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December 2020
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# The Life and Work of Nicholas Gonzalez, MD

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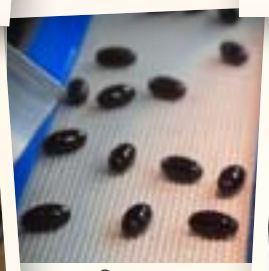

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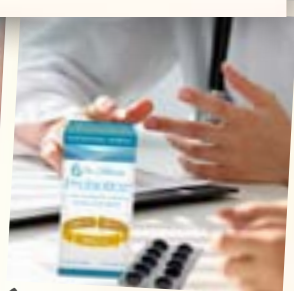

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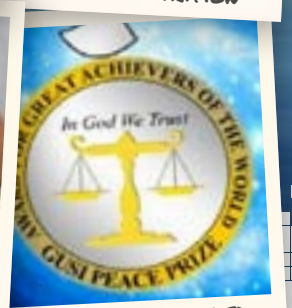


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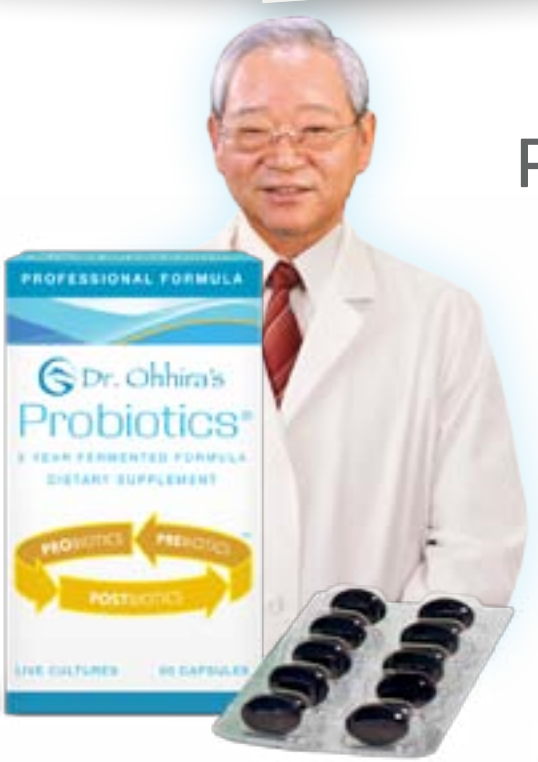


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# From the Publisher

**Townsend Letter Index**

For years our subject and author index was available, like the magazine, only on paper. With our first website we published the index online, but one would still need to find the article in the print magazine. In the last year www.townsendletter.com has been entirely redone. Not only are the current and previous issue contents easily accessible but recently posted articles, best reads, and a blog post are all available on the home page. Thanks to the work of our index editor, Jule Klotter, and our webmaster, Joy Reuther-Costa, the index has now been completely updated and made easily accessible with a simple click on the banner tool bar.

The article you read a year ago may not be so easily remembered, but you can quickly search the index on our website. If the article is online, a simple click will bring the article up for fast review. We have also created an index of keywords for examining articles from past issues. Give a look-see of our website in the near future and be sure to include inspection of the newly accessible index.

**Bioinformatics Tools for COVID-19 Management by Peter D'Adamo, ND**

Over the past several months we have had a "deluge" of contributions from writers and readers about COVID-19. While many of these articles have appeared in the print

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# Letter from the Publisher

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and e-edition of the *Townsend Letter,* we have published others online only on our website, www.townsendletter.com (accessed by clicking on the "New Coronavirus Reports" green tab at the top of the website.) Located half-way down this page of diverse, colorfully illustrated article tabs is one labelled: "Generativity: Bioinformatics Tools for COVID-19 Management by Peter D'Adamo, ND." I have given you these directions to find his article rather than a simple link because D'Adamo's interactive article will also ask for your step-wise participation. Located all in one place, using an AI-structured, algorithmic, data-based program, practitioners are invited to key in patient diagnostics and best-evidenced therapeutics are mapped out for treatment of COVID-19. The data powered by datapunk.net is updated continuously, and hyperlinked journal references are immediately accessible for review. While D'Adamo's bioinformatics tool has been posted for many months, we have neglected to give it its fair due in the print magazine. This is my request for you to take the effort to go to our website and access his column and spend some time learning how to "play" with this very well researched, physiological-mechanism-based, evidence-rated compendium of pharmacological and herbal treatments for COVID-19 and related viruses.

