isolation, Holt-Lunstad et al defined these terms and then analyzed aggregated data to determine associated health outcomes.[41] ***Social isolation*** was defined as living alone, having infrequent social contacts, and having sparse social network connections. ***Loneliness*** represented the subjective experience of social isolation, resulting from disparities between one's desire

➤

➤

for social relationships and one's actual social relationships. The results of the meta-analytic review showed social isolation and loneliness to yield weighted average effect sizes that increase the risk of mortality in a manner comparable to other health risk factors like obesity, substance abuse, physical inactivity, and mental health problems. Specifically, the odds ratio of increased mortality was 1.29 (29%) for social isolation, 1.26 (26%) for loneliness, and 1.32 (32%) for living alone.

In a review paper, Cacioppo and Hawkley described underlying mechanisms associated with social isolation.[42] Individuals that perceive themselves to be socially isolated often experience insecure adult attachments that beget physiological changes characterized by activation of the sympathetic nervous system (SNS), the sympathetic adrenomedullary (SAM) system, and the hypothalamic-pituitary-adrenal (HPA) axis. Additionally, perceived social isolation becomes its own stressor and produces negative emotions (e.g., depression and anxiety), negative reactivity (e.g., hostility, mistrust, and irritability), and reduced feelings of self-worth, happiness, and life satisfaction. The autonomic patterning of socially isolated individuals is also characterized by a higher total peripheral resistance, and lower cardiac output. These latter effects degrade both central and peripheral hemodynamics leading to increased vascular resistance and decreased vascular compliance, and the likely development of hypertension. Perceived social isolation also undermines repair and maintenance functions and weakens anabolic processes, such as wound healing time and restorative sleep (i.e., lower sleep efficiency and higher wake times after sleep onset).

Similar to social isolation and loneliness, SES is also a significant stressor since it imposes disadvantages and impediments that undermine a person's ability to succeed in life for countless reasons. McEwen and Getz cited several sources when documenting the deleterious effects of low SES and perceived SES.[7] They cited research demonstrating that individuals having low SES are at greater risk for "predisease" conditions, such as obesity, metabolic syndrome, substance abuse and psychiatric disorders (p.S23). Similarly, they noted other research that showed an association between perceived low SES and a poor sense of control and low self-esteem.

The brain is the primary organ that mediates how a person perceives and responds to chronic stressors.

With respect to brain changes, there is evidence of deleterious effects arising from social isolation, loneliness, and SES. For example, the chronic stress associated with individuals perceiving themselves to have a low social standing (i.e., a composite marker that includes standard measures of SES) was linked to reduced grey matter volume in the ***anterior cingulate*** cortex (ACC) located proximally to the prefrontal cortex (PFC).[43] This was deemed important because this particular neuroanatomical area plays a role in how people experience emotions and regulate their behavioral and physiological reactivity to psychosocial stress. Even low perceived parental standing – known to be a likely indicator of socioeconomic hardship during childhood and adolescence – was "associated with greater amygdala reactivity to threatening (angry) facial expressions" in "healthy individuals who had not yet reached their adult SES" (p.203).[44] This finding was believed to represent a neurobiological pathway by which early SES experiences become biologically embedded, impacting allostatic systems, and likely future health and disease vulnerability.[44]

Research on social isolation has reviewed brain changes among individuals that spent 14 months living in isolation in the Antarctic.[45] The results showed statistically significant reductions compared to controls in the hippocampal volume of the ***dentate gyrus*** from before to after the expedition. This particular part of the hippocampus contributes to the formation of episodic memories.[46] The results showed that other hippocampal regions and even several regions of the PFC had reduced volumes compared to controls but these changes did not reach statistical significance.[45] Serum BDNF levels were also measured before and after the expedition. Compared to serum measurements before, BDNF levels dropped during the expedition and did not recover to their pre-expedition levels when assessed 1.5 months after the expedition had ended. The decreased serum BDNF levels that happened during the expedition were also associated with reductions in the hippocampal volume of the dentate gyrus, and reduced cognitive performance (i.e., as shown by tests of spatial processing and selective attention). The results of this study demonstrated how vulnerable the dentate gyrus of the hippocampus is to environmental deprivation, and revealed similarities to animal studies in which "neurogenesis, stress-induced behavioral changes, and environmental deprivation" adversely impacted this particular hippocampal region as well (pp.2274-2275).[45] Even though the sample size was very small in this study (n=9) and other factors might have contributed to the observed brain changes from environmental deprivation, it is clinically plausible that similar brain changes and reductions in BDNF and cognitive performance will be found among people living socially isolated lives.

Chronic Stress and Personality

It would seem important to consider personality as a potential influencer of chronic stress, as it plays an essential role in facilitating and/or moderating how the brain and body respond to ongoing challenges. Canli extensively reviewed extraversion (E) and neuroticism (N) – both of which are heritable personality traits – and determined associated brain imaging mechanisms.[47] ***Neuroticism*** as a personality trait encompasses individuals that are more likely to be moody and to experience feelings such as worry, fear, anxiety, anger, frustration,

guilt, depressed mood, and loneliness. ***Extroversion*** as a personality trait refers to individuals that are sociable, talkative, assertive, excitable, have lots of energy, and tend to be full of life and energy. Canli's study showed that Individuals with dominant E traits experience more positive affect in their daily lives compared to individuals with dominant N traits that experience more negative affect in their daily lives. These personality orientations were enduring and noted to last "for periods of up to 10 years" (p.1106). The affective associations between individuals with E and N personality dispositions may also be mediated to some extent "by cognitive biases in the processing of emotional stimuli" (p.1107).[47]

When Canli evaluated subjects with brain imaging, he found differences between these two types of personality dispositions.[47] Individuals high in E showed greater activation of the amygdala when positive images or happy faces were shown. Individuals high in N exhibited greater activation of the amygdala when negative images were shown. Why does this seem important? The amygdalar activation was oriented towards positive and negative stimuli and was specific to these personality types. These brain differences in personality were also postulated to have some involvement in resilience and vulnerability factors for specific types of psychopathologies. Cited data pertaining to individuals high in N (or higher N relative to lower E) showed more vulnerability towards the development of eating disorders, low self-esteem, post-stroke depression, and more unfavorable outcomes when being treated for depression.

Interested readers may want to additionally review an important cohort study that documented increased all-cause mortality among individuals having a N personality disposition (i.e., based on a composite of pessimistic, anxious, and depressive personality traits).[48] These individuals were assessed early in life, and their N personality disposition had significant negative consequences on mortality when evaluated over four decades (i.e. a hazard ratio of 1.42 or 42% in the primary analysis). Other studies were also cited showing a relationship between N personality traits and increased mortality (see Table 5, p.498).[48] Some of the biological mechanisms believed to be responsible for the increased all-cause mortality among individuals with a dominant N personality disposition included the following: hippocampal atrophy and other brain lesions; stress and depression causing "increased heart rate, hypertension, increased plasma norepinephrine levels, or changes in blood coagulation that may increase the risk of cardiovascular disease"; and stress causing reduced immune system responsiveness and a greater risk of cancer (p.496). Other mechanisms attributed to individuals with the N personality disposition and the finding of increased all-cause mortality included poor self-care, unhealthy behaviors, and underutilizing healthcare resources and/or poor compliance with treatment.

There are certainly other personality types – i.e., other than N and E – that modulate chronic stress, impact the brain, and are also associated with diverse health outcomes. The N personality type was highlighted here because it seems to more commonly occur in my clinical practice and is perhaps more deleterious than other personality types in relation to chronic stress and adverse health outcomes.

Chronic Stress and Medical Disease

As mentioned near the beginning of this paper, there are four different types of allostatic responses, and for three of them the resulting biological adaptations would be required to manage alterations in cortisol[9] (as well as adaptations resulting from activation

Stressed Brain

of the SAM system[49]) over prolonged periods of time. In this section, I will briefly review the links between chronic stress and medical (i.e., physical) disease, and highlight what happens when the body is unable to cope with stress resulting in a breakdown of bodily resources. For example, chronically elevated cortisol levels due to persistent or poorly managed psychosocial stress could promote insulin resistance leading to weight gain and obesity. In one such publication, the dichotomous roles of cortisol were described in relation to what it does in the short-term compared to its deleterious effects when there is persistent and poorly managed psychosocial stress over the long-term.[50] When the physiological stress response leads to the release of cortisol, there will be an abrupt impairment of insulin secretion and an increase in the production of hepatic glucose. However, should the stress response persist for a prolonged duration, it will inhibit insulin secretion, impair insulin-mediated glucose uptake, and disrupt insulin signaling within skeletal muscle. Individuals can compensate homeostatically by increasing pancreatic beta-cell function, or by increasing the release of insulin. However, when stress becomes prolonged, insulin resistance develops, or becomes worsened by established obesity, resulting in biological adaptations that cause hyperglycemia and adverse metabolic consequences.

In addition to weight gain, obesity, and metabolic consequences, there

➤

➤

are other stress-related diseases that are presumed to result from prolonged biological adaptations to cortisol secretion, including biological adaptations resulting from activation of the SAM system. The list includes asthma, gastrointestinal diseases (e.g., ulcerative colitis), functional gastrointestinal diseases, coronary heart disease, rheumatoid arthritis, migraine headaches, being more susceptible to cold viruses, nonalcoholic liver disease, neurodegenerative disorders (e.g., Alzheimer's and Parkinson's disease), and even cancer.[51,52] The list of diseases that are stress-related, however, is likely to be much greater since prolonged (i.e., chronic) stress is considered a common risk factor in 75%-90% of all diseases.[52]

The implicating factor in all these diseases involves an inability to discharge or effectively manage perceived stress over time, which of course strongly implicates the brain because it is the primary organ that mediates how a person perceives and responds to chronic stressors. In fact, the continued ***uncertainty*** (i.e., when anticipated outcomes are unexpected) associated with chronic stress is believed to create a situation in which the brain cannot meet its demand for extra energy, and because of ***failed stress habituation*** (i.e., the inability to "attenuate autonomic, endocrine, and metabolic reactions when repeatedly exposed to the same hostile environment"), the resulting AL and subsequent AO yields both systemic pathology (as described above), as well as brain malfunction or pathology (will be described in the next section; p.167).[53]

Chronic Stress, Psychiatric Illness (Mental Disorders), Suicide, and Brain Mechanisms in General Terms

When faced with chronic stress, which seems to always be adjoined with the subjective experience of uncertainty, some individuals will be able to habituate (a.k.a., habituators) and attenuate their biological stress mechanisms. However, some individuals will be unable to habituate, and therefore their biological stress mechanisms will continue to disrupt the healthy functioning of their entire biological system (i.e., resulting in AL), which adversely impacts both the brain and body. As pointed out by Peters et al, when uncertainty cannot be resolved this leads to a "vicious cycle of altered brain architecture and systemic pathophysiology, which further damages the capability of the subject to cope with uncertainty" (p.168).[53] When this proceeds for too long or when resources to attenuate the chronic stress become depleted and damaged, AO ensues, and gives rise to brain malfunction or pathology.[53]

It is of no surprise then that life events, such as the unexpected COVID-19 pandemic, are major players in the difficult subjective experience of uncertainty. The brain must have sufficient energy to meet its high metabolic demands in the face of chronic stress and uncertainty. When there is failed habituation, which happens for some individuals, the levels of self-esteem and locus of control are significantly diminished, placing the individual at high risk of ***mental morbidity*** and mortality.[53] With respect to mental morbidity, there also exists a significant body of literature demonstrating a relationship between life events and the onset of psychiatric illness. Apparently, the strength of associations between stressful life events (i.e., also often mired in uncertainty) and psychiatric illness is stronger than similar associations and the development of medical disease.[51]

Though the names of psychiatric illnesses differ diagnostically, what is apparent is that the brain mechanisms implicated in chronic stress are more similar than dissimilar across a broad range of neuropsychiatric phenomena. For example, when an individual is faced with uncertainty arising from chronic stress and cannot habituate, specific areas of the PFC activate the ACC because it "assesses the degree of uncertainty about whether future outcomes are uncertain"(p.166).[53] This results in activation of the amygdala and an ensuing stress response - mediated by the release of norepinephrine - that leads to a hypervigilant state, and simultaneous activation of the SNS (increases glucose for energy utilization) and the HPA axis (increases cortisol) that plays a vital role in synaptic plasticity and learning after stress.[53] The released cortisol passes through the blood-brain-barrier and binds to glucocorticoid receptors in and on neurons of the amygdala, hippocampus, and PFC (i.e., three key brain structures mentioned earlier in this paper).[51] In simple terms, the net result leads to feelings of threat and loss of control, concomitant with damaging alterations to brain architecture within these three key brain areas, and greater bottom-up control via the ACC-amygdala complex that is not being properly attenuated by specific areas within the PFC.[53]

When looking at a broad range of psychiatric illnesses, it should come as no surprise that many of the same brain mechanisms are implicated. This strongly suggests that chronic stress is a significant or major underlying trigger for the majority of psychiatric illnesses. As Patriquin and Mathew pointed out, "Chronic stress may be one cross-cutting construct or dimension (i.e., that occurs across diagnostic categories defined by

Table 3. Mediators and outcomes of chronic stress

Mediators of AL and AO	Implicated brain structures	Possible health outcomes that further mediate AL and AO
Stress-vulnerability Prenatal and postnatal early life experiences Social isolation, loneliness, and SES Neuroticism personality type Uncertainty	Prefrontal cortex Amygdala Hippocampus	Atrophy and damage to these brain structures Low self-esteem Diminished locus of control Premature mortality Poor quality of life Medical disease Mental morbidity, psychiatric illness and/or suicide

the DSM-5) related to GAD, as well as other diagnoses (such as highly related MDD)" (p.2).[54] In the section below, I will review brain mechanisms in general terms that become triggered by chronic stress for several common psychiatric illnesses, such as generalized anxiety disorder (GAD), major depressive disorder (MDD), PTSD, and even borderline personality disorder (BPD).

In GAD, for example, the ACC-amygdala complex gets activated under situations of chronic stress, resulting in decreased connectivity between the amygdala and PFC, making it very difficult for such individuals to effectively regulate their emotions.[54] These brain circuit issues are implicated in symptoms, such as anxious arousal, attentional bias to threat, avoidance, and even helplessness behavior.[54] Similarly, in MDD, chronic stress leads to impairment in PFC function, an overactivated amygdala resulting in more fear-based or bottom-up control, and a concomitant downgrading of hippocampal functioning.[55] Some of the common features of MDD, such as neurocognitive impairment, withdrawing from aversive environments, and anhedonia are linked to these brain circuit issues.[55] In PTSD, there is impaired PFC function, elevated cortico-amygdala activity resulting in heightened vigilance and reactions to threatening stimuli, and reduced cortico-basal ganglia reward sensitivity.[56] In an older publication on PTSD, the amygdala was noted to exert an overarching influence upon the hippocampus causing reduced functionality and hypermnesia for stressful experiences, behavioral disinhibition, and impaired PFC function.[57] In BPD, affect dysregulation happens because certain areas within the PFC are known to be impaired (i.e., as evidenced by abnormal neuronal activity and prefrontal hypometabolism), and is also associated with top-down processing problems.[58] Disruptions in prefrontal-limbic circuitry have also been found among people with BPD due to functional disconnectivity between the amygdala and various regions of the PFC with associated volume reductions noted in the amygdala, hippocampus, and in several other subcortical brain regions.[58] The amygdala is also believed to be overactive or poorly controlled among BDP patients, such that it directs "their unfiltered attention to predominantly negative and threatening social stimuli" (p.842).[58]

Outside of psychiatric illnesses, suicide has not specifically been addressed though chronic stress and vulnerability have been proposed as the key triggers toward dying by suicide. Heeringen and Mann noted that "suicide is the result of an interaction between state-dependent (environmental) stressors and a trait-like diathesis or susceptibility to suicidal behaviour, independent of psychiatric disorders" (p.63).[59] For a brief review of additional theoretical models of suicide see the reference noted here.[60] Similar to our previous discussion on childhood adverse experiences, early life adversity appears to affect suicide risk because of alterations to brain architecture, dysregulation of the stress response, and likely cytotoxic effects from excessive concentrations of increased CRH and glucocorticoids.[59] In terms of neurobiological mechanisms, certain genetic variants (i.e., alleles for lower expression of the serotonin transporter gene 5HTTLPR) associated with suicide are linked to "impaired connectivity between the prefrontal cortex, amygdala, and anterior cingulate" (p.68).[59]

Though the clinical manifestations of the aforementioned psychiatric illnesses are both similar and different, they are also principally related to the same key brain areas. Suicide and certain genetic variants were also noted to involve the PFC, amygdala, as well as other brain areas. The genetics and epigenetics, however, of the noted psychiatric illnesses (as well as others) and suicide is very complex and plays an important role in how the brain mediates stress, and the ensuing biological responses. Interested readers should review the following references[(i.e., 54-59, 61)] to further understand this complex subject matter.

Conclusion

There ought to be no further dispute or controversy about the devastation that chronic stress imposes on both the body and brain. Chronic stress, as noted earlier, is pathological and happens when allostatic mechanisms fail to adapt because resources have been exhausted. The brain, the principal organ that perceives and determines how an individual responds to the world, is subject to multiple stressful and chronic insults that increase the risks of body and brain damage, disease, psychiatric illness, and other health outcomes (Table 3). Thus, understanding what stresses the brain is of paramount importance for any clinician whose aim is to provide treatment that regulates the brain and alters a patient's current and future morbidity and mortality. ◆

Full article (Parts 1 and 2) and the references are posted online at www.townsendletter.com.

Dr. Jonathan E. Prousky graduated from Bastyr University (Kenmore, Washington) in 1998 with a doctorate in naturopathic medicine. He furthered his clinical training by completing a family practice residency sponsored by the National College of Naturopathic Medicine (now the National University of Natural Medicine). In 2008 he obtained a master of science degree in international primary health care from the University of London, which focused on clinical epidemiology and evidence-based research. In 2016 he obtained a master of arts degree in counselling psychology from Yorkville University.

At the Canadian College of Naturopathic Medicine, Dr. Prousky's primary responsibility is the delivery of safe and effective naturopathic medical care in his role as the chief naturopathic medical officer. He was the first naturopathic doctor to receive the "Orthomolecular Doctor of the Year" award in 2010. In 2017 he was also the first naturopathic doctor to be recognized for his longstanding commitment to mental health by being inducted into the "Orthomolecular Hall of Fame." Dr. Prousky is the author of several texts, such as *Textbook of Integrative Clinical Nutrition*, and *Anxiety: Orthomolecular Diagnosis and Treatment.*

Estrogen Vindication, Part 3: The Tamoxifen Connection and Hormone Therapy

by Devaki Lindsey Berkson, DC

All three parts of this article are posted with appendices and references online at www.townsendletter.com.

Medical practitioners thought tamoxifen worked because it was an anti-estrogen. But tamoxifen works in a wide variety of anti-cancer mechanisms, not just by tamping down estrogen. In fact, tamoxifen can often raise estrogen levels. Of the 20 studies between 1980 and 2008 that showed estrogen was not only safe for breast cancer patients but was also protective, only the HABITS study found an increased risk of recurrence in breast cancer patients on HRT. This risk only occurred if the women were on tamoxifen, which "blocked" the action of estrogen.

Tamoxifen

A major argument that estrogen causes or promotes breast cancer is that tamoxifen helps to reduce or retard the growth of ER positive breast cancer by competitively blocking the binding of estrogen to the estrogen receptor on breast cancer cells. Several lines of research, according to correspondence with Dr. Avrum Bluming, a California oncologist and co-author of *Estrogen Matters*, dispute this belief.

- When tamoxifen is given to premenopausal women, their natural estrogen levels increase up to five-fold.
- This rise in estrogen should block any competitive binding of tamoxifen, yet it doesn't. Tamoxifen's protective effect against breast cancer works as well in premenopausal as postmenopausal women.
- Approximately 40% of ER+ patients fail to respond to tamoxifen.
- Cancer is "growth out of control" worsened by "growth factors." Tamoxifen inhibits growth factor stimulatory effects involved in breast cancer even in the absence of estrogen, pointing a finger at initiators of breast cancer other than estrogen.
- Estrogen added to tamoxifen can help make tamoxifen work better. After treatment with tamoxifen, some breast cancer cells acquire the ability to proliferate. These cells become "resistant" to the protective action of tamoxifen. But when low doses of estrogen are then given, this helps cancer cells die (apoptosis). Estrogen therapy helps breast cancer cells overcome tamoxifen resistance by adding estrogen.
- Tamoxifen has also been shown to have a therapeutic effect on ER *negative* breast cancer cells, both in laboratory studies and in human patients, pointing to other cancer protective effects of tamoxifen than affecting estrogen receptors.

In summary, tamoxifen works through a protective number of portals that have nothing to do with the estrogen receptors. Exactly how tamoxifen protects against breast cancer isn't completely known. But it's inaccurate to say tamoxifen mainly works as an anti-estrogen, and thus estrogen is the main driver of breast cancer.

In 1980, Torbin Palshof from Copenhagen, Denmark, published the results of a study comparing adjuvant estrogen with adjuvant tamoxifen in the management of patients with treated breast cancer. From 1975 to 1978, 387 patients who were admitted to three breast cancer clinics in Copenhagen entered the study. Subjects were women younger than 70 years of age, with T1 to T4, N0 to N3, M0 breast cancers. There could be no history of previous or concomitant malignancy. Treatment involved simple mastectomy without routine axillary dissection and postoperative irradiation. Two weeks after surgery, patients were randomized to double-blind endocrine therapy for two years.

After a median duration of observation of three years, 91 recurrences were observed.

The investigators concluded that despite the limited number of patients and time of observation, a marked effect of tamoxifen on recurrence rate was observed in postmenopausal patients as well as:

- An even higher reduction in the rate of recurrence was achieved when estrogen was added to the tamoxifen therapy.
- ER assay positivity did not correlate adversely with prognosis among patients treated with estrogen.
- There were no recurrences among the ER-positive patients who received adjuvant estrogen therapy.

DES vs. Tamoxifen

Dr. JoAnn Manson, one of the lead researchers on the WHI, has come around to looking at estrogen in a new way. Dr. Manson said the breast protective effects seen in the estrogen-only arm in the WHI was probably due to estrogen's ability to act like tamoxifen. But tamoxifen is an anti-estrogen. How can an estrogen act like an anti-estrogen? Oy veh.

To answer this question, we have to go back to DES (diethylstilbestrol), the most powerful synthetic and pharmaceutical estrogen ever invented, fifty times more powerful than our own naturally made estrogen. Sir Charles Dodds, the same

doctor and scientist who invented plastics (which are also estrogenic), created it.

DES was given to many millions of pregnant women for 36 years. It was outlawed in 1971 when it was finally proven to be the most powerful endocrine-disrupting and cancer-causing drug even invented. It is now labeled a Class-1 carcinogen, never to be used during pregnancy. But it was the preferred method of treating metastatic breast cancer in the 1960s and 1970s. Metastatic cancer is when cancer cells have spread from the initial primary tumor out into other parts of the body. This is diagnosed as a life-threatening stage 4 cancer.

How can that be? The original studies showed it shrank tumors in many women with breast cancer. DES was so effective that it was described as making tumors dissolve in 30% of women treated with it.

Craig Jordan, PhD, (credited with getting tamoxifen recognized as a breast cancer treatment and now working on hormone therapies for breast cancer patients so they don't miss out on a higher quality of life), said, "Large tumors would just melt away, but you needed sledgehammer doses to do it – 50 times more than a woman would normally have in her body." Thus, DES was used until tamoxifen was found to work as well – not better, but with less adverse effects; DES was being linked to other nasty things. When the Mayo Clinic's 1981 head-to-head comparison of tamoxifen with DES showed similar response rates – and far fewer adverse responses in tamoxifen users – breast oncologists switched *en masse* to the newer agent. By that time, DES had also gained a reputation for producing a rare vaginal tumor cancer in the daughters of women who used DES to sustain their pregnancy.

The longer-term follow-up studies were rather mind-bending. The Mayo Clinic ran a follow-up analysis of one of its older studies comparing DES treatment to tamoxifen treatment on breast cancer patients. This follow-up study showed that some breast cancer patients treated with DES actually lived longer compared to those treated with tamoxifen. How? The Mayo Clinic researchers were able to show that estrogens, given at the right time (and the "timing" is a big part of this deal) can deliver signals to breast cancer cells to instruct them to "die." This is exactly what Dr. Jordan had been talking about.

Sometimes robust estrogens, like DES, can make breast cancer cells that were not responsive to drugs like tamoxifen start to respond. A Norwegian study published in 2001 showed that half of 32 breast cancer patients who had become resistant to tamoxifen or other endocrine therapies, once treated with high-dose DES then became responsive to the endocrine therapies. This meant that a woman who had become non-responsive to tamoxifen or an anti-aromatase inhibitor could be rebooted to once again respond to them by the use of a powerful estrogen.

Tamoxifen works through a protective number of portals that have nothing to do with the estrogen receptors.

The natural next question was: Could a woman's own home-grown estrogen be protective like DES, too? The answer was yes.

Matthew Ellis, MD, PhD, director of the breast cancer program at Washington University in St. Louis, answered this question and published his results. Dr. Ellis showed that giving both high-dose natural estrogen (30 mg/day) or low-dose estrogen (6 mg/day) to women with metastatic breast cancer, who had failed aromatase inhibitors, helped effectively kill breast cancer cells. These women were given oral estradiol, identical to the active form of estrogen inside a women's body. The estradiol shrank tumors in 30% of the women. The adverse side effects from the estrogen therapy, especially the lower dose, were less toxic than from chemo, and certainly less costly.

It always boggles my mind when some women come to me after working with other doctors trying to find the right HRT dosage but getting no or bad results on high dosages of estrogen. Why? You just learned. High dosages of estrogen "*turn off*" the estrogen receptor. They are not to be regularly used as hormone therapies, but rather cancer therapies.

Interest in DES rekindled following the 1999 long-term follow-up of the original Mayo Clinic study that showed patients treated with DES had increased survival compared to tamoxifen-treated patients. Then, in 2001, a Norwegian study of 32 breast cancer patients who had become resistant to endocrine therapy showed that almost half of the participants responded to high-dose DES.

We are not recommending DES to treat cancer but rather showing that estrogenic compounds can be cancer killing and protective.