One reason that this article was posted online rather than printed is that "bioinformatics" works infinitely better on a screen than on a paper page. It may be ideal, if possible, to use two devices, a phone and a laptop or tablet, so that while the article is being read, the datapunk site can be viewed simultaneously. If nothing else the tabulated table of putative coronavirus agents that include some 100 drugs, herbs, and vitamins is a wealth of information. Each agent is hyperlinked to a Wikipedia entry providing an immediate description of drug or herb. Each agent is rated as to its effective activity against COVID-19 as well as corona, influenza, herpes, HIV, and hepatitis viruses. The evidence is rated as evidence-based, observational, case report, in-vitro testing, and speculative. The reference for the evidence is accessible for immediate reading directly from the table – this enables comparison of drug vs drug and herb vs herb as well as drug vs herb.

Using D'Adamo's tool allows the user to enter clinical data about an individual patient. Symptom entries include temperature and symptoms such as myalgia, chills, cough, fatigue, dyspnea, dermatitis, oxygen saturation, heart rate, and more. Based on symptom entry the program identifies the stage of illness and then determines the top therapeutic indications graded by stage. Therapies are differentiated

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into those having highest level of significance, lower level of significance, possibly contraindicated, and requiring watchful monitoring. An indication strength of 1.0 would be absolutely indicated; a strength of 0.0 would be not indicated whatsoever. The therapeutic indications for the specific patient are then listed in numerical order with ratings of 1.0-0.0 (highest to lowest). Each remedy is sorted for stage of illness and symptom specificity.

The ultimate bioinformatics tool is a "Requisite Variety Matrix," which appears as a spatial diagram. The matrix separates out several key physiological mechanisms that offer best synergistic support. Each therapeutic is spatially linked linearly to its key synergistic mechanism. The value here is that the AI-based algorithm is delineating therapeutics based on the patient's diagnostics.

Is this the future of medicine – are we going to enter diagnostic symptoms and an AI-based program will determine best-evidence based treatment? Perhaps. One thing that separates D'Adamo's tool is that he includes herbals with drugs; in certain cases, an herb offers as much support as a drug. It is doubtful that medical academia will include herbals in their algorithm tools.

**"Erectile Dysfunction: The Canary in the Cardiovascular Coalmine?" by Erica Zelfand, ND**

Not too long ago, Viagra and Cialis were the most widely advertised pharmaceutical products in print and on television. Both are phosphodiesterase inhibitors, which are effective in helping a man with ED develop an erection. However, they are a temporary solution only – when not used, the erectile dysfunction persists. Over the past decade "low-T" (low testosterone) treatment has become the panacea for loss of vitality as well as ED. Clinics dedicated to diagnosing and treating low-T have sprung up throughout the US and internationally. While testosterone has proven to be unsurpassed in "awakening" grumpy old men, it has not been nearly as successful in reversing impotency. Hence, many low-T treated men still require Viagra or Cialis to take care of business in the bedroom. But is there a better solution for ED?

Erica Zelfand, ND, posits that the approach we focus upon in managing erectile dysfunction ignores the role that nitric oxide plays in tumescence (penile erection). NO is the principal molecule that enables the relaxation of the cavernous musculature permitting the blood engorgement of an erection. Like testosterone, NO levels decrease as one ages.

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# Letter from the Publisher

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Nitric oxide can be nutritionally increased by eating foods abundant in nitrates such as beets. However, dietary nitrates require bacteria in the mouth to convert nitrates to nitrites. Further without adequate hydrochloric acid in the stomach, nitrites may not convert to nitric oxide.

Concurrently NO can be synthesized from the amino acid, L-arginine. The enzyme nitric oxide synthase, which converts arginine to NO, depends on multiple co-factors emphasizing the need for nutritional management, exercise, and improving overall cardiovascular health.

Zelfand's article is an excellent primer to share with men who fail to take their health seriously.

**Cover Story: Nicholas Gonzalez, MD**

Before the 2000s, cancer care was largely based on surgical excision, radiation treatment, and chemotherapy. This was before immunotherapy, biological treatments, and targeted therapy. Despite cheerleading by the American Cancer Society (ACS), long-term survival with nearly all cancer diagnoses was uniformly poor if the malignancy progressed beyond a Stage 1 tumor. As would be expected, alternative cancer therapies developed here and abroad. While clinics in Germany and Mexico integrated conventional and alternative cancer therapies, alternative cancer centers in the US largely offered proprietary therapies independent of conventional care. Quackbusters, including hematologist Victor Herbert, MD, decried alternative cancer treatments, labelling practitioners as quacks.

Politically the public who wished the freedom of choice to seek out alternative care demanded Congress to investigate why such treatment was being attacked by medical boards, the AMA, and the ACS. In 1987 the Office of Technology Assessment (OTA) set up a study of unconventional cancer treatment. Despite the lackluster characterization of such treatments by the OTA, Congress appropriated funding in 1991 for an Office of Alternative Medicine at the NIH; that office became the National Center of Complementary and Alternative Medicine at the NIH.



Among the many cancer protocols and practitioners the OTA examined was the work of Nicholas Gonzalez, MD, a treatment protocol based on specialized diet, extensive supplementation including high dose pancreatic glandular supplements, and complementary treatments such as coffee enemas. While Dr. Gonzalez died in 2015, his treatment protocol continues to be administered by practitioners, for example, Linda Isaacs, MD. This month Gonzalez's authorized biography, *The Maverick M.D. – Dr. Nicholas Gonzalez and His Fight for a New Cancer Treatment* by Mary Swander, has been published. An excerpt from the biography appears in this issue together with a special report for the *Townsend Letter* by Swander of her experience being treated by Gonzalez.

Gonzalez's protocol was based largely on the work of a renegade dentist, William Donald Kelley, who putatively survived a diagnosis of pancreatic cancer with a metabolic-based diet and high doses of glandular pancreatic enzymes. (See Carrie Decker's article from Aug/Sept. 2019: "Pancreatic Glandular Therapies: From Absorption to Cellular Interaction in Cancer" at www.townsendletter.com). Unlike Kelley, Gonzalez was an individual soundly trained in medicine and science completing post-graduate work with renowned immunologist Robert A. Good, MD, at Sloan Kettering Cancer Center and at the University of Oklahoma. Gonzalez decided in 1987 to devote his energies to perfecting the Kelley protocol, necessitating his decision to step away from conventional cancer centers who were unwilling to welcome his use of unconventional cancer care.

The National Cancer Institute and NCCAM did fund an experimental study comparing a chemotherapeutic agent, Gemcitabine, with Gonzalez's regimen of specialized diet and pancreatic enzyme therapy in patients with advanced pancreatic cancer. The results, unfortunately, did not prove efficacy of Gonzalez's approach; the NIH report showed survival in the Gonzalez treatment group was four months compared to 14 months in the Gemcitabine group. Gonzalez decried the study design and the statistical analysis; when he requested investigators at Columbia University review the study, he was stunned by their confirmation in 2009 condemning the treatment effectiveness. Gonzalez subsequently authored a book denigrating the report's faulty analyses and conclusions – the excerpt from Swander's book in this issue details Gonzalez's plight with the university investigators and the NIH.

Does a specialized diet and glandular enzymes play a role in cancer care in 2020? Despite the blanket condemnation offered by *Wikipedia* of Gonzalez's regimen, patients still need alternative cancer options now. Survival for most advanced cancers may have been modestly improved in the past decade with expensive immunotherapies, but five-year survival rates remain low. Unless a patient is content with limiting oneself to only what is available in "evidence-based" medicine, quality-based long-term survival will necessitate alternative treatment interventions. Not everyone benefits using the Gonzalez approach, but everyone should be permitted the freedom to use it when no other options are forthcoming.