Breast Cancer Risk and Hormone Therapy: The Science

In 1990, Darcey Spicer from the Kenneth Norris Jr. Comprehensive Cancer Center, USC Medical School, Los Angeles, said: "While there is a general belief that hormone replacement therapy will increase the risk of recurrence of breast cancer, there are, in fact, no data to support this notion."

A very thorough review of the research up to 1994 from cancer doctors at Rush-Presbyterian-St. Luke's Medical Center in Chicago, and colleagues in the Breast Cancer Committees of the Eastern Cooperative Oncology group, wrote: "A major concern over prescribing ERT for women with a history of breast cancer is that dormant tumor cells might be activated. There is surprisingly little clinical information to substantiate such concern."

Up to 20 scientific human studies published in peer review, most of them taking place at prestigious cancer institutes, have shown that breast cancer patients given prescriptive estrogen therapy (most of the time as Premarin or estradiol), in studies lasting an average of two to five years, had the following:

- Statistically significant "less" risk of breast cancer recurrence.
- Quite a number of these studies also demonstrated less risk of death from breast cancers.
- In a number of these studies, breast cancer patients had less risk of dying prematurely from a wide range of non-cancer issues, called "all-cause mortality." (See the Appendix for details on the human trials.)

Yet many doctors are still reluctant to recommend hormonal therapies, especially to high-risk women – such as those with breast cancer or close family members with history of breast cancer.

Pelin Batur, MD, an internist at the Cleveland Clinic, published a review of

➤

➤

15 studies totaling 1,416 breast cancer survivors using hormonal therapies (most started two to four years post diagnosis) compared to 1,998 not using HRT. The women were followed for three years and findings showed the following:

- *Women on hormones had a 10% reduced risk of recurrence of breast cancer*.
- There was a slightly significant decreased risk of mortality from cancer and all-causes at a seven-year follow-up.
- Protection of estrogen continues after stopping therapies, as was stated in the re-analysis 19-year follow-up study headed by Dr. Chlebowski.

The Stockholm study was similar in size to the HABITS study. This was a prospective and randomized trial, with 188 women randomized to HRT and 190 not given hormones. There was no difference in the rate of new breast cancers, which held up over a 10-year follow-up.

A variety of scientists like Dr. LaCroix started to refer to the WHI as the first randomized trial to give evidence that if you give healthy women estrogen therapy within 10 years from the initiation of their menopause, or to post-menopausal women without a uterus, this reduced the risk of getting breast cancer.

Two other researchers agreed. Dr. Craig Jordan, the estrogen and cancer scientist who put tamoxifen on the cancer map, and Leslie Ford, MD, associate director for clinic research at the National Cancer Institute's Division of Cancer Prevention, wrote an article called "Clinical Paradoxical Effect of Estrogen on Breast Cancer Risk." This research showed that sometimes estrogens not only prevent breast cancer, they also cause breast cancer cells to die. The ability of estrogen to do this seems to be activated by a period of lack of estrogen exposure (menopause or anti-estrogen therapy) and then re-exposure to estrogen. The absence of estrogen and then re-exposure retriggers breast cancer cells to die in some women. Dr. Jordan commented on this rebooting of response to endocrine therapies by estrogen: "After five years of anti-estrogen therapy, a switch takes place inside breast cancer cells which makes them resistant to these anti-estrogen agents. When estrogen is then used, it triggers breast cancer cell death, not growth."

Dr. Jordan is a big fan of estrogen. Presently he is a cancer director at the renowned MD Anderson Medical Center, researching safe estrogen therapies for breast cancer patients (meaning patentable).

So, research is showing that estrogens help prevent breast cancer in some women, help eradicate sleeping breast cancer cells, and help some women become responsive once again to breast cancer therapy that had stopped working.

The Benefits of Estrogen

By the early 1990s, researchers had summarized the benefits of estrogen therapies and documented them in the medical literature.

- Estrogen controls menopausal symptoms.
- If given early, it helps prevent strokes and bone loss and fractures for many years, even after discontinuation.
- Estrogen significantly reduces the risk of heart disease,
- Estrogen significantly reduces the risk of fracture (Framingham study showed a 50% drop in osteoporosis-hip fracture),
- Estrogen significantly decreases risk colorectal cancer, and
- It significantly reduces the risk of cognitive decline and Alzheimer's disease. The Cache County studies (which had the bad karma to come out only months after the WHI and was not noticed) showed that if women had been on 10 years of estrogen therapies, they had a 30 to 50% reduction in incidence of AD.
- Estrogen has now been found to have hundreds of other pleotropic effects, such as helping epigenetics and protecting mitochondria (our energy organelles) from damage, so it helps in maintaining the energy production needed for a positive lifestyle effort.
- Estrogen helps maintain volume, plasticity, and protection from injury of the hippocampus, where memories live in the brain.

Now we see that estrogen *protects* against breast cancer in a woman who has not yet had it and even in those that already have. To age without individualized hormonal support is to age at the speed of an accelerating bullet, while hormonal therapies allow us to live younger longer and healthier.

Vindication

Let 2020 be the year that estrogen is vindicated.

I had breast cancer 26 years ago and have been on estrogen and other hormone therapies for 21 years now. I would not be the person, physician, or author that I am if I were not on hormones. I am passionate about passing this information forward.

I get email after email from women all over the world saying that their doctor will not prescribe estrogen for them. I hope this article makes it possible for more women to enjoy the benefits of this hormone.

This article is written for women to hand to their doctors or for doctors to feel vindicated (and safe) about prescribing hormones. ◆

All three parts of this article are posted with appendices and references online at www.townsendletter.com.

D. Lindsey Berkson, DC, has been a leader in functional medicine, with an emphasis on the gut, hormones, and the environment for several decades. Dr. Berkson has been teaching certification relicensing courses for MDs, pharmacists, NPs, NDs and chiropractors for decades – in the last few years focusing on the gastroenterology module for A4M and hormones and oxytocin for PCCA.

Dr. Berkson formulated Metagenic's first female nutrient line for physicians. Dr. Berkson was a scholar at an estrogen think tank at Tulane University where she worked with the top scientists that discovered "receptor physiology" and growing epidemic of competitive inhibitors found in endocrine disruptors.

Dr. Berkson has authored 21 books; several have been best sellers. She also hosts the Dr. Berkson's Best Health Radio, writes the Berkson Blog (@ DrLindseyBerkson.com), and is a research fellow with Health Sciences Collegium.

Pulsed Electromagnetic Fields in the Treatment of Chronic Pain

by William Pawluk, MD, MSc

References for this article are available at www.DrPawluk.

When I was still active in hospital care, there was a one-month period in which I became aware that several patients had been admitted for stomach bleeds. One of them died. These were all pain patients taking ibuprofen or aspirin as recommended by their doctor. Gastric bleeding was a known and accepted side effect of these widely used over-the-counter medications. With no better options to help patients manage their pain, these complications continue to be, unfortunately, accepted. More than 16,000 North American arthritis patients die each year from gastric bleeding. That number could easily be doubled when all the pain conditions are considered for which NSAIDs are used. (Today we must also factor in the 15,000 deaths annually from opioids prescribed for pain management.) Thousands of others suffering with pain have permanent kidney damage from the use of NSAIDs, requiring dialysis. This began my journey in search of better alternatives.

As I gained experience within holistic/integrative medicine, I was not confident in pain reduction relying solely on using nutrition, supplements, or emotional/cognitive approaches. For the more significant pain problems that typically still resulted in reliance on narcotics, I felt that something else was needed. Even though I was trained in acupuncture, it was not always helpful in mitigating more severe pain. This is where magnetic therapy becomes a treatment par excellence, whether in a practitioner's office or for home use. Most significantly, PEMFs do not just help to relieve the symptoms but also address the underlying causes of the pain, particularly inflammation. Addressing the causal factors are more likely to produce a durable response, eventually offering the possibility of healing the dysfunction. In my experience, almost everyone benefits from PEMF therapy, and patients are frequently able to avoid procedures and to decrease or avoid the use of medications. Research has shown that PEMFs work for numerous pain-related conditions, including the following:

- Abdominal pain
- Angina
- Arthritis
- Bruises
- Burns
- Bursitis
- Carpal tunnel syndrome
- Cervical disc injuries
- Dental pain
- Fibrocystic breast disease
- Fibromyalgia
- Fractures
- Intermittent claudication
- Ischemia
- Muscle spasms and tears
- Nerve entrapment
- Nerve pain
- Neuroma
- Painful shoulder
- Pelvic pain
- Peripheral neuropathy
- Phantom pain
- Plantar fasciitis
- PMS
- Post-workout aching
- Postoperative pain
- Reflex sympathetic dystrophy
- Sinus pain
- Sprains
- Strains
- TMJ
- Tendonitis
- Tennis elbow
- Trauma
- Whiplash

Population-Wide Pain Syndromes. The issue of pain treatment is an extremely urgent public health and socioeconomic problem. In the US alone, chronic pain affects at least 116 million American adults, more than the total affected by heart disease, cancer, and diabetes combined. At least 17% of people ages 15 and older suffer from chronic pain to such a degree that it interferes with their daily life. Pain, in acute, recurrent, and chronic forms, is prevalent across age, cultural background, and gender and costs North American adults an estimated $10,000–$15,000 per person annually. At any given moment, at least one in four adults in North America is suffering from some form of pain.

The Regulatory Environment. FDA approval is not required for devices that are used or marketed primarily for wellness (FDA, 2016). This has resulted in a dramatic proliferation of relatively lower-cost, easily accessible, commercially available "wellness" PEMF systems. This position of FDA most likely results from the perspective that low-intensity, low-frequency PEMF systems are generally regarded as safe (GRAS).

PEMF as Complementary Therapy

Several authors have reviewed the experience with PEMFs in Eastern Europe and elsewhere and provided a synthesis of the typical physiologic findings of practical use to clinicians, resulting from magnetic therapies. Animal studies have shown that PEMFs reduce pain perception in the brain. In some research, PEMFs were found to be equivalent to 10 mg of morphine.

Mechanisms of action include, at a minimum, reduction in inflammation, edema, and muscle spasms/contractions, enhanced tissue repair, and natural antinociception. Magnetic fields (MFs) affect pain perception both directly and indirectly, with an impact on neuron firing, calcium ion movement, membrane potentials, endorphins, dopamine, nitric oxide, and nerve regeneration. Indirect benefits of MFs from physiologic function enhancement can improve circulation, cellular metabolism, tissue oxygen, and prostaglandins. For soft tissue and musculoskeletal injuries and for postsurgical, post-traumatic, and chronic wounds, edema reduction must take place in order to accelerate healing and reduce associated pain. These are the fundamentals of cell injury repair. (For research and references on more than 20 mechanisms of PEMF action, please see the October 2020 issue of *Townsend Letter*, available online.)

Frequency, Intensity, Duration. PEMF therapeutic devices are designed for specific frequencies and intensities.

➤

➤

- Frequency patterns, expressed in Hertz, refer to those commonly recorded on standard EEG evaluations, patterns first described in the literature (1929) by the German psychiatrist Hans Berger, inventor of the EEG device. The low end of the range, ELF (extremely low frequency) devices are 3 to 1000 Hz, and include familiar frequencies from delta (1-4 Hz), theta (5-8 Hz), alpha (9-13 Hz), beta (14-25 Hz) and gamma (26-100 Hz).
- Intensity refers to the strength of the magnetic field. On consumer devices, peak intensity ranges from 0.1 mT (1 gauss) to 800 mT (8,000 gauss). In contrast, a standard MRI unit is 1,000 to 2,000 mT (10,000 to 20,000 gauss) or 1 – 2 Tesla. Repetitive transcranial magnetic stimulation (rTMS) units provided in hospitals and psychiatry practices typically have a strength of 800 mT (8,000 gauss).

  Even weak magnetic fields of very low intensity can affect pain perception and pain-related EEG changes in humans. For example, a two-hour exposure to just 0.02–0.07 mT (0.2-0.7 gauss) magnetic field can cause a significant positive change in pain-related EEG patterns. Neuroimaging research has revealed changes in specific areas of the brain with pain stimuli that were definitely modified by low-intensity PEMF exposure.
- In terms of duration, a determination always needs to be made regarding the length of the course of treatment. The rule of thumb is that higher intensity PEMFs typically need shorter treatment times and course of treatment for pain reduction. Patients are often happy to simply have a reduction in symptoms and improvement in function. However, simply because the pain is gone does not mean that the problem is gone. Without resolution of the underlying cause, the pain will tend to recur.

PEMFs offer clinicians a tool that amplifies treatments they are already providing. It also broadens the range of indications they can treat successfully and deepens the benefits of the therapies they are applying, whether provided in the clinic or self-administered at home. At its most effective, PEMF therapy benefits from informed supervision and guidance by the practitioner. In the clinical setting, the fact that PEMFs penetrate clothing, casts, or bandages without attenuation means that therapy can be applied without having to expose or come in direct contact with the skin or target tissue. This allows simple focused application to organs within the body usually without concern for harm or negative effects to intervening tissue.

Reduction in the Need for Pain Medication. PEMF therapy is also frequently performed concomitantly with medication management. PEMFs are commonly seen clinically to not only decrease pain, but also reduce dependence on pain medications. In one study using very high-frequency PEMFs for the treatment of cervical dorsal root ganglion pain, the need for pain medication continued to be significantly reduced in the active group after six months. A study on knee pain found that even after follow-up at one year, 85% reported pain reduction beyond the time of stimulation. Medication consumption decreased by 39% at eight weeks and by almost 90% in the follow-up period after eight weeks. Rohde et al.(2010) documented a 2.2-fold reduction in narcotic use by PEMF-treated, post-surgical patients.

Musculoskeletal Disorders

Musculoskeletal disorders make up the vast majority of pain sources commonly treated with PEMFs. These include arthritis, tendonitis, sprains and strains, fractures, post-op pain, osteoporosis, wounds, neuralgias, neuropathies, hip disorders, muscle spasms, spinal cord injury, and trauma, as well as burns, neuromas, heel spurs, phantom pain, carpal tunnel syndrome, headaches, tennis elbow, reflex sympathetic dystrophy (RSD), and so on.

A series of 240 patient cases, treated in an orthopedic practice with PEMF, documented decreased pain from rheumatic illnesses, delayed healing process in bones, and pseudo-arthritis, including those with infections, fractures, aseptic necrosis, venous and arterial circulation, RSD (all stages), osteochondritis dissecans, osteomyelitis, and sprains, strains and bruises. The clinically determined success rate approached 80%. X-ray evidence of continued improvement confirmed cartilage/bone reformation and healing at the joint margin. Double-blind clinical studies have shown this in chronic wound repair, acute ankle sprains, and whiplash injuries. Similar studies have been done for neck pain.

Fractures. In evaluating acute care, researchers assessed pain and swelling of distal radius fractures after an immobilization period of six weeks. In the study, 83 patients were randomly allocated 1) to receive 30 minutes of either ice plus PEMF, 2) ice plus sham PEMF, 3) PEMF alone, or 4) sham PEMF for five consecutive days. All had a standard home exercise program. The addition of PEMF to ice therapy produced better overall treatment outcomes than ice alone, or PEMF alone in pain reduction and improvement of ulnar nerve entrapment.

Whiplash. In a study of 92 patients with whiplash, pain was measured on a ten-point scale. The before/after treatment result averages were as follows: Head pain pretreatment 4.6/post-treatment 2.1 with magnetic field treatment compared with 4.2/3.5 in controls. Neck pain, 6.3/1.9 with PEMF as opposed to controls 5.3/4.6. For pain in the shoulder and arm, 2.4/0.8 with PEMF compared to controls 2.8/2.2.

Back Pain. More than 15% of the entire US population experiences lower back pain at any given time. Spinal stenosis and arthritis of the back, for example, are conditions that are not usually reversible. Frequently they persist for the rest of a patient's life and are typically progressive. Benefit using PEMF has been shown for patients suffering from stenosis, arthritis, herniated discs, spondylosis, radiculopathy (spinal nerve compression), and sciatica. People who have tried other modalities and failed to find relief often experience relief with PEMFs. Research findings suggest that it is best to apply PEMF therapy on a consistent basis over an extended period to achieve the best results, and 95% of individuals achieve significant relief.

In clinical practice, I recommend PEMF for back pain because the stimulation penetrates deep into the body to heal the tissues. In contrast, a study using a static magnet pad found no relief for back pain, likely because it was too shallow in its application. Higher intensity PEMF is often necessary in more severe or chronic back pain situations to support effective pain reduction.

Lumbar osteoarthritis. Patients who were treated with 35-40 mT (350-400 gauss) PEMF found relief between 90-95% of the time. PEMF therapy also enhanced results from other rehabilitation therapies and improved related neurologic symptoms. Even PEMF of only 0.5-1.5 mT (5 to 15 gauss), used at the site of pain and related trigger points dramatically improved patients' pain. Some patients remained pain free six months after treatment. While PEMFs can be especially dramatic in resolving acute back pain, they are actually most often used for chronic back pain.

*Failed back syndrome***.** Chronic pain can be an unfortunate consequence of back surgery, and largely unpredictable. In these situations, PEMF therapy can make a huge difference in the ability to function. While PEMF may not be able to eliminate the pain because of the degree of damage to the back, severe pain may become tolerable, mild pain.

Lumbar radiculopathy. A study involving 100 patients with lumbar pain received magnetic field treatment and controls received standard medication. Group 1 had low intensity PEMF therapy twice a day for two weeks. The average time to pain relief and painless walking was eight days in the PEMF group and 12 days in controls. In another randomized controlled clinical trial, 40 patients with lumbar disc prolapse were randomly assigned to either a PEMF group or a control group. PEMF produced better results on the Oswestry Low Back Disability index in terms of personal care, lifting, walking, sitting, standing, sleeping, social life, and employment, as well as evidence of improvement of nerve damage and nerve root compression.

Osteoarthritis (OA). These conditions affect approximately 40 million people in the US. The most optimal approach is to prevent progression of the OA process at the earliest stages. Various researchers have found positive effects of PEMFs on cartilage cells and tissue cells with field intensities between 1.5 mT and 3 mT (15-30 gauss), using a 75 Hz signal. At these parameters, stimulation for six hours per day had better clinical outcomes, with decreased use of NSAIDs. In these studies, PEMF stimulation increased cell growth and extracellular matrix (ECM) production. ECM molecules include proteoglycans (PGs which provide joint lubrication), glycosaminoglycans (GAGs), collagen II, IL-1b, and IGF-1. PEMF supported production of prostaglandin E2 (PG-E2) and reduced inflammation, increasing joint capsule cells, joint tissue stem cells, and collagen synthesis.

Other research showed positive results from a PEMF application of .5 mT-2 mT (5-20 gauss) and documented changes in prostaglandin levels evident within four to 24 hours of stimulation. Reducing pain and improving function are important, but unless the underlying changes in the tissues due to the OA process are affected directly and reversed, the tissue will continue to deteriorate and more aggressive treatment will need to be taken years later, such as joint replacement.

Neuropathies

Diabetic Neuropathy. PEMFs used for at least 12 minutes every day in the treatment of patients with intense symptoms of diabetic neuropathy experienced improvement in pain, as well as reduced paresthesia and vibration sensation, with increased muscular strength in 85% of patients compared to controls.

Research on neuropathic pain (NP) using low-power, low-frequency PEMF of 600 and 800 Hz, for 30 patients, 40–68 years of age with DNP stages N1a, N1b, N2a, were randomly allocated to three groups of ten each. They found significant reduction in pain and statistically significant improvement in distal latency and nerve conduction velocity in both experimental treatment groups. Using this particular protocol, low-frequency PEMF was seen to reduce NP and slow the progression of neuropathy, even when applied for only a short span of time.

PEMF therapy is frequently performed with medication management.

Carpal Tunnel Syndrome. Another form of neuropathy, these chronic pain disorders affect the median nerve at the wrist. In a randomized, double-blind, placebo-controlled trial, ten months of active PEMF resulted in improvement in nerve conduction and subjective improvement on examination (40%) and reductions in pain scores (50%) and global symptoms (70%).

Complex Regional Pain Syndrome (CRPS). Also termed RSD (reflex sympathetic dystrophy), this form of neuropathy is extremely painful and largely unsatisfactorily treatable by standard approaches. In one report, ten 30-minute PEMF sessions at 50 Hz followed by a further ten sessions at 100 Hz plus physiotherapy and medication reduced edema and pain in 10 days. I personally treated a patient with this disorder using a 27.12 MHz PEMF signal, a nurse who was almost completely disabled in her left upper extremity. She used her device for approximately an hour a day. Within about one month, she experienced 70% recovery, and within two months, she had essentially normal function with no sensitivity to touch or changes in skin temperature. She maintained her recovery with continued treatments in the home setting.

Complex Pain Conditions

Ulcers. Resolution of gastric ulcers requires clinical skill, given that they can be caused by *H. pylori* infection and/or stress. Treatment of duodenal ulcers with a 50 Hz, 20 to 25 mT (200 to 250 gauss) PEMF was 1) applied for 1 minute to acupuncture points specific to gastrointestinal function, compared to 2) the combination of medication plus PEMF acupuncture point stimulation, and 3) standard antiulcer medication. Time to pain relief, reduction of dyspeptic symptoms, and ulcer healing were compared. Pain and dyspepsia were best controlled in the sole PEMF therapy group in 2.75 days, whereas combining PEMF and drug therapy resulted in pain control in 8.61 days. Ulcer healing with PEMF took 18.25 days, with PEMF and medication, 19 days, and with medication only, 26.6 days. Compared with other studies in which medication plus active therapy was more effective, in this study adding medication appeared to delay improvement.

Migraines. Globally, approximately 15% of people are affected by migraine headaches. A migraine study of PEMF provided treatment at 2-5 Hz and 3-4 mT (30-40 gauss) with stimulation to the head once daily for 10-15 minutes for 30 days.

➤

➤

Improvement in the PEMF group averaged 66% versus 23% in the placebo group with decreased frequency and intensity of attacks.

In a study of 90 patients with headaches resistant to medication or acupuncture, PEMF treatment was applied for 20 minutes daily for 15 days. PEMF stimulation was most effective against tension headaches with 88% reporting excellent or good results (for classic migraines, 60% of patients experienced benefit, and for cervical migraines, 68%).

In research involving 82 patients with a variety of headaches, including migraines, tension headaches, migraines and tension headaches in combination, and cluster headaches, as well as weather-related, and post-traumatic head pain, patients were evaluated in a double-blind, placebo-controlled study with four weeks of PEMF, 16 Hz at 5 mT (50 gauss). Of those receiving active treatment, 76% experienced evident or definite relief of symptoms. Only two participants had worsening of symptoms.

In a series of 20 treatments, 50 migraine patients received PEMF at 10 Hz for 15 minutes a day. Reduced frequency and intensity of attacks was experienced by 60% of patients with diminished use of medication over a three- to four-month period. In a second study, a case series, 50% to 60% of participants reported a favorable effect with PEMF therapy. A third study of PEMF at 9.6 mT (96 gauss) and 12 Hz applied to the head for one hour was found to alleviate migraines.

A migraine study with an unusual design applied PEMF treatment to the area of the femoral artery in the inner thigh. Short courses of therapy produced a 73% reduction in pain, whereas a longer course of therapy provided 90% relief.

Fibromyalgia (FM). Individuals with FM have abnormalities in central brain structures that process pain sensations, impairment in their ability to activate natural pain inhibition, and/or altered CNS processing of pain signals, resulting in hypersensitivity to pain.

A fibromyalgia study, involving 56 women with FM, ages 18 to 60, randomly assigned participants to PEMF or sham therapy, 30 minutes per session, twice a day for three weeks. They were tested for general FM status, pain, depression, and general function. After active treatment ended at four weeks, significant improvements were evident in test scores and were maintained at the twelve-week evaluations. The sham group showed general improvement at four weeks. However, there was no improvement in pain or FM symptoms, and there was some regression in general gains made by twelve weeks in the sham group.

PEMF or sham exposure treatments were provided in another study and levels of pain and anxiety were evaluated. The study was double blind, randomized, and placebo-controlled with a 30-minute magnetic field exposure, at an intensity of about 400 mT (4 gauss), < 3 kHz. There was significant benefit in reduction of pain for the FM patients with PEMF therapy.

In a double-blind, sham-controlled clinical trial involving women ages 22 to 50 years old, the active stimulation group received therapy with an 8 Hz square wave PEMF of 43 nT (0.00043 gauss) using an EEG cap with 33 small PEMF coils. Treatment sessions were provided once a week, lasting 20 minutes each time, for eight weeks. Outcome measures included blood serotonin levels, pain thresholds, activities of daily living, perceived chronic pain, and sleep quality. Improvement in pain thresholds was noted after the first stimulation session; however, improvement in other measures occurred after the sixth week. The perceived pain after eight sessions was 39% less, compared with 8% reduction in the sham group. This study makes it clear that even low intensity magnetic stimulation may offer a safe and effective treatment for chronic pain and other fibromyalgia symptoms.

Centralized Pain

In the presence of pain, nerve signals move from the source of the pain upstream to the brain. Foot pain, for example, can become established in the brain, and the brain can then become the chronic source of the pain (termed centralization or colloquially, “pain brain”). In this situation, treating the brain is the most appropriate approach. In fact, many chronic pain conditions centralize quickly. The brain may perpetuate the pain signal even though the initial pain stimulus is now relatively weak. Therefore, dual approaches, treating the localized source (the foot, in the example of a foot injury) and the brain, may produce the best, fastest results. In these situations, PEMF systems are recommended that will allow whole-body and localized treatment simultaneously.

Conversely, treatment should address the injured area and the spinal cord at the same time or in the same treatment session. In other cases, pain may be conducted downstream as well (a hip problem can cause knee pain, for instance). For this reason, it is ideal to treat the source of the pain, not the region to which the pain is referred. Further, identifying the cause, not just the referred location, is critical to appropriate and enduring relief. In sum, the most effective chronic pain management involves treating the source of the pain and also apply treatments to the brain or along the spine. This combination allows for management of the cause of the pain and at the same time controls the pain signaling to the brain where the pain is ultimately recognized and where it may continue to reverberate.

Healing does not typically occur overnight. More powerful PEMFs may be necessary. Weaker PEMF systems usually take significantly longer to provide benefit, particularly when the source of the pain is deeper in the body.