Jonathan Collin, MD

# Pathways to Healing

**by Elaine Zablocki**

## Coalition Mobilizes to Protect Compounded Bioidentical Hormones

In July the National Academies of Science, Engineering, and Medicine (NASEM) released a report on compounded bioidentical hormone therapy,[1] and recommended that it no longer be allowed except in exceedingly rare circumstances.

For decades women experiencing menopause have used pharmaceutically manufactured hormone replacement therapy – to prevent bone loss, reduce hot flashes, and to address the many deleterious effects of hormone loss in menopause. However, now over half of US women seeking treatment for menopause use compounded bioidentical hormones,[2,3] also known as cBHRT. These preparations are prescribed by physicians and other licensed healthcare providers, then compounded individually for each woman by a specialized, licensed and regulated compounding pharmacy.

"Some women experience lower hormone levels in as early as their 30s. At menopause all women lose their powerful ovarian hormones," says Daved Rosensweet, MD. "This is critical for their general health. The hormones protect women's energy and sleep, their bones and brain, their vagina and bladder, their arteries, and quite a bit more."

Dr Rosensweet is a holistic medical doctor who has specialized in treating menopausal women with bioidentical hormones for 25 years. Nowadays he spends most of his professional time training and mentoring physicians, nurse practitioners, and other licensed providers in specializing and mastering menopause medicine. He is the author of the book *Happy Healthy Hormones: How to Thrive in Menopause.*

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Bioidentical hormone treatment is individualized for each patient. There is usually a three-month multi-consultation period in which the woman and the practitioner work to discover her optimal dosage levels and balance. After clinical symptom alleviation, she is tested to confirm optimal dosage range – not too much and not too little. Then she returns annually for tests and further adjustments. "Women vary enormously in what levels of estrogens, progesterone and testosterone they are used to," Rosensweet says. "A tall, thin, small-breasted women can have a very different hormone profile compared to a short, large-breasted woman. Women also vary as to how much they absorb from the hormones they put on their skin, as well as to how sensitive they are to what they are receiving."

**Daved Rosensweet, MD**

One thing the NASEM panel failed to consider is the manner in which cBHRT is used clinically and the positive outcomes patients often experience. Here are a few examples.

*Gina*: I'm now age 50. About three and a half years ago, I developed chronic insomnia. There were mornings when I would wake up and cry at the thought of getting out of bed, I was so tired. Sleeping pills didn't help. Due to lack of sleep, I was irritable and short-tempered; I was snapping at my kids and our relationships were suffering. A friend of mine suggested I might be suffering from a hormone imbalance due to menopause. That changed my life. From the very first night when I started taking bioidentical hormones, I experienced super-deep restful sleep. It's been three and a half years now, and I intend to keep taking them until the day I die.

*April*: I had a surgical hysterectomy at age 26. I have tried many different methods for hot flashes. I tried estrogen pills, creams, many different options, and I struggled with hot flashes for 20 years. Now I've found that compounded hormonal therapy really works. I've had relief from vaginal dryness. I sleep better at night using them consistently as recommended, morning and evening. I just cannot recommend it enough!

*Betsy*: I had a hysterectomy when I was 27, and they put me on Premarin. I stayed on it until I was 50, when the doctors took me off it. For two years, I went downhill. My quality of life took a nosedive. Finally, a doctor asked me, "Have you considered bioidentical hormones?" It was a godsend; it was a total game-changer for me. I think one big part of it is that bioidenticals address all the hormones – estrogen, progesterone, testosterone, DHEA – and balances them. But what's most important to me, and to all women, is to have a choice. Had I known about bioidenticals, I don't think I'd have stayed on Premarin for 23 years!