William Pawluk, MD, MSc is a holistic physician located in Townsend, Maryland, in the Baltimore metropolitan area, with past appointments at Johns Hopkins University and the University of Maryland. With a background in family medicine, he has additional training in functional medicine, nutrition, acupuncture, homeopathy, hypnotherapy, bodywork, and energy medicine. He is the foremost authority on Pulsed Electromagnetic Field therapy in North America, with 30 years of experience in clinical applications of PEMF for healing, regeneration, and holistic pain management. Author of *Power Tools for Health*, a comprehensive book on the research and usage of PEMFs in healing, he has also written professional book chapters and numerous journal articles. and provided more than 50 interviews for radio, podcasts, magazines, and TV. He has been cohost of a two-hour holistic health radio show for the past ten years and host of the Pain Solution Summit, www.painsolutionsummit.com. In 2019, Dr. Pawluk received the ACIM Lifetime Achievement Award for work with magnetic field therapy.

Clinical Relevance

Across four decades of research on magnetic fields, there have been hundreds of studies that found benefit from PEMF and a limited number that found benefit equal to placebo. None of the research to date has found harm. In this article, we have reported those that documented clear benefit, with a range of parameters in terms of frequency, intensity, and duration of treatment.

There are numerous PEMF devices available to the clinician with a range of functional capabilities and limitations. The choice of a device should be based on the conditions to be treated and the relative strength called for to reach the target tissue or organ, as indicated by research data and clinical studies. Clinical electromagnetic (PEMF) therapy is highly relevant to conditions treated in the fields of chiropractic, physical therapy, acupuncture, biofeedback, naturopathy, and psychology, as well as orthopedics, physical medicine, pain medicine, neurosurgery, psychiatry, and the growing fields of integrative and functional medicine.

Resources

PEMF Devices. Dr. Pawluk has purchased, tested, and validated approximately 100 different PEMF devices over the 30 years he has worked in this field. Based on his experience, a number of devices are recommended and available for purchase on his website, drpawluk.com. They include local and whole-body systems, both battery and AC-powered devices. Intensities of devices range from very low intensity (<1 gauss), medium intensity (10 – 1,000 gauss), to high intensity (2,000-8,000 gauss) including devices that are able to cause muscle contractions.

Consulting services. Dr. Pawluk provides consulting services to both consumers and practitioners. Consultations are recommended for practitioners to be able to have more certainty about the most appropriate tools for the professional setting. Many professionals spend much more than they need to for PEMF systems. On the other hand, many professionals also acquire PEMF systems that are not likely to provide much benefit quickly in the practice setting.

Website. drpawluk.com is an extensive resource for patients, with basic educational information, more than 40 blogs with references, numerous videos, and a virtual store from which devices may be purchased. Once devices are purchased, Dr. Pawluk and his staff provide significant ongoing support for both initial use and subsequent informational needs.

Book. *Power Tools for Health* is a readable, highly referenced work on basic concepts in the application of PEMFs, mechanisms of action, an extensive clinical section on 50 different health conditions, and more than 500 references on clinical trials and laboratory findings.

Editorial Support
Nancy Faass, MSW, MPH – info@HealthWritersGroup.com
Jerry Stine, CNC – Lifespan2@comcast.net

References for this article are available at www.DrPawluk.

Fibromyalgia, Chronic Fatigue, and Multiple Chemical Sensitivities – A Unified Hypothesis

by Carolyn McMakin, MA, DC

References and slides are available online at www.townsendletter.com.

When they arrive in your office, they all look the same with minor variations, rather like identical suburban tract houses with different floor plans and exterior colors.

They have body pain that varies between a 4-5/10 and a 6-8/10. They don't sleep. They report being fatigued and depressed and say that walking down the soap aisle in the grocery store or standing next to someone who wears perfume gives them a headache or makes them sick for days. They seem to react to so many foods and are allergic to everything. Medications might reduce the pain a little and create side effects like fatigue and slow thinking, but it's all the doctor can do.

It doesn't matter how many doctors of what type they have seen, they get one or more of these diagnoses: fibromyalgia, chronic fatigue, multiple chemical sensitivities and recently they are often told they have mast cell activation syndrome (MCAS) or small intestine bacterial overgrowth (SIBO), gastroparesis, leaky gut, mold toxins, Epstein-Barr (EBV) or maybe Lyme (even though the Lyme tests have been negative or show only 1 band). Or they are told they really just have depression even though they are already on an antidepressant and they are prescribed an additional antidepressant or a stronger dose of the one they are already on. Or, worse yet, they are put on a "mood stabilizer" that turns out to be an "atypical antipsychotic" with severe long-term side effects we won't have time to cover in this article.

In general, no one asks them, "What happened immediately before the onset?" If the answer is, "Nothing happened, it just started," the doctor usually moves on to the next questions instead of drilling deeper. If the patient is lucky, the next question might be, "When was the last time you felt well?" And the answer is often, "I've always been sick. I think I've been like this since childhood." The next question should be but isn't usually, "What did you do for fun in grade school or high school?" That answer is often, "I played soccer, rode horses or did gymnastics or theater." Replies the doctor, "So up until that year you were fine. Then what? When exactly did the symptoms get this bad?" After that the answers might be relevant. But few doctors ask the set of questions that should come next.

My entire practice since 1998 has been the 10% of patients no one else could help, and I failed a number of them myself. But eventually through trial and error and being sick and recovering myself through the help of brilliant colleagues, I learned what I am about to tell you in this article.

In general, there is either the most basic medical blood work ordered, which will turn out normal or there may be up to $3,000 to $4,000 worth of exotic complex blood work ordered, which will show all sorts of items out of range. But the exotic blood work doesn't ever say how the analysis is done, where and on whom the normal levels were determined or published and gives very little guidance about what to do to correct the abnormal results. Patients either leave with a prescription for something that might not help much or $500-$1,000 worth of supplements to take three to four times a day that might help in a few months after they have been on an incredibly restrictive diet.

If they look on the internet, they will be even more frightened and hopeless but will feel, at least, that there are many other people who have what they have so they know now that they are not crazy. And then they come to you, for one last chance, that you might be able to help.

If you're like most practitioners, you swallow the rising panic and desperation and apply the latest thing you read or the technique you've learned that helps most patients and hope it will help this patient.

If you're the patient, you hope that this person might be the one with a solution to this thing that has made your life miserable for the last two, five, 10, or 20 years. You hope that the little glimmer of hope you have will turn desperation into a solution that makes the trip and the office visit worthwhile as you tell the story for the tenth time to the tenth doctor.

And, the truth of the matter that gives rise to this unified theory, is that these conditions and these symptoms have one thing in common that no one thinks of because they don't have a way to treat that one thing. I propose that this thing they all have in common is the vagus nerve through its role of suppressing the immune system, regulating gut motility and gut pH and therefore gut bacterial flora, and the connection of the vagus to the brain and limbic system. Once

continued on page 56 ➤

FREQUENCY SPECIFIC MICROCURRENT FOCUSING ON BRAIN HEALTH

The effects of frequency specific microcurrent on nervous system function have been documented for almost twenty years.

2000: blood samples analyzed at NIH showed log-rate reductions in all of the inflammatory cytokines by factors of 10 - 20 times in response to only one frequency combination. Only frequencies targeting the medulla and nervous system increased serotonin levels.

2003: Only one frequency combination (40/116) reduced lipoxygenase (LOX) mediated inflammation by 62% in four minutes in blinded animal research. COX mediated inflammation declined by 30% in four minutes. No other frequencies reduced inflammation.

2010: PTSD protocol reduced symptoms and scores after only four treatments in four weeks in 3-5-year chronic combat-induced PTSD. No improvement is expected when PTSD is more than two years chronic.

2013: significant and dramatic EEG changes were documented in TBI and autism patients treated with a combination of FSM and speech therapy.

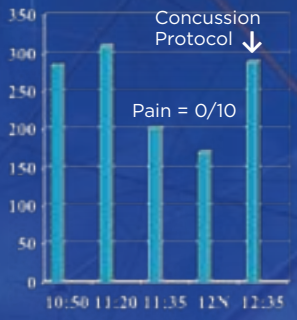
2013: only specific frequencies targeting the sympathetic and parasympathetic nervous systems changed autonomic function and heart rate variability dramatically and quickly.

The data suggests that combining FSM rapid effects with nutrition makes treating the brain more effective, more efficient and less expensive.

ONLY ONE FREQUENCY SEQUENCE INCREASED SEROTONIN

#1 Serotonin = 285.6
#2 Serotonin = 309.2
#3 Serotonin = 202.1
#4 Serotonin = 169.5
#5 Serotonin = 289.6

Serotonin
normal=100-300 ng/ml



- Serotonin dropped during pain treatment (40/10) as endorphins rose.
- Pain was 0/10 at 12N
- Only one protocol increased serotonin levels by as much as double in 35 minutes in every patient
- Serotonin was the only parameter that changed direction with that protocol

TREATING PTSD WITH FREQUENCIES ALONE

Case #1 Combat exposure score 28 (high)

4 years chronic (2006)
5 Treatments

	6/24/10	7/24/10
BDI	43	13
GAD 7	21/21	2/21
PTSD-M	77/85	60/85
PTSD-C	79/85	58/85

Case #2 Combat exposure score 35 (Heavy Exposure)

3 years chronic (2007)
4 Treatments

	3/17/10	3/30/10
BDI	47	32
GAD 7	19/21	2/21
PTSD-M	78/85	60/85
PTSD-C	79/85	61/85

Case #3 Combat exposure score 27 (high)

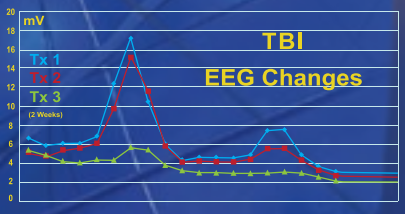
DOI 2005, Dx 2007
4 Treatments

	4/2/10	4/27/10
BDI	29	not done
GAD 7	8/21	4/21
PTSD-M	43/85	22/85
PTSD-C	44/85	22/85

THE PERFECT COMBINATION

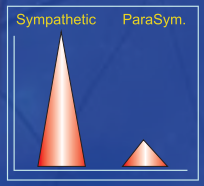
- **Specific frequencies change cell signaling to reduce inflammation**
- **Frequencies change neurotransmitters quickly and safely**
- **Specific frequencies change the brain**
- **Support those changes with nutrition and lifestyle**

Frequencies Change The Brain

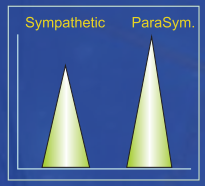


Change Autonomic Balance

Pre-Treatment

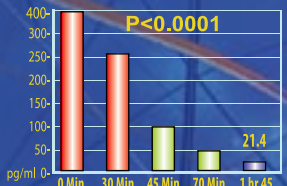


Post-Treatment

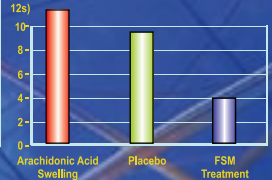


Reduce Inflammation

Reduce IL-1



Reduce LOX 62%



Dr. McMakin's™ Frequency Specific Microcurrent

Treating the brain can be more effective, more efficient and less expensive

www.frequencyspecific.com

➤*continued from page 54*

you have a way to treat the vagus fairly quickly and you can see the results and improvement fairly quickly, then the connections begin to be obvious and the patients improve.

It should be said up front that I developed Frequency Specific Microcurrent™ (FSM) in 1996, and FSM is what I add to treat all of these patients as an adjunct to what most practitioners already do. It has to be said that I don't know how I would treat any of these conditions without FSM, so this article can only tell you the unified theory based on treatment experience; it won't teach you how to use FSM, but it might give you a reason to look into it. It is hoped that the theory will be interesting whether FSM appeals to you or not.

Fibromyalgia (FMS) is a neuro-endocrine condition characterized by chronic full body pain in all four quadrants, chronic non-restorative sleep, and central pain sensitization lasting more than three months. Fibromyalgia patients have reduced levels of growth hormone due to reduced levels of growth hormone releasing hormone (GHRH) in the brain and loss of stage 4 sleep during which 85% of growth hormone is generated. Growth hormone in an adult facilitates transport of amino acids into muscle cells for repair. Fibromyalgia patients do not tolerate exercise because they don't have enough growth hormone and can't repair the normal wear and tear produced by even minor exercise. They have reduced levels of branch chain amino acids, and there are consistent hormone and neurotransmitter abnormalities across all fibromyalgia patients no matter what caused the fibromyalgia.

After treating over 500 fibromyalgia patients in 23 years, it has become obvious that there are at least five different and distinct causes of fibromyalgia. The literature says that 27% of cases are caused by physical trauma. Clinical experience puts that number at closer to 40%. The other causes are organic chemical exposure, severe prolonged stress, viral illness, and there is a genetic type characterized by genetic defects in the serotonin pathways that affect pain processing or genetic defects in other neuroendocrine pathways. Fibromyalgia may start from any one or from a combination of these causes. Regardless of how they start out, fibromyalgia patients end up looking like the patient described in the first section of this article.

Chronic fatigue syndrome (CFS) is distinct from fibromyalgia although both diagnoses are sometimes used as a garbage-can diagnosis by many of the physicians who treat these patients. Chronic fatigue is associated with a positive Epstein-Barr titer and tender lymph nodes suggesting some infectious influence. Some researchers question whether EBV causes CFS or is opportunistic. There is some support for the idea that CFS is an advanced form or variant of fibromyalgia but that is not well accepted. In CFS, fatigue and cognitive problems are the overwhelming complaints, along with non-exudative pharyngitis, swollen cervical lymph nodes and low-grade fever. In one study substance P was not elevated in the spinal fluid of CFS patients whereas it is generally elevated in fibromyalgia patients.

Multiple chemical sensitivities (MCS) is a controversial diagnosis unless you are the patient who has it. The medical community is still trying to decide whether it is a clinical diagnosis or not. Many in the medical community consider MCS symptoms to be a physical manifestation of psychiatric illness rather than a primary medical illness. This attitude prevailed towards fibromyalgia for many years until there was finally enough research to demonstrate consistent physiological abnormalities among fibromyalgia patients. There are those in the medical community and patient advocate groups who agree that multiple chemical sensitivity is a negative physical reaction to certain chemicals. Which patients have which symptoms may depend on individual genetic variants in individual liver detoxification pathways and neurochemical and metabolic pathways. There is still debate as to whether multiple chemical sensitivity can be a diagnostic illness on its own.

The most common symptoms of multiple chemical sensitivity may include headaches, rashes, asthma, muscle and joint aches, body pain, fatigue, memory loss, and confusion exacerbated by exposure to specific organic chemicals, fragrances or volatile organic chemicals (VOCs) that outgas off of carpets, synthetic fibers or paints. Each patient experiences symptoms differently, which may be why the medical community has difficulty deciding that this is one diagnosis.

A **Unified Hypothesis** for these three conditions isn't meant to suggest that they are the same thing; this hypothesis suggests that the vagus nerve plays a role in the cause and perpetuation of the symptoms in these conditions.

The vagus nerve starts in the medulla, part of the brain stem, and it has dense upwards connections to the limbic system, the stress centers in the brain, made up of the amygdala, the hippocampus, the prefrontal cortex and the cingulate gyrus. When it leaves the skull and descends down through the neck into the trunk, it becomes the longest and most complex nerve in the body.

The vagus motor fibers start in the nucleus ambiguous and control every muscle that controls speech and swallowing and even some muscles of the face. The recurrent laryngeal nerve opens the vocal cords so you can breathe, and a different branch closes the vocal cords so you can make sounds. The vagus nerve is why you can speak. The superior laryngeal branch of the vagus is why you can scream or sing high notes. The vagus supplies the pre-ganglionic neurons for the heart muscle. It beats your heart. The vagus moves your digestive system and vagus secretory fibers are why you have saliva and mucous in your pharynx and larynx. The vagus controls the smooth muscles in your bronchi and esophagus. The vagus is why you can swallow. The left side of the vagus slows the left ventricle (AV node) and it is why you do not have ventricular tachycardia. The right vagus slows the atria (sino-atrial, SA node) and it is why you don't have atrial fibrillation.

The motor fibers of the vagus follow the esophagus through the diaphragm and control the esophageal sphincter that keeps the contents of the stomach out of your esophagus. The vagus is why you don't have reflux.

When you're under stress, your muscles and brain need glucose from the blood. The vagus has fibers to the

liver that stop the liver from producing glucose. These vagus fibers need to be quiet when the stress response from the sympathetic nerves and the adrenal glands send signals to the liver to pump out more glucose so you can run.

The visceral sensory fibers of the vagus are why you know you have pain anyplace in your abdomen – the stomach, the liver, pancreas, spleen, and the gut. The vagus has stretch receptors in the stomach that tell you when you should stop eating. The vagus sensory fibers are why you feel hunger, satiety and nausea. The visceral pain information from your heart, esophagus, and trachea travel up the vagus and make you cough and tell you you're having angina. The pressure receptors in the aortic arch and the airways tell your heart to slow down before something bursts. There are chemo receptors from the vagus in the aorta that tell your system that you need more bicarbonate from the pancreas. The vagus chemo receptors in the upper small intestine make you crave certain foods because you need certain nutrients. Those chemo receptors could also be responding to organic chemicals in the blood that cannot be processed by your liver because you lack the enzymes or substrate to take them apart. There aren't good references for this hypothesis, but it's a reasonable guess.

The recurrent branches of the vagus follow the posterior meningeal artery from the upper cervical spine into the skull. This branch is sensitive to dilation of the blood vessels in the posterior portion of the dura. This contributes to the sensation of headaches that happen when air pressure drops. Vagal nerve stimulators are approved for the treatment of migraine.

The vagus general sensory fibers carry sensations of touch, pain and temperature from the ear pharynx and larynx. The branch of the vagus for the ear (auricular branch) enters the superior vagal jugular ganglion and joins up with the C2-3 nerve root and the mandibular (lower) branch of cranial nerve V. The general sensory fibers from the pharynx and larynx join with the motor fibers.

This gets complicated but stay with it. It all makes sense and once you see it, you can't ever un-see it.

All of the general sensory fibers of this portion of the vagus synapse within the spinal nucleus of Cranial Nerve V at the place where the cervical 3, 4 and 5 nerve roots exit the spine. Why is this important? In neurology you learn a memory trick, "C3-4-5 keep the diaphragm alive." It's why you cough when you put a cotton swab too far into your ear. It's why you cough when you get something in your throat that you didn't even know you swallowed. The sensory fibers of the vagus join up with the motor fibers of the nerve roots that control your diaphragm and make you cough before you even know you need to. It's automatic.

Basically, the vagus nerve keeps you alive. It beats and controls your heart, moves your digestive system, keeps you from choking, allows you to empty your bowels and tells you what to eat and when you're full, tells you that you have inflammation in your liver, pancreas or gut, regulates your blood sugar and allows you to breathe and speak.

And the vagus controls your immune system. This is where the vagus becomes crucial in FMS, CFS, and MCS. The vagus quiets the immune system by fibers that go from the celiac ganglion to the spleen to quiet T-cells and macrophages, and from the splenic nerve to the spleen to control antibody responses. Signals from the (afferent) vagus tell the brain when there is threat from infection, stress, or physical trauma. The brain sends signals down the vagus that tell the vagus to turn itself off or down. The (efferent) vagus by way of the celiac and splenic ganglia are now NOT turning off the macrophages, T-cells and antibodies in the spleen. If there is infection, stress, threat, or trauma, the vagus needs to be off to help with survival. The spleen and the immune system need to increase inflammation to fight infection and repair trauma.

Take a moment and think about that. When life is good, the vagus slows the heart, digests your food, reduces inflammation, and quiets immune response. When there is threat, stress, infection or trauma you don't need to digest your food, therefore you don't need digestive enzymes or stomach acid or gut motility. You don't need bronchial relaxation or a slow heart rate; you need stress hormones and the sympathetic nerves to dilate the bronchi and speed up your heart so you can run. You don't need to sleep right now because you might miss your chance to run away if the threat eases for even a moment. You need to run away from the "tiger" that is chasing you.

The symptoms of fibromyalgia, chronic fatigue, and multiple chemical sensitivity indicate vagal dysfunction.

When the vagus tells the brain that there is infection, threat, stress, or trauma, it sends those signals up from the body to the vagal nuclei in the medulla and that message goes directly up to the midbrain limbic system stress centers, the amygdala and the hippocampus, and others. The amygdala registers and mediates emotions and feelings. The hippocampus puts into subconscious, rarely conscious or sometimes conscious memory every "tiger" you've ever encountered. Every infection, every physical trauma, emotional trauma and every stress or threat is stored in the hippocampus so that the next time that threat is encountered, the hippocampus can remember how to get away from it faster. Short-term memory is reduced. There is only the "tiger." Long-term memory is specific for every bad thing that has ever happened because the only thing you need to remember is how you got away from the "tiger" the last time. That's why patients can only remember being sick since childhood. The threat receptors literally fire faster in the presence of very little objective external stimulus because the hippocampus remembers the last time this "tiger" was a threat.

And it doesn't matter what the "tiger" is. The "tiger" response is primitive and exactly the same whether it is a stressful job, an abusive spouse, hunger and lack of nutrients, a broken leg, torn connective tissue because you have Ehlers Danlos syndrome and your connective tissue is constantly stretching past its integrity, or toxic chemical exposure, a virus, parasite, worm or dental or mold infection. If there

➤

➤

is infection, stress or trauma, the vagus goes down or off, the immune system is unregulated, inflammation increases, and nothing works right.

Now go back and look at the symptoms of fibromyalgia, chronic fatigue, and MCS. The common features, the unifying factor, once you know all of the things the vagus does, is vagal dysfunction. But no one ever seems to think of it that way because there is no easy or risk-free way to treat the vagus. No one is going to install a vagal nerve stimulator because you have multiple chemical sensitivities, which they're not even sure are real. No one is going to install a vagal nerve stimulator because you have a sore throat and swollen lymph glands from a chronic infection that they call chronic fatigue syndrome. And they don't use vagal nerve stimulators for fibromyalgia even though 86% of fibromyalgia patients have irritable bowel and don't digest their food well. It's just too risky to install them and there are too many potential side effects, and it is really just easier to tell the patient to go on this diet, take these pills, and learn to live with it.

If you're lucky and have the right skills, you can treat the trauma, resolve the mold, virus, dental or parasite infection and the patient is not inherently sensitized from some early childhood trauma and the hippocampus tells the vagus that the threat is gone and it is OK to come back on. The vagus comes back on and the patient recovers. If you and your patient are both lucky.

Case Report

The patient was a 49-year-old female who had fibromyalgia for 18 years following an auto accident. Her pain had been between 4/10 and 8/10 for 18 years. Her symptoms included headaches, burning midscapular pain, hand, arm, leg, foot, neck, back and jaw pain. Over the years she had developed asthma, allergies, acne and irritable bowel syndrome and had been diagnosed with digestive system candida overgrowth.

Fortunately, her body pain responded to the Frequency Specific Microcurrent treatment for fibromyalgia associated with spine trauma. When the pain decreased so that it was consistently below a 4/10, her digestion improved, her immune system quieted down, the allergies to food and environmental factors disappeared, the asthma resolved, her sleep improved and her fatigue resolved as her adrenal function and diurnal rhythm returned.

She had twenty treatments between December 8 and March 15, and she used a home microcurrent unit as often as needed to keep her body pain below a 4/10 at all times. She had physical therapy to repair the pain generators in her neck and two sets of facet injections. She used one combination supplement for repairing her gut. Her acne and night vision cleared up when she was given an oil-based vitamin A supplement. No genetic testing was done, but it has been suggested that some patients can't convert beta-carotene into the active form of vitamin A. By February 8, after eight weeks of treatment, she no longer met the diagnostic criteria for fibromyalgia. Her pain was consistently between a 2/10 and a 4/10 without medication. She slept well without medication and her irritable bowel syndrome resolved. By March 15 she was discharged from treatment and in June she moved to Colorado where her recovery was maintained for at least six years.

Think about all of the confusing, multi-system symptoms that were simply a result of body pain that remained between a 4/10 and 8/10 for 18 years. The body pain was eliminated by treating inflammation in the spinal cord, but the immune system activation, allergies and asthma were from the vagus.

Irritable bowel and candida. If your gut doesn't move, and your pancreas continues to secrete bicarbonate, but your stomach doesn't secrete as much acid as usual, your gut contents become alkaline and candida loves an alkaline environment. The friendly acid-loving bacteria don't thrive, and they aren't creating the short chain fatty acids and other products that repair your gut wall. The vagus. Again.

Sleep disruption resolved because the "tiger" was gone. The amygdala and hippocampus kept the threat response high because if the pain was a 7/10 there must be a "tiger." When the pain was a 2-4/10, the tiger was gone, and sleep was welcome.

We were lucky because she had no early childhood trauma to maintain the sensitization and the vagus came back on by itself once the pain resolved. In 2000, when she was a patient, the vagal treatment had not yet been developed.

In 2020, the vagus can be treated with FSM and treating the vagus can improve the speed of response; but if the cause of vagal dysfunction is not corrected, the limbic system can turn the vagus off faster than it can be turned back on. Knowing how the vagus works and how it creates symptoms in so many body systems helps make sense of it all and makes the patient presentation less overwhelming.

If you look for the cause of the infection, stress, threat, pain or trauma and resolve that, and if you're lucky, the limbic system will calm down and the vagus will come back on. If you need a little extra luck, Frequency Specific Microcurrent can give you a tool to help quiet the limbic system directly and turn the vagus back on.

◆

References and slides are available online at www.townsendletter.com.

Carolyn McMakin, MA, DC, developed Frequency Specific Microcurrent™ (FSM) in 1995 and began teaching it in 1997. She has a part-time practice treating chronic pain, does clinical research, and teaches FSM seminars in the US and abroad. She has lectured at the National Institutes of Health and at conferences on fibromyalgia and chronic pain in the US, Australia, England, Kuwait, Taiwan, and Germany. Her textbook *Frequency Specific Microcurrent in Pain Management* was published in 2010 (Elsevier). *The Resonance Effect; How Frequency Specific Microcurrent is changing medicine* was published in 2017 by North Atlantic Books. www.frequencyspecific.com

Treatment of Strained Hamstring with Acupuncture and Medical Massage

by Dr. Sabrina Brunner, DACM

Abstract
Acupuncture combined with cupping, medical massage, and Zhen Gu Shui topical appointment is safe and effective for strain of the hamstring, according to clinical experience. There is no other supporting acupuncture research at this time. Studies that have been linked to hamstring strain include dry needling (achi points) in physical therapy research. The studies that I have used came from physical therapy resources. Acupuncture is still growing and developing its way through the medical community.

Athletes of all shapes, sizes, and professions are subjected to injuries every now and again. If an injury is not tended to or the wrong treatment is given, this can set an athlete up for a chronic injury or worsening of the injury. I have been treating soft tissue injuries with athletes for over 20 years. In the last 10 years of working with professional athletes and their injuries, I have noticed that when acupuncture, cupping, medical massage, and herbal tinctures are used together in one treatment the recovery time is cut by 50-70%.

A patient sought treatment for muscle spasms, pain and knots, and tingling in his right hamstring. Mr. Jaguar said that he was squatting 500 pounds and felt a pop in his right hamstring. He instantly felt pain and spasms; he presented with a knot in the very center of the right hamstring. Palpable finding suggested a pulled right long head and short head of the biceps femoris hamstring. The area presented itself with edema, redness, hot to the touch, and pain on palpitation. I diagnosed the condition as qi and blood stagnation in the UB channel. The meridian runs straight up the injured part of the hamstring.

A combination of medical massage and a topical Zhen Gu Shui (a traditional Chinese liniment) was used in addition to acupuncture and cupping. The purpose of "achi" acupuncture was to free up the pain and energy stuck in the hamstring. "Dry Needling has been shown to increase ROM [range of motion] in the upper and lower hamstring quarter."[1] Cupping is used to create a reverse suction on the skin that pulls up blood, lymph, and muscle waste from deep inside the muscle up to the surface of the muscle and skin. Zhen Gu Shui was applied topically to reduce stiffness and soreness. Then medical massage is applied to flush out the muscle. The

➤

Date Pain Scale 0-6	Interventions	Acupuncture Points, Location, depth	Outcomes
02/27/19 Before TX.... 5 After TX 5	20 minutes of acupuncture Cupping 5-7 minutes Med Mass 45 minutes	Si 3, Ub 62, Ub 40 Gauge .20x30 superficial 10 achi per hamstring Gauge .25x60 @ 2 inches	MYMop marks 5 on hamstring spasm, pain, walking, wellbeing
03/02/19 Before TX.... 5 After TX..... 4	Same as 02/27/19 Add hamstring stretch	On right hamstring Zheng Gu Shui applied before Med Mass	Hamstring not as painful to the touch or walking
03/07/19 Before TX.... 4 After TX..... 3	20 minutes of acupuncture Cupping 5-7 minutes Med Mass 45 minutes	Li4, Lr3, Ub 40, Gb34 Gauge .20x30 superficial 10 achi per hamstring Gauge .25x60 @ 2 inches	Walking is easier, stretching is easier
03/09/19 Before TX.... 3 After TX..... 2	Same as 03/07/19 Continue with stretch	On both hamstring Zheng Gu Shui applied before Med Mass	Hamstring Is less, painful, spasms calmed down
03/14/19 Before TX.... 2 After TX..... 2	20 minutes of acupuncture Cupping 5-7 minutes Med Mass 45 minutes	Si 3, Ub 62, Ub 40 Gauge .20x30 superficial 10 achi per hamstring Gauge .25x60 @ 2 inches	Hamstring is tolerable and back to lifting
03/21/19 Before TX.... 2 After TX..... 1	20 minutes of acupuncture Cupping 5-7 minutes Med Mass 45 minutes	Li4, Lr2, Ub 40, Gb34 Gauge .20x30 superficial 10 achi per hamstring Gauge .25x60 @ 2 inches	Mymop-FollowUP marks 1 on hamstring spasm, pain, walking, wellbeing

Strained Hamstring

➤

purpose of medical massage is to move old blood, lymph, and muscle waste out of the hamstring and to facilitate entry of new nutrients and lengthen the muscle. Medical massage to the muscle and tendon tissues increased hamstring extensibility.[2] Administration of a topical foam has also been shown to remarkably reduce muscle tightness and stiffness.[3] Self-performed hamstring stretches were assigned to gently lengthen the hamstring: "Self myofascial stretching immediately increased hamstring muscle flexibility."[4]

Mr. Jaguar was advised to rest the hamstring for three weeks and was allowed to work out the other parts of his body lightly. The MYMOP (Measure Yourself Medical Outcome Profile) was utilized to monitor spasm, pain, activity, and wellbeing over the four-week treatment process. Initially, MYMOP2 showed scores of five in hamstring spasm, hamstring pain, walking, and wellbeing. Patient participated in all recommended changes and by the end of the four weeks the hamstring spasms, pain, walking, and wellbeing improved. MYMOP2 follow-up showed scores of one in hamstring spasm, hamstring pain, walking, and wellbeing.

This is just one example of many success stories for injured athletes.

References

1. Geist K, et al. Clinical effects of dry needling among asymptomatic individuals with hamstring tightness: A randomized control trial. *Human Kinetics Journals.* November 2016;26(6); 507-517.
2. Akazawa N, et al. Effects of long-term self-massage at the musculotendinous junction on hamstring extensibility, stiffness, stretch tolerance, and structural indices: A randomized control trial. *Physical Therapy in Sport.* September 2016;21: 38-45.
3. Gervasi M, et al. The effect of topical thiocolchicoside **in preventing and reducing** the increase of muscle tone, stiffness, and soreness: A real-life study on top-level road cyclists during stage competition. *Medicine (Baltimore).* July 2017; 30. Retrieved from
4. Sung-Hak C, et al. Immediate effects of stretching and ultrasound on hamstring flexibility and proprioception. *Journal of Physical Therapy Science.* June 2016;28(6):1806-1808.

Sabrina Brunner is a doctoral graduate in acupuncture and Oriental medicine from the Pacific College of Oriental Medicine. She has a double masters from Yo San University of Traditional Chinese Medicine and Acupuncture in Los Angeles, California. She has 20 years of professional experience with peewee and professional athletes while specializing in sports injuries. Sabrina is licensed through the State Medical Board of Ohio for acupuncture and medical massage. She also has national certifications in both acupuncture (NCCAOM) and massage (NCTMB). Dr. Sabrina Brunner, DACM is very well known in Cincinnati for her successful treatments that consist of acupuncture, cupping, medical massage, and tincture of her choice.

◆

A Proposed Micronutrient Protocol for COVID-19 Pandemic

by Michalis Leotsinidis,[1] Constantine Kotsanis,[2*] and Nakos Kotsanis[3*]

References are available online at www.townsendletter.com.

Introduction

The recent world epidemic with coronavirus is only six months old. Humanity has seen such epidemics come and go. We theorize that the coronavirus is behaving similarly to the common flu virus, but it is much more contagious and virulent. The scientific community often provides desirable solutions against microbes with antibiotics, antivirals, antifungals and vaccines. However, such scientific wonders take an average of one to five years from development to implementation. We must be aware of the fact that mutations are the rule in the prokaryotic world. In clinical medicine we need considerable time to prove the efficacy of a concept or the effectiveness of a new drug. Even minor mutations can alter the effectiveness of new drug discoveries. As echoed by the philosopher Heraclitus "Τα Πάντα Ρεί *[egl.Ta Panda Rhei]*" – *"everything is in a state of flux and change*" is more true today than any time in history.

The question is what do we do in the meantime or in the event that new medicines or new vaccinations do not make ends meet in due time? We find that a strong immune system is an appropriate answer for many diseases. Optimal nutrition along with micronutrient support is historically considered the most effective way to limit infections and especially COVID-19.[1,2] In addition to this we have considerable experience in the use of oxidative interventions using high doses of vitamin C, medical grade ozone, and photodynamic therapy with methylene blue to be potent interventions against infections.[3-5] This is consistent with clinical reports over a number of years suggesting promising outcomes.[6-7]

Following in the footsteps of highly credible physicians of the past like Drs. FR Klenner, RF Cathcart, LJ Hoffer, and A Kalokerinos, all have used vitamin C extensively to strengthen the immune system and fight infections and other degenerative disease successfully. For the past 75 years we and a plethora of physicians around the world have successfully used micronutrients, and vitamin C to support patients against antibiotic, antiviral, and antifungal drug-resistant infections. If one were to revisit Dr. Klenner's work, one will see that vitamin C is very effective against drug-resistant infections. Actually Drs. Klenner, Cathcart, Hoffer, Cameron, and Kalokerinos, to name a few, used IVC only when necessary. Humanity might benefit greatly from combining the wisdom of the past with today's technological advances and other novel interventions/therapies.

One may argue that novel interventions are anecdotal and do not meet the rigorous scientific criteria of academia or the FDA. However, the incorporation by the scientific community of novel and or anecdotal interventions should be examined as we are currently facing a pandemic and the death of tens of thousands of people. This is in line with paragraph 37 of the World Medical Association (WMA) Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects.

The pandemic killer virus has no political or academic affiliations. The management of patients that suffer from COVID-19 should be reassigned exclusively to the clinically based physicians that live in the frontlines with the pandemic. Academia and the three-letter agencies like the CDC and the FDA should step back and wait to implement their treatments once the research has been completed. At this juncture medicine needs to incorporate all appropriate methods to help the patients and prevent a socio-economic and societal collapse. Now is the time for the research scientific community and all the regulatory bodies to become more tolerant and more supportive to the frontline doctors that are brave enough to use medicines and remedies that have shown promise but were ignored.

As treating physicians and scientists, we salute the efforts of academia and the three-letter agencies that use the "quantitative scientific method" to verify the efficacy and safety of new drugs and new vaccines. Epidemiologists estimate that there are about 140 emerging virulent pathogens that can show up anytime in the future.[8] Each time a new emerging pathogen infects humanity, it takes about two years to come up with new medicines and new vaccines. If we were to close down society for one

➤

[1]Professor and Chairman, Lab. of Public Health Medical School University of Patras. University Campus, 26504, Greece; email: micleon@upatras.gr.

[2]Medical Director Kotsanis Institute-Health Clinic, Grapevine, Dallas Texas, USA; email: gusatwork@aol.com

[3]Research Assistant and Micronutrient Scientific Advisor Kotsanis Institute - Palladion Rehabilitation Centre Tripoli Arcadia, Greece; email: aktouariosp@gmail.com

*Corresponding Author: *E-mail address:*gusatwork@aol.com (Kotsanis K.)

➤

to two years every time an emerging epidemic shows up, we could potentially place society and all businesses under house arrest for the next 280 years.

Using common sense to solve the problem should enter the minds of every government, every regulatory agency and academia. The solution to every pandemic should follow two scientific steps. In "Step One" we should utilize the qualitative scientific method. Step Two utilizes the quantitative method.

Step One. The qualitative scientific method has been in use for thousands of years dating back to Alkmeon (6th century BC), and Hippocrates (5th century BC). This means, the physicians in the frontlines that face patients every day, should utilize all their experiences and knowledge to fight the epidemic using all known FDA-approved pharmaceuticals as well as all anecdotally effective non-FDA approved remedies/interventions. The first job of the clinical physician is to stop the epidemic with all his/her knowledge. To save patients from a lethal epidemic, the treating physician should not fear the authorities for doing his/her job. In short, the frontline physician should practice his/her trade and art and be allowed to offer "quantitative" and qualitative" remedies to save his/her patients.

Step Two. Once the epidemic is under control, then we should allow academia and the government agencies to implement pharmaceuticals and vaccinations that have stood the vigorous standards of the "quantitative method."

Historical Facts

COVID-19 has spread exponentially at a global level. The epidemics of the past help us to understand the behavior of this new virus and options for the future.

A survey conducted by the EU concerning public opinion about the influenza pandemic revealed that EU citizens did not trust most sources of information about the swine influenza pandemic in 2009.[9] During the H1N1 epidemic Europeans only accepted as real the scientific findings of scientists and health care professionals. People were reluctant to change their social and personal behavior. In this survey three quarters of the respondents (75%) had not changed their daily routine. A worldwide threat, such as a pandemic, involves a lot of controversy that cannot be ignored. The fog of war is a feature of crises in general and not limited to military conflict.

The Spanish flu pandemic in 1918 killed 35-100 million people. A similar pandemic today could lead to the deaths of hundreds of millions. What is astonishing was the fact that 50% of the pandemic's deaths were in a period of about 10 weeks in the autumn of 1918. The estimated R0 of Spanish flu was 1.4 – 2.8 while seasonal flu is only slightly lower 0.9-2.1.[10] The COVID-19 virus had R0 estimates somewhat larger than the Spanish flu since the basic reproductive number (R*0*) of COVID-19 was initially estimated by the World Health Organization (WHO) to range between 1.4 and 2.5, as declared on 23th January 2020,[11] but data, based on the early phase outbreak in Italy, estimated it to be in the range 2.43 to 3.10.[12]

Making light of the seriousness of the Spanish flu in those days, arrogance prevailed over prudency. False reassurances resulted in lack of trust in authorities.[13] Keeping people isolated and nourishing social-phobia, led to a deteriorating society and increased hunger, not from lack of goods but because of reluctance to sell-give and deliver-donate. Building trust helps societies sustain infrastructure during crises. For example, the measures taken by the state of California, then, resulted in audacious behavior from the citizens. In California personal hygiene (masks, hand washing, keeping a distance), respect towards health care workers (unnecessary visits, home detainment) and volunteering to keep the community going were more effective since the population were given the data instead of authorities attempting to manage risk communication tactics.[13]

The Coronavirus Epidemic

There are no FDA-approved drugs or vaccines to prevent this coronavirus infection. The CDC itself reports that "*nonpharmaceutical interventions would be the most important response strategy.*"[14] This comes in line with a recent study in having revealed that the COVID-19 is unique in its structure, meaning that a new virus has emerged with a spike glycoprotein in its RNA genome that may provide efficient spreading in human population.[15]

We propose that a micronutrient protocol must be utilized so as to protect, prevent, ameliorate, and most importantly *confine the COVID-19 outbreak.* Protection, prevention, and confinement are our main focus. Nutritional deficiencies affect the immune response to infections.[16-17] Micronutrients and vitamins can boost immunity. Vitamin C, for example, was reported to be effective at eradicating an influenza virus.[18-20] Inactivation of viruses by ascorbic acid in vitro was first recorded by Jungebult in 1935.[21]

With the emergence of a new pandemic virus, vaccines are generally unavailable in time to provide protection.[22] Prudent utilization of vitamins, micronutrients and oxidative therapies against this pandemic virus is not a rejection of conventional medicine. We conducted a PubMed literature search on *"social distancing,"* which does not appear to be double-blind placebo-controlled or otherwise derived from evidence-based medicine. It's just common sense and the knowledge of epidemic control throughout history.

Actually, in the treatment of Severe Acute Respiratory Syndrome (SARS) in China, traditional herbal medicine had a prominent role in the strategy to contain and treat this outbreak.[23] Micronutrients such as 1) magnesium (a cofactor in any DNA repair mechanisms and chromosome segregation), 2) zinc (a cofactor for Cu/Zn superoxide dismutase, endonuclease IV, function of p53, FAPY-DNA glycosylase, and in zinc-finger proteins such as PARP) and 3) manganese (the vital component of mitochondrial manganese superoxide dismutase), to name few, are required to secure and protect genome stability and sustain all body functions such as immunity.[24] Finally, Dr. Cheng, member of the Medical and Scientific Advisory Board to the International Intravenous Vitamin C China Epidemic Medical Support Team, announced, from China, clinical trials for prevention and treatment with vitamin C. Dr Cheng has already been approved

to conduct three clinical trials, two that will focus on intravenous vitamin C (IVC) at high pharmacological doses and a third one that will use liposomal-encapsulated vitamin C since this can be applied more rapidly to the population on a national scale.

Scientists around the globe are recommending micronutrient protocols to *boost immunity* as a first line of defense against this pandemic, since there are no other promising options at this time to help treat dying patients from coronavirus. We are of the opinion that a micronutrient cocktail could assure a shield against emerging new viral outbreaks.

Our position in treating COVID-19 virus or any emerging epidemic must be done by a well-trained licensed physician that is familiar with all the pharmaceuticals and nutraceuticals recommended in the following protocol.

Vitamin C

> "*I have not seen any flu yet that was not cured or markedly ameliorated by massive doses of vitamin C.*"
> *(Robert F. Cathcart, MD)*

Ascorbic acid also known as vitamin C is an essential vitamin. Humans do not have the capability of manufacturing vitamin C; it must be supplied exogenously.[25] When used correctly it has no known toxicity other than loose stools.[26-28] However, patients with very low G6PD enzyme levels can undergo hemolysis. It is thus necessary to check the blood levels of G6PD enzymes prior to high dosage administration of ascorbic acid.

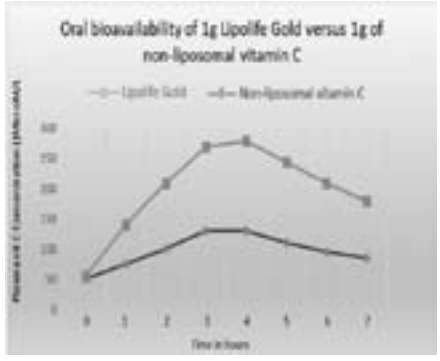
During this pandemic with COVID-19, vitamin C supplementation is crucial. It is well documented in the literature that vitamin C is rapidly depleted during an infectious disease and if not replenished poor outcomes will be observed.[29] Low levels of vitamin C (close to scurvy) are associated with respiratory tract infections, especially pneumonia.[30] Therefore, when dealing with a serious respiratory disease like pneumonia, vitamin C becomes a necessary supportive measure. Low blood levels of ascorbic acid are consistently found in patients with viral diseases.[31,32]

There are reports from throughout the world that prominent physicians have exceptional anecdotal outcomes when prescribing ascorbic acid for advanced staged infectious diseases. To name a few, Dr. FR Klenner recommended >4.5 grams C, 2-4 hours /daily; Dr. RF Cathcart proposed a bolus dosage till bowel tolerance; Dr. Linus Pauling published the effective use of vitamin C during a flu disease; and Dr. A Kalokerinos advocated its use against all diseases.[8] Scientists advocating its use have published data about the "*Quantity – Frequency – Duration*" of vitamin C use.[21,25-26,29,32] Effective dosing of vitamin C pharmacokinetics as an anti-viral molecule is dependent upon achieving sustained high plasma concentrations of vitamin C.[30,31,33]

The importance of vitamin C in health and disease has been acknowledged for every disease, even serious diseases such as viral diseases and cancer.[34-37] One of the main concerns of oral vitamin C consumption is whether or not oral vitamin C can achieve maximum therapeutic blood plasma levels against viral infections of the lungs. Orally, the maximum levels that can be reached, should be at least 250 µmol/L (4.05mg/dL).[38-40]

Scientists have emphasized the importance of the steady high blood plasma concentration of ascorbic acid of more than 200 µmol/L.[29,41] By keeping a constant high vitamin C plasma level, the body pool will reach its maximum tissue storage. As a result, during a viral disease at the onset, vitamin C will be available to quench the pathogen infection.[41-43] Hume and Weyers reported that supplementation of 6 grams per day of vitamin C abolished the decline of vitamin C concentration in leukocytes by the common cold.[44] Subsequently, it is documented that when blood plasma concentrations are high our body will efficaciously respond to any oxidative stress stimuli.[43, 45-47, 48]

Recently according to Hickey and Roberts (2008)[46] and Davis et al (2016),[48] vitamin C blood plasma concentration could exceed the oral barrier of 230 µMol/L if supplementation is taken with the liposomal form. Specifically, they observed that plasma concentrations of vitamin C >250 µMol/L could be obtained by a single one-gram dose of liposomal-encapsulated ascorbic acid. Most interesting is the fact that liposomal vitamin C can achieve plasma levels of 600 microM/L or more. Moreover, a combination of simple ascorbic acid with liposomal-encapsulated C are absorbed independently and can produce higher levels.[47] A single dose of liposomal-encapsulated C can keep steady concentrations of reasonably high vitamin C concentrations in the plasma more than four hours.[48] (See the graph, which was obtained from Dr. Hickey S. with permission of LipoLife Gold.)



The asymmetric behavior of COVID-19 and poor outcomes from patients appears to involve hemoglobin. This is probably due to the insult that red blood cells are up against from COVID-19 impairing hemoglobin, hence unlatching the iron atom. Scientists are trying to understand the biochemistry behind iron deposition and the pandemic virus.[49] This is probably due to the fact that confirmed COVID-19 patients appear to have elevated levels of ferritin. For this reason, vitamin C could be an asset in regulating iron.[50]

Finally, a recent review argues that there is a high probability that the immune system will respond to vitamin C adjuvant utilization on COVID-19 patients.[51] To be more specific, Boretti and Banik (2020) report that intravenous vitamin C seems to pose a dual function (antiviral-antioxidant) that may enhance immunity so as to cope with 1) the "cytokine storm" that characterizes the Acute Respiratory Distress Syndrome (ARDS) that appears in the later cycle of the COVID-19 infectious disease and 2) the oxidative stress that accompanies ARDS through the release of free radicals

➤

➤

and cytokines.[51] It appears that this new virus initiates a "*storm*" of cytokines since COVID-19 patients show an increase of C-reactive protein (hsCRP).[52]

There is no doubt that vitamin C pharmacodynamics has been observed to be clinically safe and successful in responding to viral ARDS and inhibiting the acceleration of a "*cytokine storm*" in *critically-ill* patients from infectious diseases such as COVID-19.[53] Of course, subsequent clinical research is needed as soon as possible to utilize IV vitamin C (VC) and oral VC (such as liposomal-encapsulated VC) as an adjuvant intervention-choice for COVID-19.

The methods we propose have been in use for many decades and in some cases over a century.

Recommendation

Prevention
Dosage: 1-2 grams/every 3 hours per day

Mild Influenza Onset
Dosage: Day 1-7 start with 3-5 grams/hour/day, Day 8-15: 2-3 g/2 hours/day, then after 1-2 g/3 hours/day

Serious Influenza Onset
Dosage: IVC *may be required*, Large dosage every half hour (3-5 grams) titrating to bowel of tolerance

*****Note: a) encapsulated Liposomal C is better b) unencapsulated Vit C and adjunct use with Vitamin E, R-a-Lipoic acid is prudent*

Vitamin D

Thirty years ago, Dr. Hope-Simpson theorized that "seasonal stimulus" linked to solar radiation could explain the remarkable seasonality of epidemic influenza. Solar radiation activates a vigorous seasonal vitamin D production in the skin that can have profound results in human immunity.[54]

1,25(OH)2D modulates our immune system to a point that can prevent excessive expression of inflammatory cytokines and increase the 'oxidative burst' potential of macrophages. Moreover, it stimulates the expression of anti-microbial peptides, present in neutrophils, monocytes, natural killer cells, and importantly in epithelial cells of the respiratory tract, which protect against lung infections.[55] The release of pro-inflammatory cytokines with COVID 19 is dependent on the virulence of the virus. Similarly, recent research confirms that the clinical phenotype of influenza correlates well with the amount of cytokines released.[55,56]

Furthermore, 1,25(OH)2D induces gene expression that in turn can enhance immunity. Almost every human tissue has vitamin D receptors. In turn the vitamin D receptors control gene expression from homeostatic control of mineral metabolism to focal activities that are essential for growth and immune function.[57] Vitamin D either directly or indirectly regulates the expression of up to 5% of the human genome or about 1250 genes. For example, vitamin D supplementation caused at least a 1.5-fold change in the expression of 291 genes that are involved in apoptosis, immune function, transcriptional regulation, epigenetic modification, response to stress, cell cycle activity and differentiation.[58,59] In a recent study 66 genes showed a significant change in their expression when supplemented with 2,000 IUs vitamin D3. Of the 66 genes, 52 genes increased their expression in response to vitamin D3 supplementation. Specifically, in genes coded for T Cell intracellular antigen-1 (TIA1), there was a 26-fold increased expression; and in those coded for immune function and zinc finger protein 287(ZNF287), there was a 6.8-fold increase.[58] Supplementing with vitamin D3 would be a prudent approach. There is, however, a caveat for vitamin D3 supplementation. The action of vitamin D3 depends upon the available magnesium levels since magnesium is required in eight crucial biochemical steps.[60]

A recent review reported that vitamin D supplementation reduced the risk of acute respiratory tract infection.[61] The prevention of acute respiratory tract infection is a critically important indication for vitamin D supplementation. People, especially those who are very deficient, experience substantial benefit when receiving daily or weekly vitamin D without bolus dosages. In general, vitamin D treatment was linked with a substantial degree of protection against acute respiratory tract infection among those who took part in the analysis with baseline circulating 25-hydroxyvitamin D concentrations less than 25 nmol/L.[61]

In line with this is the very enlightening article by Ilie et.al (May 2020), stressing the potential relationship between the mean levels of vitamin D with COVID patients and mortality.[62] It was revealed that in COVID-19 cases vitamin D levels were critically low, from the data acquired by 20 European countries. To be more specific the authors mention that not only in Nordic countries but in Southern Europe countries the levels were less than 30 nMol/L, but the aging population that experienced poor outcomes were those with the most deficit vitamin D levels. Thus, the potential association between COVID-19 therapy and vitamin D supplementation could not be ignored.

From a pharmacodynamic angle, there is solid scientific background that favors its utilization in early and later phases of the severe acute respiratory syndrome coronavirus 2, thus, reducing the impact of COVID-19 in populations that are characterized to be deficient in vitamin D. It appears that the data promotes supplementation so as to attenuate serious COVID-19 incidences.[63]

Recommendation

Prevention
Dosage: 400 - 5,000 IU per day

Mild Influenza Onset
Dosage: Day 1-7 start with 10,000 IU/day; Day 8-15: 5,000 IU/day, Day 16-30: 2,000 IU/day

Serious Influenza Onset
Dosage: Day 1 start with 20,000 IU/day; Day 2-7: 10,000 IU/day, Day 8-30: 5,000 IU/day

*****Note: Adjunct with Magnesium, Vit K_2 and Omega-3*

Magnesium

Approximately 800 enzyme systems require magnesium for their optimal functioning. It is well documented that magnesium deficiency is common reaching even 80% in some groups.[64]

Mitochondrial dysfunction is attributed to low levels of magnesium. Six out of the eight steps that produce ATP (adenosine triphosphate) in the mitochondria via the Krebs cycle require adequate levels on magnesium (magnesium is a cofactor for ATP production). We need optimum cellular energy to cope with viral disease because it comes with great metabolic and energetic costs. Incidentally, magnesium also seems to be able to insult the avian influenza PA endopolymerase and provides an anti-influenza target with optimum levels of magnesium.[65]

The potential role of magnesium in the development and activation of the immune system is profound.[66] Magnesium is a cofactor in most immune responses.[67] Magnesium is an option for someone wanting to boost their immune system in a viral epidemic.

Recommendation
Dosage: 400-2000 mg per day

Zinc

The essentiality of zinc on immune function has been well documented.[68] The results of more than three decades of work indicate that zinc deficiency rapidly diminishes antibody- and cell-mediated responses in both humans and animals.[69] Zinc deficiency has been linked to immune dysfunctions mainly affecting T-helper cells and decreasing natural killer (NK) cell activity. Moreover, zinc supports innate immunity and not only facilitates normal development and function of macrophages, NK cells, and neutrophils but also affects T and B cells function and growth.[70] Subsequently studies have revealed that macrophages and monocytes are stressed during zinc deficiency, as a result generating inflammatory cytokines such as TNF-a and IL-1b.[70]

In a Cochrane review, 13 randomized placebo-controlled trials revealed that, when taking zinc immediately upon appearance of common cold symptoms, there was a significant reduction not only in the duration but also in the severity of symptoms.[71]

It has been referred that excess zinc is not stored in the human body, thus consumption of this mineral, through diet or supplementation, is important in maintaining not only the integrity of the immune system but also body homeostasis since zinc deficiency is responsible for serious respiratory infections worldwide.[72,73]

Finally, a recent exemplary study argues the prophylactic effect that zinc may pose on COVID-19 (SARS-CoV-2).[74] Specifically, the article discusses how changes in zinc homeostasis could be linked with most of the common symptoms of COVID-19. Zinc's direct anti-infectious properties will only benefit against viral and respiratory tract cases; zinc is vital so as to 1) safeguard the respiratory epithelium inhibiting any pathogen entry, 2) increase ciliary length and movement, 3) balance every immune cells function multifariously, 4) prevent the formation of platelet aggregates and 5) inhibit viral replication, to mention a few effects.[74] The article presents numerous studies that reveal its effectiveness in coping with respiratory infections; but severity, frequency, and duration of the illness depends on the concentration, zinc's compound structure, and the time it is taken after the initial symptoms.[74]

Recommendation
Prophylaxis: Dosage: 10-25 mg per day
Onset of Infection: Dosage 60 mg per day
(*according to physician's discretion)*

Conclusion

This open letter is designed to bring light and hope to the dying and afflicted patients and to the devastated economies around the world. Given the above, and since we are in the midst of a global pandemic, time is of the essence. Exhaustive, randomized controlled trials cannot replace successful clinical results when it is necessary to act quickly and prevent physical and economic death and destruction. The methods we propose have been in use for many decades and in some cases over a century.

Wisdom involves making rational decisions.[75,76] We must endorse the plethora of available *quantitative* and *qualitative* data and the efficacy of "*the obvious,*" which in turn will definitely enhance clinical decisions especially when objective evidence has been collectively accumulated and revealed to us over generations.[77]

Our group is in support of any proposal that has been shown safe by government or academia, provided it is in accordance with the Helsinki Declaration. We respectfully request from all authorities that they allow all schools of thought to be employed against this common COVID-19 enemy.

We are facing a formidable viral epidemic. We must not limit the fight to drugs and vaccines, especially where strong evidence exists to back micronutritional support and other medical interventions. Our group strongly endorses the use of pharmaceuticals and vaccines in combination with micronutrient protocols and the use of anecdotal remedies that have a good clinical track record. We need methods that work! ◆

References are available online at www.townsendletter.com.

My Bioidentical Hormone Creams Are Killing Me!

by Jeffrey Dach, MD

With the publication of the July 2020 NASEM report, I was astonished to learn that for the past 20 years, compounded bioidentical hormones have been killing everyone.[1] If only we had used FDA-approved hormone pills and patches manufactured by the pharmaceutical industry, everything could have been so much better.

This Is All Nonsense

Of course, this is all nonsense, because over the past 20 years of prescribing compounded bio-identical hormones to thousands of patients, I can attest to good outcomes in patients on compounded bioidentical hormones, with relief of menopausal symptoms and good quality of life (QOL). Of course, adverse side effects can occur, most commonly related to excess hormone dosage. These are easily managed by adjusting dosage under the supervision of a knowledgeable physician.

Here is the conclusion of the NASEM Report: "Evidence does not support the clinical utility of compounded bioidentical hormone therapies and their use should be limited to patients who cannot use products approved by the US Food and Drug Administration (FDA)."[1]

This NASEM report reminds me of the last time this came up in 2016 when the Endocrine Society advised doctors against using compounded bioidentical hormones. Four years ago, I wrote an article suggesting the organization should change their name to the "Endocrine Nonsense Society." Similarly, NASEM, which stands for National Academy of Science, Engineering, and Medicine, should change its name to the "National Academy of Nonsense, Engineering, and Medicine."[2]

Compounded Bioidentical Hormones Are on the Chopping Block

The drug industry has a long history using unethical and illegal activities, including "dirty tricks" to advance its financial interests. Indeed, the drug industry has paid out 35 billion dollars in penalties for criminal and civil violations. One of the "dirty tricks' over the years is the seeding of medical literature with "ghost-written" articles, disparaging bioidentical hormones and promoting their own patented synthetic hormones.[3-5]

Pharmaceutical Industry as Organized Crime Syndicate

Books by two eminent physicians Drs. Peter Gøtzsche, and Marcia Angell have documented the enormous corruption of the pharmaceutical industry. Dr. Peter Gøtzsche has gone so far as to compare the pharmaceutical industry with an organized crime cartel that has captured our legislative bodies, regulatory agencies, medical societies, medical meetings, medical research, and the mainstream media, thus wielding enormous power over our society.[4,5]

Insidious New Campaign to Eliminate Compounded Hormones

With the publication of the NASEM report, the pharmaceutical industry has launched an insidious new campaign to eliminate compounded bioidentical hormones. This campaign is based on the NASEM report claim that only randomized placebo-controlled trials represent "medical evidence." The FDA, an agency captured by the drug industry, funded a report by NASEM to come up with the predestined conclusion: Since there is no evidence for efficacy or safety for bioidentical hormones, therefore bioidentical hormones should be placed on the FDA "Difficult to Compound List," a regulatory move which essentially bans compounded bioidentical hormones, eliminating a major economic competitor. It's just business. Two consequences will be 1) Post-menopausal women will have no access to the compounded hormone creams they are currently using; 2) Compounding pharmacies across the nation will go out of business.

The basis for the FDA-funded NASEM report is an old gimmick used over and over again by the drug industry to eliminate competing natural substances, and thereby gain market share. According to patent law, natural substances, such a bioidentical hormones, cannot be patented, so there is no money for expensive clinical trials.

The old gimmick is to "declare" that the only acceptable "evidence" is the randomized double-blind placebo-controlled drug trial of the type required for FDA new drug approval. Although the randomized double-blind placebo-controlled trial is considered the gold standard for FDA drug approval, this type of drug trial is not practical for natural substances, which cannot be patented, nor for off-label drug use. The reason patent protection is required is the cost involved in

a randomized trial is prohibitively expensive in the range of 100 to 250 million dollars. No drug company in their right mind would incur this expense without patent protection to guarantee profits on the back end. The same is true for most off-label drug use, usually involving off-patent drugs, meaning these are old drugs with expired patents.

To make the claim that the only acceptable "evidence" is a randomized placebo-controlled drug trial is false; and it is a standard gimmick or ploy used by the pharmaceutical industry for decades. Off-label prescribing is in the same boat, since there are no randomized placebo-controlled trials to support off-label use of an old drug. So, such an attack on compounded hormone preparations is also an attack on off-label prescribing, comprising 20% of all prescriptions

The Privilege of Off-Label Prescribing

New drugs are FDA approved for a specific "indication," a medical condition placed on the drug label. However, about twenty percent (one-fifth) of all drug prescriptions are prescribed off label.[1] This means the drug is prescribed for a different indication unrelated to the original FDA approval.

An example of off-label use is the prescribing of clarithromycin for multiple myeloma by Dr. Tomer Mark of Cornell as a repurposed anti-cancer drug. Clarithromycin's original FDA approved indication is an antibiotic to treat bacterial infection, not as a repurposed anti-cancer drug.[6,7]

This common medical practice of off-label use of a drug has always been accepted by all medical societies and regulatory agencies as a prerogative and privilege of the prescribing physician. Since twenty percent of prescriptions are not based on a randomized double-blind placebo-controlled trial (typically used for FDA new drug approval), the next obvious question is: What other types of evidence are used to justify off-label prescribing of drugs?

Evidence for Prescribing Drugs Off-Label

Doctors rely on many other types of evidence such as in-vitro and in-vivo animal studies, human observational trials, and registry trials. Another powerful and highly accepted type of medical evidence is called challenge-rechallenge, which proves drug causality. Challenge-Rechallenge is accepted by medical science as well as our legal system (a court of law) and is used in medical research to show causality of a drug or treatment.

Of course, the doctor must understand the physiology, the basic science showing the drug's mechanism of action. The importance of this cannot be over-emphasized, as it provides confidence that the drug is effective and can be used, or ineffective and should not be used.

NASEM Committee Rejects All Other Types of Medical Evidence

All of these other perfectly valid types of medical evidence have been rejected by the esteemed doctors of the NASEM committee, who came to their ridiculous conclusion that there is no evidence of clinical utility of compounded bioidentical hormones. Needless to say, this amounts to a form of scientific deception and fraud which, in a free society, should not be tolerated. This erosion of scientific integrity is real, and if unchecked by a grassroots movement of enraged post-menopausal women, this insidious campaign against compounded hormone replacement is likely to prevail, resulting in catastrophic consequences for millions of post-menopausal women and their compounding pharmacies.

FDA-Approved Bioidentical Hormones Preparations

All the hormones used in compounded preparations have been FDA approved and are used off-label in compounded preparations. Below is a partial list of FDA-approved hormone preparations for estradiol, progesterone, and testosterone.

As you can see with the chart, the bioidentical hormones, estradiol, progesterone, and testosterone have all been FDA approved for specific indications on the basis of randomized placebo-controlled trials. Off-Label use of these drugs and other drugs is a common physician practice. Compounded formulations of combinations of these three hormones is a form of off-label use and as such, the NASEM report requirement of placebo-controlled randomized trial for each compounded formulation is a ridiculous proposal; and in fact, it has never been required in the history of medicine for off-label prescribing by a physician.

Medical Evidence Supporting Off-Label Use of Bioidentical Hormones

The next obvious question is where is all this medical evidence excluded by the NASEM report supporting the clinical utility, safety and efficacy of bioidentical hormones for off-label prescribing? This evidence is abundant in the medical literature. For starters, I refer the reader to two excellent review articles by Drs. Kent Holtorf, Erika Schwartz, and David Brownstein.[8,9] There are many others.[10-18] A Google Scholar search for the key words, "**bioidentical hormones**" yields 5,200 articles in the scientific literature. Go take a look.

➤

Hormone Product	Year of FDA Approval	Manufacturer
Alora (estradiol)	1996	Watson Labs
Climara (estradiol)	1994	Bayer
FemPatch (estradiol)	1997	Parke Davis
Vivelle-Dot (estradiol)	1994	Novartis
Estraderm (estradiol)	1986	Novartis
Esclim (estradiol)	1998	Women's First Healthcare
Estrace (estradiol)	1993	Bristol Myers Squibb
Estring (estradiol)	1996	Pharmacia UpJohn
Prometrium (progesterone)	1998	Solvay Pharmaceuticals
Crinone (progesterone)	1997	Columbia Labs
AndroGel (testosterone)	1999	Unimed / Abbott
Testim (testosterone)	2002	Auxilium

➤

Hormone Replacement Is Not a Stand Alone Program

The one pill, one clinical trial, one FDA indication mentality of the drug industry is inadequate for the complexities of actual clinical practice prescribing bioidentical hormones for the typical post-menopausal patient. A bioidentical hormone program should not be considered a stand-alone medical intervention. A more holistic, integrative approach is required to achieve the best results. A complete patient evaluation that addresses micro-nutrient deficiencies, thyroid function, and gluten sensitivity is included in the program. I would recommend adding a cancer prevention program, as well, with testing for and supplementation with iodine, vitamin D3, selenium, and DIM (Di-Indole Methane).

Subservience to the Pharmaceutical Industry

In most of the NASEM reports, subservience to the pharmaceutical industry agenda is not so obvious. This one is very blatant. This NASEM "decree" reminds me of a scene in a Woody Allen movie, *Bananas*. The little island of San Marcos has a new dictator, and his first proclamation is "All subjects are to wear their underwear on the outside." Oh well, just another day for George Orwell's "Ministry of Health and Truth."

Conclusion

In the 1940s an obscure Penn State chemist by the name of Russell Marker devised the marker degradation process, which opened the door for manufacturing bioidentical hormones inexpensively in large volumes. Russell Marker gave this process as a gift to the world, declining to obtain a patent for his chemical formulation. Since the 1940s, bioidentical hormones have been prescribed by physicians for the betterment of human life, specifically to relieve post-menopausal symptoms. The FDA is seeking to change that by using a fraudulent NASEM report to ban the use of compounded bioidentical hormones. This is the most evil, despicable thing I have seen in a long time. Where is the outrage?

References

1. National Academies of Sciences, Engineering, and Medicine. 2020. The Clinical Utility of Compounded Bioidentical Hormone Therapy: A Review of Safety, Effectiveness, and Use. Washington, DC: The National Academies Press. https://doi.org/10.17226/25791.
2. Santoro N, et al. Compounded Bioidentical Hormones in Endocrinology Practice: An Endocrine Society Scientific Statement. *Journal of Clinical Endocrinology & Metabolism.* 2016;101(4): 1318-1343.
3. Fugh-Berman AJ. The haunting of medical journals: how ghostwriting sold "HRT. *PLoS Med.* 2010;7(9): e1000335.
4. Angell M. *The Truth About the Drug Companies: How they deceive us and what to do about it.* Random House Incorporated, 2005.
5. Gøtzsche P. *Deadly Medicines and Organised Crime: How Big Pharma Has Corrupted Healthcare.* London: Radcliffe (2013).
6. Mark TM, Coleman M. It's time to take clarithromycin seriously in multiple myeloma. *Acta haematologica*. 2016;135(2):101-102.
7. Mark TM, et al. Phase 2 study of clarithromycin, pomalidomide, and dexamethasone in relapsed or refractory multiple myeloma. *Blood Advances. 2019;*3(4): 603-611.
8. Schwartz ET, Holtorf K. Hormones in wellness and disease prevention: common practices, current state of the evidence, and questions for the future. *Primary Care: Clinics in Office Practice* 2008;35(4): 669-705.
9. Holtorf, Kent. The bioidentical hormone debate: are bioidentical hormones (estradiol, estriol, and progesterone) safer or more efficacious than commonly used synthetic versions in hormone replacement therapy? *Postgraduate Medicine*. 2009;121(1): 73-85.
10. Ruiz AD, et al. Effectiveness of compounded bioidentical hormone replacement therapy: an observational cohort study. *BMC Women's Health*. 2011;11(1): 27.
11. Martins V, et al. Compounded bioidentical HRT improves quality of life and reduces menopausal symptoms. *Journal of Prescribing Practice.* 2020;2(7): 384-390.
12. De Lignieres B, et al. Combined hormone replacement therapy and risk of breast cancer in a French cohort study of 3175 women. *Climacteric*. 2002;5(4): 332-340.
13. De Lignieres, B. Effects of progestogens on the postmenopausal breast. *Climacteric*. 2002;5(3): 229-235.
14. Fournier A, et al. Breast cancer risk in relation to different types of hormone replacement therapy in the E3N-EPIC cohort. *International Journal of Cancer.* 2005;114(3): 448-454.
15. Wood CE, et al. Effects of estradiol with micronized progesterone or medroxyprogesterone acetate on risk markers for breast cancer in postmenopausal monkeys. *Breast cancer research and treatment*. 2007;101(2): 125-134.
16. Hargrove JT, et al. Menopausal hormone replacement therapy with continuous daily oral micronized estradiol and progesterone. *Obstetrics and Gynecology*. 1989;73(4): 606-612.
17. L'Hermite M. Custom-compounded bioidentical hormone therapy: why so popular despite potential harm? The case against routine use. *Climacteric*. 2017;20(3): 205-211. HT can be optimized by continuously combining transdermal estradiol with progesterone (when required).
18. Thompson JJ, Ritenbaugh C, Nichter M. Why women choose compounded bioidentical hormone therapy: lessons from a qualitative study of menopausal decision-making. *BMC Women's Health*. 2017;17(1): 97.

◆

Dr Dach was originially trained in clinical medicine, and worked as an emergency room doctor in Illinois. He then worked 25 years as a hospital-based physician as a diagnostic and interventional radiologist. After retiring from radiology in 2004, Dr. Dach returned to clinical medicine and founded a new clinic specializing in bioidentical hormones, and natural thyroid for the low thyroid condition. Dr. Dach also prescribes low dose naltrexone (LDN) for a variety of inflammatory and autoimmune conditions.

drdach.com

Letters to the Editor

Re: Germanium and Kidney Function

My philosophy is usually not to comment on other colleagues' articles because first I have no time and I prefer not to interfere, even if I believe I found some mistake(s) or wrong interpretation that should be explained. However, I read in the June 2020 *Townsend Letter*, an article called, "The Canary in the Coal Mine or How to Improve Kidney Function," by Dr. Douglas Lobay, BSc, ND. I was attracted, at least, to the title. Another reason is that I earlier wrote a similar article in *Townsend Letter* called, "How to Reverse Kidney Atrophy with Naturopathic Medicine." I like to learn from other colleagues. Overall I found Dr. Lobay's article excellent and well documented, except it really needed a major correction on the last page of the article. He gave a list of substances, herbs, and other dietary supplements that were toxic for the kidney, including germanium.

Here I found a major issue. I was surprised and could not believe that a colleague in our profession still wrote categorically that germanium is toxic. Previously at the request of Dr. Collin, I wrote an article called "My Experience with Organic Germanium and Cancer" (January 2018, available online). I have been using GeOxy132 since 1973 to treat not only cancer but a variety of diseases. In 1990, I published in France my first book on germanium. During this period, using organic germanium even with a high dosage, nobody complained or died as a result of kidney damage. Now I may believe that Dr. Douglas G. Lobay has missed my article in the *Townsend Letter* and perhaps he was not aware of the difference between germanium dioxide and organic germanium Ge-132.

The problem of germanium being toxic started around 1990, being largely reported by the media and medical corporations in several countries. This included TV programs with so-called medical doctors from hospitals, university professors who have never previously heard about germanium, who did not know what germanium was, and had no experience using organic germanium. Suddenly they all were on TV directly warning people about taking germanium that, according to them, destroys the kidney with a high risk of death? How can this be?

Who organized this campaign? Big Pharma in England spent 12 million dollars on TV programs and articles to destroy the image of germanium. For what reason? I believe that germanium was over publicized regarding its anticancer properties, after which one incident that happened in Japan served as a detonator to destroy germanium's public image. This soon led to having germanium banned in various countries in Europe.

As I previously explained in 1990, three cancer patients, all elderly women with kidney problems, died of kidney failure after taking a high dosage of toxic germanium dioxide. Inorganic germanium is toxic to the human body but not the organic germanium compound Ge-132 known as carboxyethyl germanium sesquioxide. Ge-132 was first synthesized in 1967 by the Japanese scientist K. Asai and was proven very safe.

Ge-132 has different health functions – immunomodulatory actions (macrophages, NK cells, interferon γ), antioxidant effects, anti-inflammatory effects, anti-viral properties (now being widely used in Japan to protect against the coronavirus); and it detoxifies, and has the ability to expel heavy metals such as mercury. This is in addition to other anti-cancer properties. Organic germanium has a different structure. First of all, organic germanium is soluble in water and is expelled by the kidney and does not accumulate. After 20-30 hours you will find no trace of germanium in the body, only a very small quantity remains in the kidney, about 15 ppm (nothing in fact to damage kidney).

In 1971, I met K. Asai who introduced me to his organic germanium. Toxicology testing, made by the Asai Germanium Institute, the University of Kitasado's department of pharmaceutical sciences, the Saitama Medical University, and in 1972, the Japan Experimental Medical Research Institute

➤

➤

found that organic germanium, GeOxy-132, was incredibly safe, even with high dosages. Also, more recent research has evaluated the total safety of germanium sesquioxide compared to germanium dioxide, which has been shown to induce renal toxicity. So it was and continues to be a major mistake to say categorically that germanium is toxic to the kidneys and kills patients because we must differentiate between the two germaniums. For instance, we know that organic germanium eliminates heavy metals such as mercury via the urine. Therefore in my opinion it makes no sense if we say that it concentrates in the kidney to inflict damage!

Now germanium dioxide, I'll repeat, has a different structure than organic germanium. Inorganic germanium dioxide has difficulty being expelled, remains longer in the kidney, and may induce damage. However, the damage was done on aged women with cancer but not to middle-aged or young patients.

More recently, out of context, a 63-year-old male patient came to me with a case of rectal cancer. Chemotherapy had badly damaged his kidney function forcing him to go on dialysis. Are we going to stop chemotherapy just for that!? In my kidney article which you can read on my blog, I had prescribed high dosages of Ge-Oxy132 at that time, (the original Asai Organic Germanium) to this patient with kidney atrophy. After 40 years he is still here, feels healthy, and still comes to my clinic for consultation at 71 years of age. I do hope now that readers can understand that when you refer to germanium, you need to be sure it is organic germanium, which is very safe and does not induce kidney damage. Be sure it is not germanium dioxide.

I'll be happy to send information including a more recent report on the toxicological evaluation of organic germanium to interested doctors who wish to know more. I hope Dr. Lobay will forgive me for this intrusion, but I have over 47 years of clinical experience with organic germanium, accumulated scientific reports, and have been in permanent contact with Japan.

In my book on germanium, I describe several cancer cases that recovered from the disease, including some advanced cancers with no hope, such as brain cancer. We have ample documentation that demonstrates not only its safety with various physiological functions but its efficacy with anticancer action. My experience has shown that organic germanium is truly a bodily regenerator besides being very efficient to treat cancer disease and other diseases that I have had the opportunity to treat over past decades. I am available to colleagues who wish to learn more about organic germanium and how to use it with patients.

Serge Jurasunas, MD (hc), ND, MD(hom)
Email: sergejurasunas@gmail.com
Blog: naturopathiconcology.blogspot.com

Nephrotoxicity and neurotoxicity in humans from organogermanium compounds and germanium dioxide

by Alexander G. Schauss

Biological Trace Element Research. 1991;29:267–280

Abstract

There is no known biological requirement for germanium (Ge), germanates, or any organogermanium compound. Ge deficiency has not been demonstrated in any animal. The estimated average dietary intake of Ge in humans is 1.5 mg/d. Ge is widely distributed in edible foods, all of which, with few exceptions, contain less than 5 ppm Ge, since higher levels are toxic to most plants. Ingestion of Ge compounds has been shown to produce toxic effects in experimental animals.

In recent years inorganic germanium salts and novel organogermanium compounds, such as carboxyethyl germanium sesquioxide (Ge-132) and lactate-citrate-germanate (Ge lactate citrate) have been sold as "nutritional supplements" in some countries for their purported immunomodulatory effects or as health-producing elixirs, resulting sulting in intakes of Ge significantly exceeding the estimated average dietary intake. Since 1982, there have been 18 reported cases of acute renal dysfunction or failure, including two deaths, linked to oral intake of Ge elixirs containing germanium dioxide (GeO2) or Ge-132. In these cases, biopsies show vacuolar degeneration in renal tubular epithelial cells, without proteinuria or hematuria, in the absence of glomerular changes. Serum creatinine levels have been well above 400 µmol/L in such patients. In 17 of 18 cases, accumulated elemental Ge intakes reportedly ranged between 16 to 328 g over a 4–36 mo period, or between 100 to 2000 times the average estimated dietary intake for human. In surviving patients, renal function improved after discontinuation of Ge supplementation. However, in no case was recovery complete.

One organogermanium compound, an azaspiran organogermanium compound, 2-aza-8-germanspiro[4,5] decane-2-propamine-8,8-diethyl-*N,N*-dimethyl dichloride (spirogermanium), has been found to cause both neurotoxicity and pulmonary toxicity in phase I and II studies examining its chemotherapeutic potential as an antitumor drug in the treatment of various malignancies. In cancer patients given the drug spirogermanium, 40% experienced marked, yet transient neurotoxicity. Two patients suffered from pulmonary toxicity. Results of phases I and II human cancer trials for spirogermanium have not been favorable, with the exception of moderate benefits for three types of malignancies.

It is recommended that patients exposed to long-term (>3 mo) Ge supplementation at levels well above the estimated daily intake be medically supervised and monitored for potential renal-, pulmonary- or neurotoxicity. Further study regarding the mechanism of Ge induced nephrotoxicity in human is warranted.

Wikipedia's Bias Against Natural Medicine – A Petition

You can help stop it with a single email

The online encyclopedia Wikipedia has been exceedingly antagonistic against practitioners of alternative medical therapies. Medical professionals are increasingly aware of Wikipedia bias against entire medical systems that are regarded as "natural" or unconventional. This disturbing anti-health trend, which continues to worsen, can be traced back at least to 2006 when Paul Lee, the former listmaster of Dr. Stephen Barrett's Quackwatch, host of the then Skeptic Webring and a volunteer Wikipedia editor, put out a call on the International Skeptic Forum to invite Skeptics to come forward to begin writing content on the encyclopedia.

In his post to the Forum, Lee wrote, "There are many subjects for skeptics to get involved with, and we really need help. There are plenty of loons out there doing the editing right now and far too few skeptics to keep them at bay." He was also fully aware that he was acting in direct violation of Wikipedia's early neutrality policies. Ergo he writes, "Any coordination of efforts should be done by private email, since Wikipedia keeps a very public history of every little edit, and you can't get them removed. We don't need any accusations of a conspiracy."[1] Among the subjects Lee posted on his "watchlist" are orthomolecular medicine, complementary and alternative medicine, applied kinesiology, chiropractic, and aspartame.

Today, Paul Lee is a senior Wikipedia administrator with special editorial privileges.

Skeptic editors now far outnumber those trying to make efforts to write in favor of alternative medical therapies. Repeatedly I hear that efforts to correct the numerous inaccuracies, misinformation, biases and derogatory terms against these medical interventions, and complementary and alternative (CAM or integrative) medicine in general, are exercises in futility. The encyclopedia's parent organization, the WikiMedia Foundation, has been repeatedly unresponsive to demands for corrections and refuses to enforce its volunteer editors to abide by its editorial rules of neutrality when dealing with subjects regarding alternative medicine and the living biographies of its advocates.

Since Wikipedia is ranked as the number one website that people turn to for information about general health, illnesses, and possible treatments, I am convinced that numerous people have been wrongfully misled and dissuaded from seeking out alternative medical therapies as a course of disease prevention and treatment. Aside from depriving sick people from potential relief of suffering, by discrediting CAM practices, Wikipedia has also served as an economic weapon at the behest of pharmaceutical drug interests.

Despite my and others' numerous attempts and failures to deal directly with the Foundation's legal department and Board members to have misinformation corrected, there is an option that can be pursued on behalf of all alternative medical modalities and individual practitioners and advocates thereof who have been ridiculed, shamed, and wrongfully characterized on Wikipedia.

In 2012, the Center for Media and Democracy coordinated a nationwide campaign to reach out to the Koch Brothers-funded American Legislative Exchange Council (ALEC) corporate members, who pay annual dues of upwards to $50,000 in addition to awarding separate grants. ALEC has been described as a "corporate bill mill" for private interests and as a means to gain direct access to elected state legislators.[2] Due to ALEC's hosting of individuals with national reputations for espousing white supremacist and racist views as conference keynote speakers, a grassroots effort was undertaken to encourage ALEC corporate members to be ethically responsible and cease their memberships. The success of this campaign resulted in 114 major private corporations (representing a total market cap value of over $7 trillion) and 19 nonprofit organizations to cut their ties or allow their memberships to lapse, thereby exerting a significant blow to ALEC's financial base.[3]

I believe a similar strategy will be highly effective against the WikiMedia Foundation and may force the Foundation to finally take serious notice and act to correct the serious systemic problems plaguing the encyclopedia. It may be added that Wikipedia's co-founder Jimmy Wales, although now removed from the organization's direct administration, has continued to be one of the Foundation's major fundraisers. He takes this role very personally. Yet Wales also endorses skepticism's efforts to use the encyclopedia to wage its assault against alternative medical practices it happens to disagree with.

Therefore, we have drafted *a petition letter to send to Wikipedia's 500-plus principle benefactors (i.e. grant-giving foundations, charitable family trusts, corporate institutions and private individual donors) with the request to sever their financial relationships with the Foundation and withhold future grants and donations.* The vast majority of the benefactors who will be in receipt of the petition will be learning about Wikipedia's biases against and demeaning characterization of alternative health as a pseudoscience and quackery for the first time. Based upon the statistics of alternative medicine's increasing popularity, it is very likely many recipients of the petition either use or have used one or more non-conventional methods for their personal health.

The link to the petition letter that has been prepared is https://prn.fm/wp-content/uploads/2019/01/Letter-Wikipedia-benefactors-1.pdf. I ask and welcome you to be a signatory. The more high profile individuals and practicing medical professionals who sign (e.g. executives of professional associations, deans of colleges, chief editors of journals and

➤

➤

publications, university professors, and journalists, and certified and licensed practitioners in these medical disciplines, etc.), the greater will be the petition's impact to persuade donors to act from a higher moral principle of conscience. The goal is to present the Wikimedia Foundation's benefactors with evidence that the encyclopedia has a deep and serious problem and their charitable giving may be better served elsewhere.

If you agree to be a signatory, please send an email to **WikipediaWatch@protonmail.com** with your full name, degree (PhD, MD, DO, ND, etc.), your professional title, affiliated institution as you wish it to appear on the petition and city and state/country.

Please share this petition letter with others who you believe would and should be signatories.

With the growing consolidation of skeptic organizations into a reactionary movement and skeptics' increasing presence on Wikipedia, this is a critical moment for us to take the upper hand.

Gary Null, PhD

References

1. http://www.internationalskeptics.com/forums/showthread.php?t=52557
2. https://www.sourcewatch.org/index.php/American_Legislative_Exchange_Council
3. https://www.prwatch.org/news/2018/11/13426/alec-lost-membership-worth-over-7-trillion-market-cap

Promising Observations on Treating COVID-19

Recent news reports of successful treatments of COVID-19 infected patients provoked me to revisit the mechanisms of action for drugs that I have used for years in the treatment of "deep blood fungus" issues. That is my term for documented parasite infections identified by next-generation DNA sequencing testing developed in 2015 by Stephen Fry, MD (frylabs.com). Prominent among eukaryotes identified in blood specimens are *Funneliformis mosseae* (plant fungus), *Perkinsus* species (as from oysters), *Hydrurus foetidus* (stream algae), Spumella species (aquatic organisms), *Saccharomyces cervisiae* (yeast valuable for food production), and *Toxoplasma gondii* (protozoan parasite that can be found in unwashed produce), among others.

My clinical experience suggests that deep blood fungus (DBF) organisms play a contributory role in the development and progression of a wide range of "inexplicable" diseases, often treated with cortisone or chemotherapy. These include various cancers, blood cancers, severe skin conditions, sudden kidney failure, sudden worsening of diabetes, MS (multiple sclerosis), ALS (Lou Gehrig's disease), RA (rheumatoid arthritis), SLE (lupus), vague immune defense system disorders, Lyme disease, chronic fatigue syndrome, and others. Fry Laboratories tests have also confirmed DBF evidence in the plaque blocking heart arteries (our *leading* cause of death) and in other body organs. With research reports now suggesting that Alzheimer's dementia (and perhaps most others) involves infections in the brain, the possibility that many or most of our chronic pathologies result from unsuspected, untested, and undetected infections that remain *untreated*.

The question arises: why would hydroxychloroquine (anti-malarial) and azithromycin (anti-bacterial) play a role in rapid reduction of life-threatening COVID-19 symptoms? Particularly impressive are improvements with pulmonary symptoms, even when patients have deteriorated to the point of ventilation assist. Such recoveries have been attributed to interruption of the "cytokine storm," proposed as an exaggerated immune response that inadvertently challenges survival. Simply stated, anti*viral* drugs available today have not shown desired results for *this* virus, but *other* "anti*biotic*" medications have.

Over the past four-and-a-half years since genetic testing has been available, my work and others have confirmed that combinations of various drugs have provided (sometimes significant) clinical improvement for a laundry list of "we-don't-know-the-cause" distressing diseases. For dozens of years patients have enjoyed the benefits of treating rheumatoid arthritis and lupus arthritis with hydroxychloroquine – an anti-malarial. Similar results from combining metronidazole (anti-fungal) with allopurinol (gout treatment) have been seen since 1976, when Professor Roger Wyburn-Mason speculated that rheumatoid patients were suffering from amoeba invasion in support tissues. Recent studies have suggested that both of these drugs have powerful anti-inflammatory effects in many organ systems not just joints. (Interesting perspectives are found at http://arthritistrust.org/important-articles/) (Details on DBF are revealed in my two-hour lecture "Deep Blood Fungus: Dental and Other Connections to Devastating Illnesses" presented in 2018: https://healthchoicesnow.com/26236/deep-blood-fungus-iabdm/.

Cursory literature review of the two dozen-plus drugs that have been variously combined to "treat" DBF show reports of anti-inflammatory activity, whether reduction of cell signaling or activation of aggressive immune cell responses or other mechanisms. My studies in immunology since 1968 have convinced me that simplistic explanations have little value, since the systems are intricately complex. Those who demand double-blind studies before prescribing often-successful empirical therapy will watch their patients suffer. Some will die. (These therapy-altering interactions are reviewed in my 2020 lecture "Immunity-Inflammation-Infection: Rooting Out All Degenerative Diseases?" available soon at www.healthCHOICESnow.com.)

My clinical experience suggests that anti-fungal and anti-parasite medications have an important role to play in treating (even preventing?) COVID-19 infections. More provocative is the prospect that dental infections might predispose for more serious viral episodes – perhaps even with common influenza that kills 20,000 to 60,000+ Americans *each* "flu

season." Gingivitis is quite common, periodontal disease has been implicated in deeper tissue infections. Children have far fewer complications with COVID-19 … because their gums and teeth are in better condition? Specific dental care and proper prophylaxis might emerge as fundamental for effective treatment programs. (My 2019 lecture "Could Your Dentist Cause Your Cancer – Or Many Other Deadly Diseases" shows clear evidence, available soon at www.healthCHOICESnow.com.) Other modalities that we use (ozone, hydrogen peroxide, UV light, chelation, nutritional IVs and supplements, sauna and other detoxification programs, and so on) clearly contribute to reducing infection and boosting immunity as well.

Integrative practitioners and biological dentists must assume a directing role in helping patients to restore and maintain more robust immune system function, critical for surviving any infection. Various slogans and platitudes are bandied about, but our patients need concrete advice on daily living habits for a longer life, more comfortable and capable. While many conventional physicians and pharmacists dismiss the critical role of nutrition in creating and preserving better health, COVID-19 presents us with a life-saving teaching moment. Essential minerals are lacking in "fast foods" and "ultra-processed foods," which often contain higher levels of grains that can impair mineral absorption. One such essential micronutrient is zinc. Zinc deficiency is prominent in diseases of aging and in illnesses associated with immune compromise. Of course, all nutrients are critical, but everyone needs to compare the *striking* similarity of zinc deficiency symptoms to those of COVID-19 (https://tinyurl.com/ud33ulq). Incidentally, zinc is significant for oral health.

Government and medical leaders encourage (or "order") people to "stay home, stay safe" – but simple prevention and nutritional measures (applicable to *all* communicable diseases) are far more important than economy-busting social distancing and unconstitutional quarantine orders for the general public. We need to investigate why many people who are "infected" with coronavirus show minimal or no symptoms. What "healthy" factors distinguish them from others? What is different about people who have advancing and even life-threatening symptoms of COVID-19…perhaps also those with seasonal influenza? Possibly undiagnosed problems with the yeast syndrome figure prominently. Certainly, studies are needed. But my clinical experience suggests that early treatment with combinations of medications shown useful for deep blood fungus might reduce suffering and death. And *that* is our solemn duty.

John Parks Trowbridge, MD, FACAM
Distinguished Lifetime Achievement Award, ICIM
Who's Who Top Doctor in Advanced Medicine
Who's Who Lifetime Achievement Award
DIAL 1-800-FIX-PAIN

Statistical Significance Does Not Always Mean Clinical Relevance

Well the number crunchers and statisticians are at it again. While I sadly read of the demise of niacin for the prevention of cardiovascular events in the latest Cochrane Library analysis, I was not swayed by their data "pooling" or meta-analysis. What Cochrane did was to pool large studies over the years in order to determine if niacin by itself was efficacious or if, when added to other drugs such as statins, it increased their efficacy in the prevention of cardiovascular disease. At the end of all the number crunching their conclusion was "moderate to high quality evidence suggests niacin does not reduce mortality, cardiovascular mortality, non-cardiovascular mortality, the

➤

Please Support the Advertisers in this Issue

For advertising information please call 360/385-6021

Letters

➤

number of fatal or non-fight fatal myocardial infarctions, or the number of fatal or non-fatal strokes but is associated with side effects. Benefits from niacin therapy in the prevention of cardiovascular disease events are unlikely."[1]

The question that I have is did they properly evaluate the clinical information in many of these studies? For example, the median duration of their 23 randomized controlled studies with a total of 39,125 participants, was 11.5 months and the median dose of niacin was only 2 grams a day. The two largest studies used by Cochrane that skewed the results were the Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides and Impact on Global Health Outcomes (AIM-HIGH),[2] 3400 participants, and Heart Protection Study 2–Treatment of HDL to Reduce the Incidence of Vascular Events (HPS2-THRIVE),[3] 25,000 participants. These two large studies used 1.9 grams on average daily of the niacin ER (extended release) form. First, the maximum daily recommended dose of the ER form is only 2 g while it is known that immediate release (IR) niacin is more effective and can be given in higher doses. Better results are achieved with 3 to 4 g or more (up to 6 g) of IR daily. Second, the selection of patients is crucial.

The patients that do best with niacin are those that have metabolic syndrome (MS). And yes, that would be patients who have high to very high triglyceride levels and very low HDL. In the HPS2-THRIVE and AIM-HIGH studies, baseline triglyceride (TG) levels were relatively modest or mildly elevated: 127mg/dl (HPS2-THRIVE) and 161mg/dl (AIM HIGH). The HPS2-THRIVE study alone comprised about 73% of Cochrane's entire study population. The current TG criterion for MS is 150 or higher. The HPS2-THRIVE group at study entry treated with a statin had low LDL (63) and relatively high HDL (49.6) This is a group unlikely to be helped further by niacin. The AIM HIGH at entry had LDL 71, HDL 34.9. so possibly a group to be further helped with niacin. In fact, a sub-analysis in this group of those patients with high TG (198 mg/dl or greater) and lower HDL at entry (less than 33 mg/dl) showed a potential benefit of combined statin and niacin therapy with a hazard ratio of 0.74 (p=.07).[4]

It is a well-known fact that higher triglyceride levels cause higher LDL particle counts with higher concentrations of small dense LDL, which are more atherogenic then the larger less dense LDL particles.[5] The Cochrane analysis study was swayed mostly by these two very large studies, which did not have optimal patient selection for the addition of niacin to a statin. Also, optimal doses of niacin were not used. A good paper which brings these points to bear was published just a few months after the Cochrane analysis and should be read by every practitioner.[4] These authors also point out that the IR niacin should not be given at bedtime but rather at mealtime. At bedtime when a patient is fasting or relatively fasting, it induces a sympathetic response and that also can provoke cardiovascular events. Finally, the authors also point out that the best absolute mortality benefit of any statin trial was in the Scandinavian Simvastatin Survival Study (SSSS),[5] producing

an absolute mortality benefit (AMB) of 3.5% in established coronary artery disease over 5-6 years (P=.0003). For niacin studies, the 15-year follow-up in the Coronary Drug Project[6] yielded a higher AMB of 6.2% (P=.0004) while the Stockholm Ischemic Heart Disease[7] showed a 7.8% (P=.035) AMB using niacin plus clofibrate over five years vs. no lipid medications in the placebo group. These latter niacin trials were from 1986 and 1988 and were not included in the Cochrane analysis!

It is true that some people have difficulty tolerating niacin, but many people do get used to the flushing and it can wane with time. There is a tendency of an increased risk for diabetes with niacin as with statins. But overall, the side effect profile is much better than with statins.[8] There are no muscle aches and pains, myopathies, neuropathies, memory problems, or lower steroid hormone levels that you'll see with the statins. Long term statin use can cause impairment of cardiac diastolic function[9,10] (likely due to reduction of synthesis of ubiquinone and Heme-A) and increased risk of calcification of arterial walls and connective tissue due to blockage of vitamin K2 synthesis.[9] Niacin also has anti-inflammatory properties and is also being studied in other medical conditions such as inflammatory bowel disease.[11] So niacin for cardiovascular patients is not dead, and there are many practitioners out there who are smart enough to still be using it with properly selected patients.

George Milowe, MD

References

1. *Cochrane Database Syst Rev*. 2017 Jun; 2017(6): CD009744
2. *N Engl J Med*. 2011; 365; 2255-226.
3. *N Engl J Med*. 2014;371:203-212.
4. *J Clin Lipidol*. Nov-Dec 2017;11(6):1309-1317.
5. *Lancet*. 1994 Nov 19;344(8934):1383-9.
6. *J Am Coll Cardiol*. 986;8:1245-1255.
7. *Acta Med Scand*. 1988;223:405-418.
8. *Am J Cardiol.* 2007 Mar 19;99(6A):22C-31C.
9. *Expert Rev Clin Pharmacol.* 2015 Mar;8(2):189-99.
10. *Perm J*. 2019;23:18.257.
11. *EMBO Mol Med*. 2017 May; 9(5): 571–588.

◆

Research on Chlorine Dioxide

review by Owen R Fonorow
Founder, Vitamin C Foundation

Forbidden Health: Incurable Was Yesterday (translated, Edition 2a)
by Andreas Ludwig Kalcker
ISBN 879-84-617-4272-1; Publisher: Voedia; c. 2018; 436 pages

Dr. Kalcker has a remarkably open mind and is the leading researcher today in chlorine dioxide (CDS). His lectures and books clearly explain his theory of how and why a few drops of a "water purifier" can effectively target pathogens in the human body, e.g. viruses. bacteria and parasites, even biofilm, without toxicity to the trillions of healthy cells or intestinal flora.

This targeted oxidation miracle is similar to the "Flash Oxidation" first reported by megadose vitamin C pioneer Fredrick Klenner, MD, in his 1971 paper "Observations on the Dose and Administration of Ascorbic Acid When Employed Beyond the Range of a Vitamin In Human Pathology":

> Ascorbic acid has many important functions. It is a powerful oxidizer and when given in massive amounts; that is, 50 grams to 150 grams, intravenously, for certain pathological conditions, and "run in" as fast as 20 Gauge needle will allow, it acts as a "Flash Oxidizer,"[4] often correcting the pathology within minutes.

In fact, the effects of a few drops of CDS and massive-dose vitamin C are so similar that it piqued the interest of the Vitamin C Foundation. Yes, 50 to 150 grams of intravenous vitamin C has wonderful effects for all cells, but there is no dismissing the same anti-pathogen "flash oxidation" effect with a few drops of MMS/CDS; a solution that is well within the reach of the entire human population – which probably explains the forces behind the Amazon ban.

On Pages 380 and 381 of Dr. Kalcker's *Forbidden Health* in his discussion of a drug Dioxychlor (really sodium chlorite) clinical study, he focuses on the fact that the protocol that destroyed viruses in the lab included a 15 g intravenous vitamin C drip.

> In 1986, Stanford University Microbiology lab performed a series of tests that showed the effectiveness of Dioxychlor (sodium chlorite) in the neutralization of different viruses. The concentration utilized in all these trials was 0.75 ppm. Viruses include Herpes II, HTLV III (HIV) Cytomegalovirus, and also the Pseudomonas bacteria. The electron microscope show complete eradication of viruses and Pseudomonas after treatment.

Kalcker wrote: "Apparently, no one realized that in this trial vitamin C (Ascorbic acid) was the acid that activated the sodium chlorite turning the sodium chlorite at 2.5% = Dioxychlor into chlorine dioxide (CDS)."

This book is now available in English from the Vitamin C Foundation. Proceeds benefit the foundation. The book can be ordered at https://vitamincfoundation.org/shop. Price may vary depending on demand and supply.

◆

Pathways to Healing

by Elaine Zablocki

Contemplative Care at the End of Life

Kirsten DeLeo

"Being present with dying people is not something we are taught growing up at home or in school," writes Kirsten DeLeo, a trainer in contemplative end-of-life care. "Individually and as a society we are ill-equipped to be present for those in our midst who are at the threshold of life and death."

For more than 25 years, DeLeo has served hospice and palliative care patients in various settings and has been teaching and training professional and family caregivers worldwide. DeLeo is the lead faculty of Authentic Presence, a professional training in contemplative end-of-life care that is offered in the US and Europe and integrates mindfulness and compassion techniques to strengthen resilience, self-care, and patient-care. She is a member of the Buddhist Ministry Working Group, an initiative of Harvard School of Divinity.

In her new book, *Present Through the End: A Caring Companion's Guide for Accompanying the Dying*, DeLeo offers tools for all of us to think about and prepare for what we and our family members would need when faced with incurable illness.

Her first piece of advice is, be present. Sitting at the bedside of a dying person may be challenging in many ways. "Living and dying happen in the present moment," she writes. "Being

Contemplative Care in the Time of COVID-19

We picture a good death, surrounded by loved ones. COVID-19 robs us of this opportunity. If you have a family member or friend facing the end of life, you may be unable to visit because they are cocooning; or visiting restrictions may prevent you from being there. This is a heartbreaking situation to be in. What can you do? You may find it reassuring to know more about the care the person is getting. Speak with the staff and also stay in close touch with others who are part of the person's life.

Of course, there are creative ways to connect. Phone or video calls or old-fashioned letters.

I recently talked to healthcare professionals who, whenever possible, try to facilitate virtual good-byes via Zoom and Whatsapp. They've learned this can provide comfort; but also, sometimes it can be stressful and increase the sense of distance.

A friend whose father was dying of old age on the other side of the country stayed connected with him over the phone. At scheduled times his nurse put the phone next to his ear, and my friend read his favorite poems to him. Or they sat in silence so he could hear her breath and she his. Her father died in his sleep while she was on the phone with him. She said that she felt strangely comforted by this experience.

Human touch and human presence are the hallmarks of hospice and palliative care. When COVID-19 patients are in the ICU, it can be painful for their families to see them unresponsive, attached to tubes and machines. An ICU nurse caring for COVID-19 patients told me she is acutely aware of how much her presence still matters, despite the gloves, mask and all the other protective gear. At the bedside, she imagines standing in for all the loving people who cannot be there.

So much pain stems from not knowing our loved one's wishes. Many of us have never talked about end-of-life care, and suddenly we are faced with tough decisions. Talk to your family and friends about your wishes now, and find out about theirs, as life is precious.

Kirsten DeLeo

at someone's bedside is a continual reminder to stay in the moment, to slow down, and be."

She recalls one of her first hospice patients, Charles, and their moments of connection as human beings. "Through his presence, Charles taught me how to be present for others," she writes. "He showed me that it was okay to feel vulnerable and still show up. He taught me how to stay when I wanted to run, to remain open when I felt sad or afraid."

Sometimes you want to support a dying person, but you don't really know what to say to them. You don't know what would be helpful. First, DeLeo suggests, just be present with that experience. Be aware of what is happening for you without judging your experience. "Be honest and natural," she writes. "Quietly acknowledge 'I don't know what to say but I'll just be here and we can sit together,' and then just listen."

"Sometimes people can struggle with extreme fear and anxiety when faced with the reality of their death." DeLeo writes. "Try not to talk them out of it or diminish their experience and feelings in any way.... Do let them know that they are not alone....Hold their hands, listen and extend your unconditional love to them. Love is the most powerful antidote to fear."

In addition, DeLeo suggests asking open questions that signal you are listening and present. "There is no fixed script or set formula to follow," she notes. "In essence a dying person needs to hear, feel, and be assured of three things: you matter, you are loved, and your wishes and values are respected." Possible questions might include the following:

- Tell me about your life. What has given you joy?
- Who has been most important to you?
- Is there anything weighing on your mind you would like to talk about?
- What gives you strength?
- Is there anything you would like to accomplish with the time you have left?
- Are there things that would offer you comfort?
- Who would you like me to call when death draws near?

Useful Pointers in Clear Language

This is a compact book written in clear, everyday language. It's full of useful tips, short meditations and exercises to spark new understandings. For those who have avoided thinking about death, this book offers an introduction to the tools we will need when death happens.

The section on how to support a child when a loved one is dying offers practical suggestions:

- Use clear words that are appropriate to the child's age.
- Give them the information they need at the moment and pause to check their reactions before offering more.
- Encourage them to share their inner world through art, music, or dance.

A chapter called "When Death Approaches" helps us prepare ourselves for the moment of death. DeLeo suggests steps we can take to create a peaceful atmosphere. We might say to the hospital staff, "Please disconnect all monitors and IVs that aren't needed for comfort care. Please do not attempt resuscitation."

She recalls a young man in his mid-30s who was dying of cancer. As death approached, his body went into spasms. "We all felt his pain and struggle – the family, the entire ward – yet there was always an invisible net of love and connection surrounding him," she writes. "Eventually Sam calmed down and his body and facial features relaxed right before he took his final breath. There was an incredible sense of stillness and peace in the atmosphere. We continued sitting with him in the special atmosphere, without saying a word, for what felt like a very long time."

DeLeo's work is dedicated to sharing tools so that when we die, more of us will die surrounded by an invisible net of love and connection. In addition to this book, she is also available in online and in-person courses and offers courses through Authentic Presence. The training program has online courses for family caregivers, a professional certificate program for those with a long-term commitment to end-of-life care, and special events for professionals in self-care and communication.

Resources

Website: kirstendeleo.com
DeLeo's website includes links to coming events, a blog, and a list of resources.

Authentic Presence. Website: authentic-presence.org
- 8-week Online Course for Family Caregivers: Caring for Others, Caring for Ourselves
- Professional Courses and Certificate in Contemplative End-of-Life Care: Cultivating Compassionate Presence, Mindfulness & Awareness in End-of-Life Care, Authentic Presence Immersion

These modules offer an opportunity to immerse yourself in the practice and integration of contemplative methods while expanding your professional skills and knowledge. They can be taken in any sequence, and together make up the Certificate in Contemplative End-of-Life Care. In order to be certified, participants must have experience in a professional or volunteer capacity in caring for patients or clients.

The certification process can take one to two years to complete. The modules are offered as online courses. They are also offered as in-person workshops in Australia, Germany, the Netherlands, Ireland, UK, and the US. All three courses have been approved for continuing education contact hours by the Association of Professional Chaplains and by the California Board of Registered Nursing.

Elaine Zablocki is the former editor of CHRF News Files.

◆

Curmudgeon's Corner

by Jacob Schor, ND, FABNO
drjacobschor1@msn.com

Tolle Causam: When Fish Oil Protects the Brain from Air Pollution Damage

A recent paper by Jiu-Chiuan Chen at the University of Southern California has me searching online for the origin and real meaning of "*tolle causam*." This phrase appears on every naturopathic physician's website because *tolle causam* is held out as one of the philosophic foundational cornerstones of naturopathic medicine. The National University of Natural Medicine's (NUNM) website lists it second, after the healing power of nature, on their list of the naturopathic principles of healing, even before the classic *primum non nocere*: first do no harm, which is placed third on their list.[1]

Chen et al.'s study has me wanting to fine tune the definition of *tolle causam* in order to apply it more precisely. Let me start with describing the Chen study. Back in 2015 Chen's group reported that higher exposure to air pollution, specifically the very fine particulates with diameters <2.5 µm and usually referred to as PM2.5, led to shrinkage in the brains of elderly women, especially of the white matter.[2] These PM2.5 particulates result from combustion, that is burning fuels in cars, factories, and power generating facilities. In Chen's new study, published July 15, 2020, they updated their initial report and suggested a possible way to protect against this unwanted brain shrinkage.

The purpose of Chen's current study was to determine whether omega-3 fatty acid levels modify the potential neurotoxic effects of PM2.5 exposure on normal-appearing brain volumes among dementia-free elderly women.[3] Translating that into English, they wanted to know if eating fish offered any protection. This was an observational study and followed a total of 1,315 older women (average age 70 at the study onset) who were participants in the Women's Health Initiative Memory Study-Magnetic Resonance Imaging (WHIMS-MRI) study and enrolled between 1996 and 1999. This cohort was a subgroup of the 7,427 women enrolled in the Women's Health Initiative Clinical Trials (WHI-CT) of postmenopausal hormone therapy. The Chen cohort participants underwent structural brain MRIs between 2005 and 2006.

Sophisticated software and collected data allowed the researchers to calculate PM2.5 exposures for the three years prior to each woman's brain MRI. Fish consumption was determined by food frequency questionnaires. Baseline levels of omega-3 polyunsaturated fatty acid levels were measured in the red blood cells of the participants and were compared with PM2.5 exposure and brain volumes as calculated from the MRIs.

When all was said and done, Chen et al confirmed their initial finding that greater PM2.5 exposure was associated with decreased white matter and shrunken hippocampus mass. And as they suspected, fish consumption offered protection against this damage. The benefits were significant. For each inter-quartile increment (2.02%) in omega-3 index, the average volume was 5.03 cm^3 ($P<0.01$) greater in the white matter, and 0.08 cm^3 ($P=0.03$) greater in the hippocampus. By the way, the associations with red blood cells, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) levels were similar; one fat wasn't any better than the other in this circumstance. In many ways, these findings are clinically important as they offer an accessible way to prevent at least some of the damage now associated with PM2.5 exposure.

The evidence has grown steadily in recent years that exposure to air pollutants, in particular PM2.5, increase risk of various neurological disorders, including stroke, cognitive decline, and accelerated brain aging. These particulates are also associated with cardiovascular disease and overall mortality.[4] Exposure to ambient PM2.5 is now considered an environmental risk factor for cognitive decline among the elderly.[5] This association between PM2.5 and decreased brain size, is one of the more striking measures to be reported.

PM2.5 particles are tiny enough to enter the body through the respiratory tract directly into the blood circulation system. As the blood flows through the body, these particles trigger inflammation causing damage to other systems, including the heart and brain. The omega-3 oils in fish are important components of the brain's synaptic membranes and are critical to maintaining brain structure and function as people age and these fats are associated with greater total brain volume and gray matter.[6,7] Fish oils have already been reported to reduce brain damage from environmental toxins, including lead, organic solvents, and mercury.[8-10] It doesn't take a great stretch of the imagination to wonder whether these oils might also protect the brain from fine particulate damage.

Another way to say this is that among older women living in areas with high levels of air pollution, those who had the lowest levels of omega-3 fatty acids in their blood had the greatest risk of brain shrinkage when compared to women who had higher levels. Eating fish prevents one's brain from shrinking like a prune when you get old. Even what many people would consider to be moderate fish consumption seems to be enough to counter the damage associated with this air pollution: just one to two servings of fish per week were enough to provide significant benefit. So, if all this is true, what is my problem? Why my ruminating over the *tolle causam* principles

"*Tolle causam*" is usually translated in naturopathic circles the way NUNM does on their website: "Identify and treat the cause." Google.Translate disagrees and says it means, in Latin, "Take the case."

"Tolle," assuming it is Latin (and not German in which case it means "amazing"), is the second-person singular present active imperative of the verb *tollō* (tollo, tollis, tollere), which means either to raise, lift up, take away, remove or destroy.[11] "Causam," the accusative form of the female noun *causa* that means cause or reason, is relatively straightforward. Thus, a possible translation could be "Remove the cause."

The historical origin of the other foundational phrases used in naturopathic medicine are well documented. "*Primo non nocere*" for example, dates back to the mid-1800s. Thomas Sydenham first used the English version, "First do no harm" in 1860.[12] The earlier use of the Latin version is generally attributed to the French pathologist Auguste François Chomel in about 1849.[13]

But in the case of "*tolle causam*," the history of the term eludes me. My hope that a better understanding of its origin and history would allow me to use it as a philosophic compass and tell me how to interpret Chen's fish data is going nowhere.

The Center for Disease Control says that according to their surveys just under 12% of US adults 65 or older report subjective cognitive decline.[14] That's a lot of people.

Should we actively encourage all of these people to eat two servings of non-fried fish a week? Or should we be following our philosophy, heeding that injunction to "treat the cause"?

The cause is not fish deficiency. In this particular study, it is particulate air pollution as measured by PM2.5 levels. Treating the cause by reducing PM2.5 is the approach the US Environmental Protection Agency (EPA) had been taking under the Clean Air Act, and it was helping. Fine particulate levels in the US decreased about 25% from 2009 to 2016. According to a 2019 publication from the National Bureau of Economic Research, this trend shifted in 2016 when PM2.5 levels began to increase, rising 5.5% by 2018.[15] This average increase was driven by a nearly 30% increase in levels in the Western states. A number of factors contributed to these increases, but researchers suggest that the major contributor was decreased enforcement of the Clean Air Act. This law and its updates had been responsible for the strict air pollution standards set for power plants, factories, vehicles and other sources of pollution. Enforcement of these laws had been improving air quality across the country. An estimate by the Environmental Protection Agency suggested that these regulations might prevent 230,000 early deaths in 2020--or might have if enforcement had continued.[16] It is calculated that the 5.5% increase in PM2.5 levels nationwide from 2016 to 2018 will be associated with 10,000 additional premature deaths this year. These calculations do not take in to account the risks for morbidity that have been recently linked with air quality such as the increased risk of dementia described in Chen et al.'s study.[17]

Environmental protections were further weakened in early June 2020 when regulations were altered by two Executive Orders. The first Order waived environmental reviews of infrastructure projects in order to encourage building during the current economic slowdown. The second rule changes the methodology used by the EPA to analyze cost benefits

➤

➤

resulting from Clean Air Act regulation, greatly limiting the strength of future controls on air pollution.[18] These and other recent policy changes will likely be associated with worsening air quality in the US.

Getting our patients to eat more fish as suggested by Chen et al is not a bad idea, but it is not treating, removing or in anyway, addressing the cause of the disease. Chronic PM2.5 triggered inflammation and organ damage is best treated by reducing PM2.5 levels. The right course of action seems clear, that all possible effort should be made to reduce levels of PM2.5 in the air we breathe.

This might come off as a political stance and many of us in our professional capacity as physicians strive to be publicly apolitical. Favoring health over pollution has turned into a partisan issue in recent years. No doubt there are those who will criticize my simplification of these issues and have arguments as to why reduction of pollution controls is a good strategy. I have yet to read an argument for doing so that is compelling. In the end the rationales to reduce pollution control enforcement and not limit emissions seem to be about maximizing profits and increasing income for a minority of the population at the expense of the health of everyone.

Have we translated "*tolle causam*" correctly or not? If we really do believe in treating the cause, then as a profession, we do have to take a political stand. Too often our profession's political agenda has been self-serving. We fight for licensure to keep our members in unlicensed states out of trouble. We lobby for dietary supplements and compounded medication that we sell at a profit. We lobby for insurance coverage or greater scope of practice; things that will help our own but the public only indirectly. If our goal is really to improve health for the largest number of people, it's time to take on issues that will directly do so.

CALENDAR

OCTOBER 30-NOVEMBER 1: FREQUENCY SPECIFIC MICROCURRENT MASTER CLASS in Taiwan. CONTACT: 360-695-7500; https://frequencyspecific.com/

OCTOBER 31-NOVEMBER 1: ARIZONA NATUROPATHIC MEDICAL ASSOCIATION CONFERENCE – Neurological and Musculoskeletal Issues online. CONTACT: https://www.aznma.org/

NOVEMBER 6-7: NEW HAMPSHIRE ASSOCIATION FOR NATUROPATHIC DOCTORS (NHAND) 2020 ANNUAL CONFERENCE: Science, Spirit & Clinical Pearls. Virtual Online Event. CONTACT: conference@nhand.org; https://www.nhand.org/annual-conference/

NOVEMBER 6-8: GREAT PLAINS LABORATORY presents ENVIRONMENTAL TOXIN SUMMIT online. CMEs available. CONTACT: https://www.gplworkshops.com/

NOVEMBER 6-8: FREQUENCY SPECIFIC MICROCURRENT CORE MODULE 2 – NEURO & VISCERAL in Chicago, Illinois. Also, **DECEMBER 3-5** in San Francisco, California. CONTACT: 360-695-7500; https://frequencyspecific.com/

NOVEMBER 7-8: 2nd EPIC FUNCTIONAL MEDICINE CONFERENCE in Charlotte, North Carolina. CONTACT: https://epicfmconference.com

NOVEMBER 13-15: 21st ANNUAL CONFERENCE OF THE WESTON A. PRICE FOUNDATION - Staying Healthy in a Toxic World in Atlanta, Georgia. CONTACT: https://www.wisetraditions.org/

DECEMBER 4-6: GENETIC METHYLATION SERIES 1 with Marc Harris, MD, ND, in Las Vegas, Nevada. CONTACT: 800-890-4547.

DECEMBER 6-8: FREQUENCY SPECIFIC MICROCURRENT CORE MODULE 1 – PAIN/INJURY MODULE in San Francisco, California. CONTACT: 360-695-7500; https://frequencyspecific.com/

DECEMBER 9-10: FREQUENCY SPECIFIC MICROCURRENT SEMINAR-SPORTS COURSE in San Francisco, California. CONTACT: 360-695-7500; https://frequencyspecific.com/

DECEMBER 11-13: 28th ANNUAL A4M/MMI WORLD CONGRESS virtual onlilne. CONTACT: www.a4m.com.

JANUARY 29-30, 2021: GREAT PLAINS LABORATORY PRACTITIONER WORKSHOPS on Organic Acids Testing and Environmental Toxins Testing ONLINE. CMEs. **CONTACT:** 913.341.8949; www.GPLWorkshops.com

MARCH 5-7: FLORIDA HOMEOPATHIC SOCIETY ANNUAL CONFERENCE – Homeopathy & Traditional Chinese Medicine: Where the Modalities Meet with Hilery Dorrian, L.Ac, LCH in Orlando, Florida. CONTACT: www.floridahomeopathicsociety.org; cicamp7@gmail.com

MARCH 5-7: THE FORUM FOR INTEGRATIVE MEDICINE "Navigating Recovery in Complex Chronic Illness" ONLINE. CONTACT: forumforintegrativemedicine.org

MARCH 10-14: 68th CONGRESS OF THE INTERNATIONAL COLLEGE OF INTEGRATIVE MEDICINE – Endocrine Ecosystem: Balanced Hormones and Reduced Toxicity for Patient Health and Happiness in Memphis, Tennessee. CONTACT: https://www.eventbrite.com/e/endocrine-ecosystem-balanced-hormones-and-reduced-toxicity-tickets-94725166523

APRIL 23-25: 16th ANNUAL JOINT HOMEOPATHIC CONFERENCE in Reston, Virginia. CONTACT: www.homeopathycenter.org

MAY 28-JUNE 1: 12th INTERNATIONAL CONGRESS ON AUTOIMMUNITY in Athens, Greece. Special session on diet and autoimmunity, chaired by Dr. Aristo Vojdani. CONTACT: https://autoimmunity.kenes.com/

JUNE 3-6: SASKATCHEWAN ASSOCATION OF NATUROPATHIC DOCTORS HEALING SKIES CONFERENCE in Saskatoon, Saskatchewan. CONTACT: http://www.sanp.ca/index.html

◆

References

1. https://nunm.edu/naturopathic-principles-of-healing/ accessed July 19, 2020.
2. Chen JC, Wang, X, Wellenius GA, et al. Ambient Air Pollution and Neurotoxicity on Brain Structure: Evidence from Women's Health Initiative Memory Study. Ann Neurol. 2015 Sept; 78(3): 466–476.
3. Chen C, Xun P, Kaufman JD, et al. Erythrocyte omega-3 index, ambient fine particle exposure and brain aging Neurology Jul 15;10.1212/WNL.0000000000010074.
4. Pun VC, Kazemiparkouhi F, Manjourides J, Suh HH. Long-Term PM2.5 Exposure and Respiratory, Cancer, and Cardiovascular Mortality in Older US Adults. Am J Epidemiol. 2017 Oct 15;186(8):961-969.
5. Heusinkveld HJ, Wahle T, Campbell A, et al. Neurodegenerative and neurological disorders by small inhaled particles. Neurotoxicology. 2016 Sep;56:94-106.
6. Cutuli D. Functional and structural benefits induced by omega-3 polyunsaturated fatty acids during aging. Curr Neuropharmacol. 2017;15:534-542.
7. Conklin SM, Gianaros PJ, Brown SM, et al. Long-chain omega-3 fatty acid intake is associated positively with corticolimbic gray matter volume in healthy adults. Neurosci Lett 2007;421:209-212.
8. Singh PK, Nath R, Ahmad MK, Rawat A, Babu S, Dixit RK. Attenuation of lead neurotoxicity by supplementation of polyunsaturated fatty acid in Wistar rats. Nutr Neurosci 2016;19:396-405.
9. Meydan S, Altas M, Nacar A, et al. The protective effects of omega-3 fatty acid against toluene-induced neurotoxicity in prefrontal cortex of rats. Hum Exp Toxicol 2012;31:1179-1185.
10. Kaur P, Schulz K, Aschner M, Syversen T. Role of docosahexaenoic acid in modulating methylmercury-induced neurotoxicity. Toxicol Sci 2007;100:423-432.
11. https://www.latin-is-simple.com/en/vocabulary/verb/201/ July 19, 2020 accessed
12. Cedric M Smith. Origin and uses of primum non nocere – above all, do no harm! *J Clin Pharmacol*. 2005 Apr;45(4):371-7. doi: 10.1177/0091270004273680.
13. Sharpe VA, Faden AI. Medical harm. Historical, Conceptual, and Ethical Dimensions of Iatrogenic Illness. Cambridge, UK: Cambridge University Press, 1998:42.
14. https://www.cdc.gov/aging/aginginfo/subjective-cognitive-decline-brief.html accessed July 19, 2020.
15. Karen Clay, Nicholas Z. Muller. Recent Increases in Air Pollution: Evidence and Implications for Mortality https://www.nber.org/papers/w26381, NBER Working Paper No. 26381. Issued in October 2019
16. https://www.epa.gov/clean-air-act-overview/benefits-and-costs-clean-air-act-1990-2020-second-prospective-study Benefits and Costs of the Clean Air Act 1990-2020, the Second Prospective Study. Full text: https://www.epa.gov/clean-air-act-overview/benefits-and-costs-clean-air-act-1990-2020-report-documents-and-graphics
17. https://www.nytimes.com/interactive/2019/10/24/climate/air-pollution-increase. html?search ResultPosition=3 Nadja Popovich. America's Air Quality Worsens, Ending Years of Gains, Study Says. Oct. 24, 2019, NYTimes. Accessed July 17, 2020.
18. https://www.nytimes.com/2020/06/04/climate/trump-environment-coronavirus.html?searchResultPosition=2

◆

Healing with Homeopathy

by Judyth Reichenberg-Ullman, ND, MSW
www.healthyhomeopathy.com

Depression and Isolation in the Time of COVID-19: Two Cases from the Magnolia Family

This pandemic has, so far, lasted over four months. The most common descriptors are unreal, bizarre, chaotic, isolating, lonely, disconnected, confusing, unthinkable, tragic, bewildering. The toll on lives, savings, relationships, job security, personal freedom is enormous. The amount of dissent, rebellion, and conflict is staggering. Besides the devastating effects of the virus, the amount of discord, dissention, rebellion, and fear in this country is staggering. Life as we knew it before seems but a distant memory. At first, the photos of millions of pink flamingos returning to the beaches of Mumbai and pumas roaming the streets of Santiago instilled hope of a healthier, less polluted world. But now, months later, the profound loss of lives and livelihood and most everything that we considered normal have risen to the forefront.

Worldwide, there are very few whose lives resemble anything like before the pandemic. The prospect of a vaccine brings hope to some and terror to others. Our freedom to gather socially, recreate, exercise, and do much of what we considered normal is but a distant memory. Being unable to gather physically with family members, loved ones, dear friends, neighbors, much less those who are ill or dying, is incomprehensible – as is what is happening here in the US: inadequate facilities, equipment, testing, coordination, and collapsed pandemic program.

The Magnolia Family

There is a homeopathic plant family that fits the societal picture of this pandemic remarkably well. According to the *Sensation Method* developed by Dr. Rajan Sankaran of Mumbai, each plant family has a particular theme which, if recognized, along with the miasm (hereditary layer of predisposition) of the remedy, can lead to a correct and effective match of a homeopathic remedy. One of these families, *Magnolianae* fits the picture of what is happening worldwide remarkably well. The mental state of the *Magnolias* will sound remarkably familiar and fitting at this time:

- Confusion, bewilderment
- Everything seems strange and unfamiliar
- Profound isolation
- Withdrawal from what is familiar
- Shutting out the world
- Stupefaction, collapse, sleepiness

At the beginning of the pandemic, the remedy *Camphora* (camphor) was claimed to be the number one remedy recommended by the Indian government, along with *Arsenicum album* (arsenic). There was a great deal of activity among homeopaths worldwide at the beginning of the pandemic: free webinars, impressive databases, a remarkable and free-flowing sharing of information for the healing and well-being of all. For a variety of reasons, including suppression on social media, this is no longer happening, which leads to further confusion, isolation, and disconnection. In the midst of all of this, the FDA is considering limiting access in the US to homeopathic remedies.

My Own Pandemic Bewilderment

I can attest to my personal experience of facing the pandemic, first in Chile, then in Washington state. My husband, Bob, and I found ourselves on our nine-acre property in Southern Chile when COVID-19 hit. Being quite connected on social media with our other home, Washington state, we were more informed than most and at least knew what was happening in time to buy disinfectant wipes and masks before they disappeared from the supermarket shelves. We did not feel comfortable interacting in person with any friends. We stopped interacting in person with anyone, including our Chilean caretaker family. Grocery shopping was an infrequent, masked, disinfected, and rather frightening ritual. We interacted only with our menagerie of three dogs, six cats, sheep, chickens, and ducks. We were immensely grateful to have plenty of room to roam, breathe fresh air, enjoy sunshine, and continue to marvel at the magnificence of nature. Our only contact with friends and loved ones was at a distance on the road and through Skype, Zoom, and Facetime. A strange, new world to say the least. But far more fortunate than those apartment dwellers worldwide, and even in the Chilean capital, who were

➤

➤

not permitted to even leave their cubicles or who were issued a limited number of permits per week to take care of their out-of-home needs. All of this was before the deaths soared worldwide, before healthcare workers' terrible plights and shortages came to light, and before the enormous dissention in the US over masking, BLM, political differences, and more.

Chile set up sanitation checkpoints, strict quarantines, and folks 75 and over were prohibited from leaving their homes. Period. Travel information was confusing and hard to come by. Returning to the US with our two golden retrievers seemed daunting. Six weeks went by of failed flights. I began relying on the Facebook posts of others in the country, who had managed to leave and make it home. It felt like we were going from one war zone to another. It was only through the experiences of others on Facebook that I was able to navigate the journey. We weren't even assured that our flight would leave, after having traveled by land ten hours from Southern Chile to Santiago, until arriving at the airport.

We were given contact tracing forms on the LATAM flight from Santiago to Miami, but no one ever asked to see those forms in the US. Airports seemed unreal and unpredictable, even from one terminal to the next! There were *five* other emotional support dogs on the plane to Miami…as if everyone were running for their lives and taking their beloved animal companions with them. We arrived in Miami to an empty, deserted international terminal – nothing open at all. Then, upon entering the domestic terminal, there were folks everywhere, very few masked, with no notion of social distancing – one moment stranger than the next!

On the way home from SeaTac, we had to detour due to the curfew in Seattle. Having been away from the internet for 48 hours, we knew nothing of George Floyd or the protests. In fact, we had no idea why traffic was diverted away from downtown Seattle! We made it home to Whidbey Island, Washington, bathed our golden retrievers in the dark to remove any possible contamination, then holed up for the mandatory (though never enforced) fourteen-day self-imposed quarantine. Walking on the beach in front of our house was absolutely our only activity other than staying at home. And my life is far more normal than many because I am still able to work virtually. I have no idea when I will feel safe enough to start seeing patients again in person.

Social interactions are still few and far between. We went inactive at our gym, which was unthinkable for us seniors who Zumba'd, Body Pumped, and did Pilates five days a week. Four months later, with restrictions eased somewhat here in Washington state, we have yet to go to a restaurant, even for takeout, and are pretty Zoomed out, even though some of the virtual gatherings are lifelines. There are very few aspects of our lives that are familiar or normal in pre-COVID-19 times. Our wonderful chiropractor had to move to a shared office space after 20 years of practice. We canceled our long-awaited September trip to Kenya. Yet, we know personally only one friend who has succumbed to the virus (in a nursing

home having just suffered two amputations and gangrene), and no patients with confirmed cases.

I am beyond appalled by the alarming political upheaval in our country, the growing violence, discontentment, ever-worsening COVID-19 numbers, grossly inadequate testing, contact tracing, protective gear. I could go on and on. And my services as a homeopathic doctor are more in demand than ever. I am *not* living paycheck to paycheck (although if Social Security were taken away from us, that would be disastrous). I do not have grandchildren whom I cannot see nor small children who may or may not be able to go back to school. I do not have a family member who has died or become severely ill with COVID. And we have plenty of food.

Yet, just like the *Magnolia* family picture, my life is wrought with confusion, uncertainty, unpredictability, bewilderment, and isolation. I have no idea how long it will last. I feel the pain of separation from those near and dear, except for Bob and a few friends. I wouldn't be allowed to visit most countries of the world, even if it were safe to do so – even Canada, which is only two hours away. Our beloved thirteen-and-a-half-year-old golden retriever, *Dulce de Leche*, died two days ago of hemangiosarcoma (cancer of the spleen), diagnosed only three weeks earlier, just like our last golden. Nothing seems normal. It is time to look for renters for our home for when we go to Chile in three months *if the planes fly.* Our country is due to have an election in three months *if it happens* and *if there is not martial law* before that time. Each of you, every one of our patients, friends, loved ones, and strangers, each of us has our own experience of bewilderment and unreality during this time, with no end in sight and no certainty of a cure nor vaccine. This is the picture of the *Magnolia* family.

The Magnolidae Remedies and Coping Strategies

How one copes with the strange, unfamiliar, bizarre circumstances of life depends on the situation, the miasm (hereditary layer of predisposition), and the particular remedy. The "passive reaction" to a strange and bewildering world is collapse, stupefaction, withdrawing, even fainting, a sense of floating, and even unconsciousness. The "active reaction" is an attempt to create a familiar world and shutting out the "other" bizarre world. I'll have to say that is what I have done, with more than a few moments of feeling psychically paralyzed and overwhelmed. The most common remedies belonging to the homeopathic *Magnolia* family include *Camphora* (acute miasm), *Nux moschata* or nutmeg (typhoid miasm), *Magnolia grandiflora* (malarial miasm), *Cinnamon* (sycotic miasm), *Myristica* (tubercular miasm), *Asarum* (cancer), and *Aristolochia* (leprosy miasm). The most common of these in my practice is *Nux moschata*, which I have prescribed successfully a number of times post head-injury and, recently, for a patient with neurocardiogenic syncope. I have another patient who has done beautifully on *Cinnamon* for depression with a sense of alienation.

A Case of Camphora

Around the beginning of the pandemic, a patient was referred to me who fit the picture of homeopathic *Camphora* perfectly. This remedy belongs to the acute miasm, which means he had a feeling of his life being in danger – a matter of death being just around the next corner. This was a very prominent, highly successful, wealthy, yet desperately unhappy individual. The CV of this gentleman would impress anyone. In fact, many of you would be familiar with his name. Having moved from the west coast to New York, he started to feel "strange." "I flatlined. Freaked out. Became hysterical. Out-of-my-mind anxious. I saw 80 doctors in three years…. I became hypervigilant. Started to lose touch with friends… My life went got very small from being very big. Empty. I lost my purpose, meaning, confidence."

He went from one health crisis to the next. "I felt stunned. Shocked. I had no life. I'm acute. Not myself. I am scared. Alone. I have very little hope. Lost at sea. Like I'm dying. Empty. Dead… Everyone feels like a stranger. There is no connection. I am isolated. I don't exist. Alienated. Like I'm going to die… Is this real? Is this me?" He suffered from cold hands and feet.

In the homeopathic literature, the following is characteristic of the remedy *Camphora*:

> Sudden and complete prostration of the vital force with great coldness of the external surface. Sudden attacks of weakness and fainting spells. Sudden sinking of strength. Stupefaction as if intoxicated. Sudden intense threat and shock from something strange and bewildering. The response is withdrawal.

Camphora was prescribed successfully for a number of COVID-19 cases internationally with extreme collapse, a feeling of icy coldness, and a sense of shock and bewilderment. In a case by Deborah Collins of New Zealand, a patient recounted, "I am all alone… I have been left behind in a cave of ice…. I came from a different planet." There is a feeling of despair, profound loneliness, anguish, indefinable anxiety, and an aversion to everything."

I was relieved to have found the probable remedy for this man who was suffering so profoundly, but he was afraid to take it and returned once again to his psychiatrist. Not the kind of satisfying ending I would have hoped for, but the truth. And, for far too many, this pandemic will end in profound aloneness and despair, even to the extent of dying in profound loneliness, without the comfort of a loved one – like the bodies piled into refrigerated trucks in New York City.

I apologize for ending on such a terrible note. But this is a bewildering, chilling, isolating time. Just like the *Magnolidae.* I hope fervently that we will find light at the end of the tunnel once this period passes.

Dr. Reichenberg is the author of *Whole Woman Homeopathy*, and co-author, and with Dr. Robert Ullman, coauthor of eight books on homeopathy: *Ritalin-Free Kids, Homeopathic Self Care* (with companion kit), *The Savvy Traveler's Guide to Homeopathy and Natural Medicine*, *A Drug-Free Approach to Asperger Syndrome and Autism, The Homeopathic Treatment of Depression, Anxiety, and Bipolar Disorder*, and *Rage-Free Kids* as well as *Mystics, Masters, Saints and Sages – Stories of Enlightenment*. Pioneers in their field, they have been columnists for the *Townsend Letter* since the early 90s. They taught originally at Bastyr University, then offered seminars internationally. Drs. Reichenberg-Ullman and Dr. Robert Ullman have been together 34 years, and live on Whidbey Island Washington, and in Pucón, Chile. Avid adventure travelers, they have visited nearly 50 countries, including hiking two Caminos in Spain and Portugal.

Please visit www.healthyhomeopathy.com (where you will find a wealth of articles, blogs, and more) and Facebook at Healthy Homeopathy. Dr. Reichenberg-Ullman can be reached at drreichenberg@gmail.com. Dr. Robert Ullman retired in April 2020.

◆

Women's Health Update

by Tori Hudson, ND
womanstime@aol.com

Two Botanicals for the Aging Brain

Nootropics is a term used to describe those agents that improve cognition, memory, creativity, or motivation. Nootropic substances can be as common as everyday caffeine and nicotine, or stimulants such as amphetamine and methylphenidate, or many prescription items, including levodopa. Nootropic agents can also include plants, vitamins, or other dietary supplements. The following botanicals are two of the most significant current botanicals used for their nootropic effects.

Bacopa monnieri

Bacopa monnieri, is a well-known herb native to Australia and India. While it is commonly found as a weed in rice fields, it also grows throughout East Asia and even the United States. It has a long historical use in Ayurvedic medicine in areas of memory and intelligence. The entire plant can be used as medicine. The main nootropic constituents of bacopa are believed to be of triterpenoid saponins known as bacosides, with jujubogenin or pseudo-jujubogenin moieties as aglycone units.[1] There are 12 bacopasides analogs called bacopasides I–XII that have been identified.[2-4] There are several alkaloids, including brahmine, nicotine, and herpestine as well as D-mannitol, apigenin, hersaponin, monnierasides I–III, cucurbitacins and plantainoside B. The most studied constituent, extracted from the whole plant, has been bacoside A.

While many of the pharmaceutical nootropics are potentially addictive (eg, caffeine, nicotine and psychostimulants), bacopa appears to nourish rather than deplete neurons. Historically, bacopa was used by Vedic scholars to help them memorize lengthy hymns and scriptures and many ancient texts refer to the herb's ability to sharpen intellect and improve mental deficits. It is often found in many Ayurvedic preparations for cognitive dysfunction.

There is conflicting evidence as to the effects of bacopa on cognitive function, but possible mechanisms for cognitive improvement include modulation of acetylcholine release, choline acetylase activity, and muscarinic cholinergic receptor binding. In the laboratory, bacopa inhibits acetylcholinesterase activity and may also have neuroprotective effects, including the ability to protect neurons from beta-amyloid-induced cell death.

At least six high-quality randomized, double-blind, placebo-controlled human trials have been conducted. Pase et al. conducted a systematic review, finding some evidence that bacopa could be used as a memory enhancer even in individuals without dementia.[5] These same six studies met the final inclusion criteria and were included in the systematic review. All the trials were conducted over 12 weeks. Not all the trials used the same dosage and three different bacopa extracts were used at dosages of 300-450 mg extract per day. All the reviewed trials evaluated the effects of bacopa on memory, and other cognitive function tests were less well studied. Across all the studies, bacopa improved performance on 9 of 17 tests in memory free recall. There was no real evidence of any other cognitive domain enhancement.

In a meta-analysis, Neale et al. compared the nootropic effects of *Bacopa monnier* to *Panax ginseng* and modafinil (an eugeroic-wakefulness drug).[6] Chronic bacopa use produced the most consistent and largest effect sizes of the three. Bacopa showed small- to medium-effect sizes for attention and information processing tasks. Larger-effect sizes were evident for auditory verbal learning tasks, including delayed word pair memory, delayed word recall, and for protection from proactive interference during delayed memory. The highest effect sizes for cognitive outcomes were 0.77 for modafinil (visuospatial memory accuracy), 0.86 for ginseng (simple reaction time) and 0.95 for bacopa (delayed word recall). These findings support the use of bacopa, particularly in measures of verbal recall.

Highlighting a couple of the individual studies, Stough et al. conducted a randomized double blind placebo controlled trial in 46 healthy adults, examining the effects of bacopa on cognitive function in healthy individuals, using a bacopa supplement of 300 mg/day standardized to 55% bacosides for

12 weeks.[7] A battery of eight tests was taken at five weeks and 12 weeks post administration, finding significantly improved speed of visual information processing, learning rate, memory consolidation, and state anxiety compared to placebo, with maximal effects evident after 12 weeks.

A study conducted in Portland, Oregon, evaluated the effects of *Bacopa monnieri* whole plant standardized dry extract on cognitive function in healthy elderly participants.[8] This randomized, double-blind, placebo-controlled clinical trial had a treatment period of 12 weeks. Fifty-four men 65 or older (mean of 73.5 years) without dementia were enrolled and randomized to bacopa or placebo. Forty-eight (48) completed the study with 24 in each group. Participants were given Standardized *B. monnieri* extract 300 mg/day or a similar placebo tablet orally for 12 weeks.

Bacopa participants had enhanced Rey Auditory Verbal Learning Test (AVLT) delayed word recall memory scores relative to placebo. Other cognitive measures such as the Stroop task results were similarly significant, with the bacopa group improving and the placebo group unchanged. Depression and anxiety scores and heart rate decreased over time for the bacopa group but increased for the placebo group. No effects were found on the Divided Attention Task (DAT), and the Wechsler Adult Intelligence Scale (WAIS) letter-digit test of immediate working memory. Overall, the study provided further evidence that bacopa could enhance cognitive performance in aging individuals.

Bacopa has also been studied in children for effects on cognition and learning. A systematic overview published in 2017 gives a good insight into the research and potential.[9] Nine trials met the inclusion criteria and five studies reported sufficient data for effect size analysis. Most of the improvements reported were in behavioral outcomes. Cognitive abilities and behavioral outcomes were reviewed in six studies, with visual perception, impulsivity, and attention demonstrating the greatest improvements.

Dosages, Side Effects, Toxicity, Contraindications

Bacopa has been used safely in children and adults in studies up to six months in duration. Common dosages range from 350-640 mg/day; the part used is the leaf.

Drug interactions that are moderate and thus caution should be considered include the following:

- Acetylcholinasterase inhibitors
- Anticholinergics
- Cholinergics
- Cytochrome p450 1A2 substrates
- Cytochrome p450 2C19 substrates
- Cytochrome p450 2C9 substrates
- Cytochrome p450 3A4 substrates

Minor drug interactions include thyroid hormones.

Bacopa seems to inhibit acetylcholinesterase and might increase acetylcholine levels and have cholinergic effects, and thus should be used with caution in those individuals with bradycardia, gastrointestinal or urogenital obstruction, peptic ulcer disease, asthma and chronic obstructive pulmonary disease. Thyroid might also increase thyroxine levels (T4).

Bacopa is generally well tolerated, but there are reports of increased stool frequency, nausea, and abdominal cramps. Less common side effects could include dry mouth, muscle fatigue, flatulence, bloating, decreased appetite, headache, palpitations, drowsiness, sleep issues, and vivid dreams.

Rhodiola rosea

Rhodiola rosea, or "golden root," has been used for centuries in Eastern Europe, Scandinavia, and Asia. It has remained largely unknown in the West, until recently. Traditionally, *Rhodiola rosea* was used in folk medicine with a reputation to increase physical endurance, productivity, longevity, resistance to high altitude sickness, fatigue, depression, anemia, impotence, gastrointestinal ailments, infections and disorders of the nervous system.[10]

The root of *Rhodiola rosea* has six distinct groups of chemical compounds:

- Phenylpropanoids: rosavin, rosin, rosarin
- Phenylethanol derivatives: salidroside (rhodioloside), tyrosol
- Flavonoids: rodiolin, rodionin, rodiosin, acetylrodalgin, tricin
- Monoterpenes: rosiridol, rosaridin
- Triterpenes: daucosterol, beta-sitosterol
- Phenolic acids: chlorogenic and hydroxycinnamic, gallic acids.

Rosavin is the constituent currently selected for standardization of extracts.[11]

The properties of *Rhodiola rosea* to influence the cardiopulmonary system, central nervous system, and improve the ability to adapt to stressors have been attributed primarily to its influence on the levels and activity of serotonin, dopamine, and norepinephrine in different structures in the brain. It may be that the plant inhibits the breakdown of these chemicals and facilitates the neurotransmitter transport within the brain.[12] In addition to these effects on the central nervous system, rhodiola has been reported to increase the chemicals that provide energy to the muscle of the heart and to prevent the depletion of adrenal catecholamines induced by acute stress.[13]

Historically, rhodiola was observed to act in humans as a tonic, increase attention span, memory and work performance. Two human studies were able to show that individuals with fatigue, irritability, insomnia and decline in work capacity responded favorably to a rhodiola dose of 50 mg, three times a day.[14,15]

In another human study of 128 patients aged 17-55, rhodiola alleviated fatigue, irritability, distractibility, headache and weakness in 64 percent of the cases. In a study of students, physicians and scientists, rhodiola was given for two to three weeks beginning several days before intense intellectual work such as final exams. The extract improved the amount and quality of work and prevented decreased performance due to fatigue. Using rhodiola during final exams appears to be ➤

➤

beneficial as well. Medical students took a rhodiola extract for 20 days and had significant improvements in mental fatigue, general well-being, final exam grades and physical fitness.[16]

Case studies have reported that *Rhodioa rosea* can help with depressive syndromes, memory loss, anxiety, cognitive dysfunction, and menopause related symptoms.

Practitioner Dosing, Side Effects, Toxicity and Contraindications

Rhodiola rosea has a very low level of toxicity in animal studies. The toxic dose is calculated in humans to be about 235 gm or 235,000 mg for a 70 kg man. The typical daily dose for chronic administration is 360-600 mg per day when standardized for 1% rosavin, 180-300 mg when standardized for 2% rosavin, or 100-170 mg when standardized for 2.6% rosavin. There are also products available that list the rosavins in milligrams; examples include 6 mg of rosavins per 120 mg of rhodiola root or 12 mg of rosavins per 240 mg of rhodiola root. These formulations are an even more robust 5% rosavin content; yet still, all of these provide a large margin of safety. Overall, there are very few side effects with rhodiola. Some anxious individuals may be over activated and become agitated. *Rhodiola rosea* may also interfere with sleep in some individuals and should be taken early in the day. It should be avoided in individuals with bipolar disorder who have a history of manic episodes when given antidepressants or stimulants and should be used with caution in general, in those with bipolar disorder. If use is desired just prior to an academic exam or an athletic competition, the suggested dose is three times the dose for daily consumption for one dose. Safety issues are not available for pregnancy and lactation, so rhodiola should therefore be avoided.

References

1. Sivaramakrishna C. Rao CV. Trimurtulu G. Vanisree M. Subbaraju GV. Triterpenoid glycosides from Bacopa monnieri. *Phytochemistry*. 2005;66:2719–2728.
2. Chakravarty AK, et al. Bacopaside I and II: two pseudojujubogenin glycosides from Bacopa monniera. *Phytochemistry*. 2001;58:553–556.
3. Chakravarty AK, et al. Bacopasides III–V: Three new triterpenoid glycosides from Bacopa monniera. *Chem Pharm Bull*. 2003;51:215–217.
4. Garai S, et al. Dammarane-type triterpenoid saponins from Bacopa monniera. *Phytochemistry*. 1996;42:815–820.
5. Pase MP, et al. The cognitive-enhancing effects of Bacopa monnieri: A systematic review of randomized, controlled human clinical trials. *J Altern Complement Med*. 2012;18:1–6.
6. Neale C, et al. Cognitive effects of two nutraceuticals Ginseng and Bacopa benchmarked against modafinil: a review and comparison of effect sizes. *Br J Clin Pharmacol.* 2013 Mar;75(3):728-37.
7. Stough C, et al. The chronic effects of an extract of Bacopa monniera (Brahmi) on cognitive function in healthy human subjects. *Psychopharmacology* (Berl). 2015 Jul;232(13):2427.
8. Calabrese C, et al. Effects of a standardized Bacopa monnieri extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebo-controlled trial. *J Altern Complement Med.* 2008 Jul;14(6):707-13.
9. Kean J, Downey L, Stough C. Systematic Overview of *Bacopa monnieri (L.) Wettst.* Dominant Poly-Herbal Formulas in Children and Adolescents. *Medicines.* 2017; *4*(4): 86.
10. Petkov V, et al. Effects of alcohol aqueous extract from Rhodiola rosea L. roots on learning and memory. *Acta Physiol Pharmacol Bulg*. 1986;12:3-16.
11. Boon-Niermeijer E, van den Berg A, Wikman G, Wiegant F. Phyto-adaptogens protect against environmental stress-induced death of embryos from the freshwater snail Lymnaea stagnalis. *Phytomedicine.* 2000;7:389-399.
12. Stancheva S, Mosharrof A. Effect of the extract of Rhodiola rosea L. on the content of the brain biogenic monamines. *Med Physiol*. 1987;40:85-87.
13. Maslova L, Kondrat'ev B, Maslov L, Lishmanov I. The cardioprotective and antiadrenergic activity of an extract of Rhodiola rosea in stress. *Eksp Klin Farmakol*. 1994;57:61-63. (Article in Russian).
14. Krasik E, et al. Therapy of asthenic conditions: clinical perspectives of application of Rhodiola rosea extract. In. Proceedings Modern problems in psycho-pharmacology. Kemerovo-city, Russia: Siberian Branch of Russian Academy of Sciences: 1970.p. 298-330.
15. Krasik E, et al. New data on the therapy of asthenic conditions(clinical prospects for the use of Rhodiola extract). Proceedings of All-Russia Conference: Urgent Problems in Psychopharmacology 1970 May 26-29. Sverdlovsk, Russia: Sverdlovsk Press; 1970.p. 215-7.
16. Spasov A, et al. A double-blind, placebo-controlled pilot study of the stimulating and adaptogenic effect of Rhodiola rosea SHR-% extract on the fatigue of students caused by stress during an examination period with a repeated low-dose regimen. *Phytomedicine*. 2000;7(2):85-89. ◆

➤ *continued from page 88*

one percent of the patients had measurable levels of ethanol one hour after glucose ingestion, with a mean concentration of 0.0025% (range, 0.001% to 0.007%). In 14 patients (2.7% of those tested), low concentrations of ethanol (less than 0.001%) were detected in the fasting state. The maximum blood alcohol concentration seen in this study was below the level at which functioning becomes impaired. However, considering that a 12-ounce soft drink contains eight times as much sugar as the challenge dose used in the study and that a typical Western diet provides daily more than 20 times as much sugar as the challenge dose, it would not be surprising if diet-induced increases in blood alcohol levels were sufficient to cause symptoms in some people.

The auto-brewery syndrome overlaps with, and may be a contributing factor to, a condition that has been given various names including *Candida*-related complex, *Candida* hypersensitivity syndrome, or the simple but less precise term, candidiasis. I will refer to this condition here as *Candida*-related complex (CRC). In 1978, Dr. Orian Truss introduced the concept that non-systemic yeast infections can cause a wide array of systemic symptoms and contribute to or exacerbate various disease conditions. Truss observed that CRC was a contributing factor to a wide range of symptoms and conditions, including depression, anxiety, hyperactivity, irritability, headache, difficulty with memory and concentration, chronic diarrhea, recurrent urinary tract symptoms, premenstrual syndrome, and autoimmune diseases.

In cases in which CRC was a contributing factor, oral administration of nystatin resulted in clinical improvement, sometimes dramatic.[4,5] Since that time, others have confirmed that CRC plays a role in a broad range of health conditions.[6] Today, many nutrition-oriented practitioners recommend an "anti-*Candida*" program for selected patients, although many in the mainstream medical community doubt the existence of the syndrome described by Truss. In addition to antifungal medication, an anti-*Candida* program typically requires the avoidance of simple sugars and other refined carbohydrates. The inability of CRC patients to tolerate sugar is presumably due in part to gut fermentation, although other adverse effects of sugar (such as dysinsulinism or immune-system dysregulation) may be involved as well.

Ethanol is metabolized in the body to acetaldehyde, a compound that may be even more important than ethanol as a mediator of CRC-related illness.[7] Some of the symptoms of CRC resemble those of alcohol hangovers, which are caused in large part by acetaldehyde. Acetaldehyde also interferes with a number of enzymes involved in intermediary metabolism, and it is thought to play a role in the pathogenesis of some autoimmune diseases.[8]

In my 19 years of clinical practice, I saw hundreds of patients (mostly women) who had a history consistent with possible CRC. I included this condition in the differential diagnosis if the patient had typical symptoms plus a history of recurrent vaginal yeast infections or oral thrush, or if they had taken medications that can promote the growth of *Candida* species (such as antibiotics, oral contraceptives, or glucocorticoids). Dietary modification and antifungal medication were each frequently beneficial, but combining these treatments was usually needed to achieve the best results. It was not uncommon for patients with suspected CRC to answer affirmatively when asked if eating sugar made them feel drunk. That particular symptom typically improved on the anti-*Candida* program. There is no generally accepted diagnostic test for CRC, so it remains a clinical diagnosis, and treatment is usually undertaken on an empirical basis.[9]

Alan R. Gaby, MD

References

1. Malik F, et al. Case report and literature review of auto-brewery syndrome: probably an underdiagnosed medical condition. *BMJ Open Gastroenterol*. 2019;6:e000325.
2. Iwata K. A review of the literature on drunken symptoms due to yeasts in the gastrointestinal tract. In: Iwata K, editor. Yeasts and yeast-like microorganisms in medical science: proceedings of the second International Specialized Symposium on Yeasts, Tokyo 1972. Tokyo, University of Tokyo Press, 1976:260-268.
3. Hunnisett A, et al. Gut fermentation (or the "auto-brewery") syndrome: a new clinical test with initial observations and discussion of clinical and biochemical implications. *J Nutr Med*. 1990;1:33-38.
4. Truss CO. Tissue injury induced by Candida albicans. Mental and neurologic manifestations. *J Orthomolec Psychiatry*. 1978;7:17-37.
5. Truss CO. The role of Candida albicans in human illness. *J Orthomolec Psychiatry*. 1981;10:228-38.
6. Crook WG. The Yeast Connection. Third Edition. Jackson, TN, Professional Books, 1986.
7. Truss CO. Metabolic abnormalities in patients with chronic candidiasis: the acetaldehyde hypothesis. *J Orthomolec Psychiatry*. 1983;13:66-93.
8. Whyte A. Haptenisation of serum proteins by acetaldehyde. *Lancet*. 1986;2:1340-1.
9. Gaby AR. Candidiasis. In Gaby AR. Nutritional Medicine, Second Edition. Concord, NH, 2017, doctorgaby.com, chapter 9.

◆

Getting Drunk Without Drinking: The "Auto-Brewery" Syndrome

In a recently published case report,[1] a previously healthy 46-year-old man developed memory loss, mental changes, and episodes of depression over a period of six years. These symptoms began after he received a three-week course of the broad-spectrum antibiotic, cephalexin. On one occasion he was arrested for presumed drunken driving although he claimed that he had not consumed any alcohol. Stool culture was positive for *Saccharomyces cerevisiae* (brewer's or baker's yeast) and *S. boulardii*. He was also found to have *Candida albicans* and *C. parapsilosis* in the small bowel, which were presumed to be fermenting carbohydrates to alcohol. His blood alcohol level, measured eight hours after a carbohydrate meal and while under observation so that he could not drink any alcohol, was 0.057%. For comparison, behavioral and other changes may occur at blood alcohol levels as low as 0.02%; and the legal limit for "driving under the influence" (DUI) in the US is 0.08%.

After treatment with a low-carbohydrate diet, antifungal medication, and a probiotic he became completely asymptomatic. Carbohydrates were gradually reintroduced into his diet without causing symptoms or increasing his blood alcohol level. At the time the case report was submitted to the journal, the patient had been symptom-free 1.5 years.

This case illustrates a condition that has been called the auto-brewery syndrome or the gut fermentation syndrome. It is characterized by symptoms of drunkenness after ingestion of carbohydrates. The first case of this syndrome was reported in 1952: that of a Japanese person who developed symptoms of drunkenness after eating. The condition was found to be due to excessive fermentation of food components by *Candida* species living in the stomach. As of 1976, 23 similar cases had been reported in Japan, but there had been no such case reports from other countries in the medical literature.[2] Symptoms in these patients included a drunken feeling, often associated with flushing of the face, headache, dizziness, sweating, fever, diarrhea, or palpitations. The symptoms typically began 30 minutes to 20 hours after eating a carbohydrate food and lasted 2 to 10 hours. Ethanol was detected in stomach contents, blood, urine, and expired breath. *C. albicans* or other yeasts and fungi were identified in the gastric and/or duodenal contents in these patients. Administration of antifungal drugs was dramatically effective in most cases.

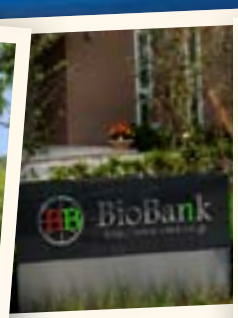
In a 1990 paper, three British doctors provided evidence that fermentation of carbohydrates to alcohol in the gastrointestinal tract is actually quite common.[3] They measured blood ethanol concentrations in 510 patients in whom chronic intestinal candidiasis or gut fermentation was suspected. Ethanol levels were measured in the fasting state and one hour after ingestion of 5 g of glucose. Sixty-

➤

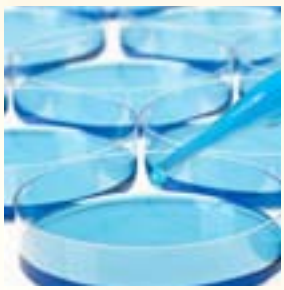
Dr. Iichiroh Ohhira: A Pioneering Genius in Probiotic Science

MALAYSIAN MYSTERY – 'DRINKING FERMENTED ELIXIR'

ADVANCED RESEARCH – OKAYAMA UNIVERSITY



FOUNDED BIOBANK

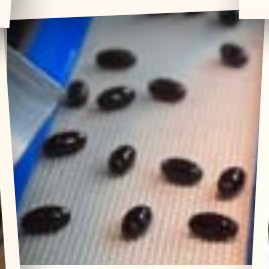


DISCOVERY LAB TH-10

TESTING FOODS FOR PEAK NUTRITION

EXCLUSIVE 5-YEAR FERMENTATION

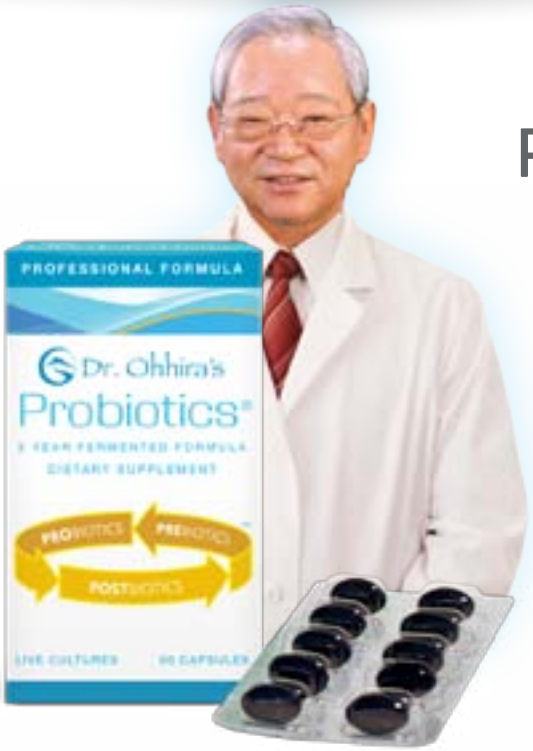
NATURE'S PERFECT PROBIOTIC W/POSTBIOTICS



PATENTED ENCAPSULATION

OFFERING "LONG LIFE AND GOOD HEALTH TO ALL!"

DR. OHHIRA AWARDED GUSI PEACE PRIZE



Developed Natures 'Perfect Probiotic' over 40 Years ago!

Dr. Ohhira has proven to be one of the world's most influential researchers in the history of probiotic science as his discoveries continue to be confirmed. He intrinsically understood restorative timeline when developing a 5-year natural temperature fermentation method that produces herculean strains of probiotics as well as therapeutic **Postbiotics Metabolites**, recently proven to be the most beneficial aspect of probiotic supplementation. Recent research on Dr. Ohhira's Probiotics revealed that his formula contains over 400 kinds of these health-promoting postbiotic metabolites!

Discover the Dr. Ohhira's Difference!™

ESSENTIAL FORMULAS®

www.EssentialFormulas.com • (972) 255-3918

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Help Ensure Your Patients' Immune Health.

With Tru Immune Support™.

Exclusively Formulated by
Dr. Chris Meletis, ND

Tru Immune Support™ Helps Optimize Immune Systems.

Nutraceuticals Innovator TruGen3® proudly introduces new Tru Immune Support™, a comprehensive combination of botanicals, vitamins, and other natural substances designed to support immune cell function and promote respiratory health. **Specially formulated by world renowned Naturopathic Doctor Chris D. Meletis**, no other immune supplement contains this effective and unique combination designed to maintain humoral and innate immunity*.

The unique Tru Immune Support™ formula contains multiple nutrients, including the botanical Astragalus, which contains high amounts of polysaccharides, flavonoids, multiple trace minerals and amino acids, all of which boast immune-supporting attributes. In addition, Tru Immune Support™ contains the proprietary ingredient, EpiCor®, a dried fermentate produced from Saccharomyces cerevisiae. Multiple studies show EpiCor® acts as an antioxidant and supports a healthy immune response during exposure to colds and flus and respiratory stresses. Tru Immune Suuport™ also contains Olive Leaf Extract, Berberine HCl , N-Acetyl-L-Cysteine and Garlic, further bolstering its efficacy†.

TruGen3® continues the Lioon family legacy of three generations and more than a half-century of nutraceutical experience, with products produced under the highest ethical standards, available exclusively through Health Professionals. Contact us to find out how you can put our highly innovative products to work for your patients, and your practice, today.

Contact us today for FREE SAMPLES and to find out how you can put our innovative, one-of-a-kind products to work for your patients, and your practice, today.

*This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
† EpiCor® is a registered trademark of Embria Health Sciences, LLC

TruGen3®

Three Generations of Truth in Nutrition

www.trugen3.com **1-844-387-8436**

733 Washington Road, Suite 211, Pittsburgh, PA 15228 (3TRUGEN)