**NASEM Report Could Limit Use of Compounded Bioidentical Hormones**

The NASEM report recommends that use of compounded bioidentical hormones should be limited to patients who have a documented allergy to FDA bioidentical hormones. Allergies to the ingredients are extremely rare, so in practice this would mean that millions of women will lose access to treatments that are working well for them.

The report recommends that "the Pharmacy Compounding Advisory Committee should review bioidentical hormone therapies as candidates for the FDA Difficult to Compound list." If compounded bioidentical hormones are placed on this list, women will lose access to them. Physicians will no longer be able to prescribe them, and compounding pharmacies will not be allowed to make them. Since they form a large portion of the work compounding pharmacies do, many compounding pharmacies would probably be forced to close their doors.

Practitioners who are recommending bioidentical hormones to their patients point out that the NASEM study committee did not include a single compounding pharmacist nor a physician with substantive experience in compounded bioidentical hormone therapy. NASEM said it based its recommendations in large part on a review of literature but only identifies 13 studies it reviewed when there are hundreds of studies on this subject that could have been considered. "In addition, there is abundant patient outcomes data that could and should have been weighed," Dr. Rosensweet says. "The clinical methods, experience and medical-scientific rationale used by those of us who prescribe cBHRT were not included in the NASEM report. The science behind the report's conclusion that these compounds fit FDA criteria for 'too difficult to compound' are not consistent with the understanding of those of us in the field with experience and expertise in their prescribing and use."

"Another major problem with their recommendations is that the FDA does not have the power to tell a licensed physician how to practice medicine," he adds. "They are over-reaching; they are interfering with the doctor-patient relationship. They are saying to doctors, you don't have the knowledge, training, wisdom or the authority to practice what you consider to be best medicine."

"Patient preference alone should not determine the use of cBHRT preparations," the report says. "They are restricting a women's choice of the physician that she wants to consult with, or the hormones she wants to use: she loses those rights," Rosensweet comments. Women attorneys, long involved in the perpetual challenge to compounded bioidentical hormones, are incensed at this overreach into women's choice. The

NASEM report is strongly challenged as yet another example of gender discrimination and attack on the rights of women.

**Coalition Forms to Support Compounded Bioidenticals**

Dr. Rosensweet and other practitioners who specialize in treatment with bioidentical hormones have formed the Coalition to Protect Compounded Bioidentical Hormones to educate women about this issue and mobilize patients to speak publicly and to Congress in support of these hormones that work so well for them.

"Once NASEM issued their report, people started coming out of the woodwork and volunteering," Dr. Rosensweet says. "We want to unify our efforts to get the truth out." The first meeting of 56 physicians, compounding pharmacists, attorneys, lobbyists, and opinion leaders volunteered to help with a wide range of projects such as interviewing women about their experiences with bioidentical hormones, grassroots organizing, developing educational materials, organizing efforts to contact congressional representatives, and reviewing and building a database of medical studies published in peer-reviewed journals. Eventually bioidentical hormone treatment for both women and men could be recognized as a board specialization, with defined standards of care.

"If you are prescribing and/or using bioidentical hormones, we want to hear from you," Dr. Rosensweet says. "There are a series of support actions you can take to protect cBHRT. Please send an email message to drr@menopausemethod.com. Our staff will respond with a list of possible actions you can take, plus proper timing. Possibilities include testimonials from you, from your patients, and signing on to letters sponsored by senators and congressional representatives. You can also join and become a part of our Coalition's professional and lay committees."

"So much knowledge and experience with bioidentical hormones has been acquired over the last 50 years," Rosensweet says. "Compounded bioidenticals help women to live their full lives as strong healthy active people. You don't want to lose your right to choose your best healthcare options, together with your physician or your nurse practitioner or your other licensed healthcare provider. Visit our website, learn more about these issues, and then work together with others to preserve your right to individualized medical care."

**Resources**

Book: *Happy Healthy Hormones: How to Thrive in Menopause* by Daved Rosensweet, MD
Coalition Website: www.cbhrtcoalition.net
Email: drr@menopausemethod.com

**References**


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Elaine Zablocki is the former editor of CHRF News Files.

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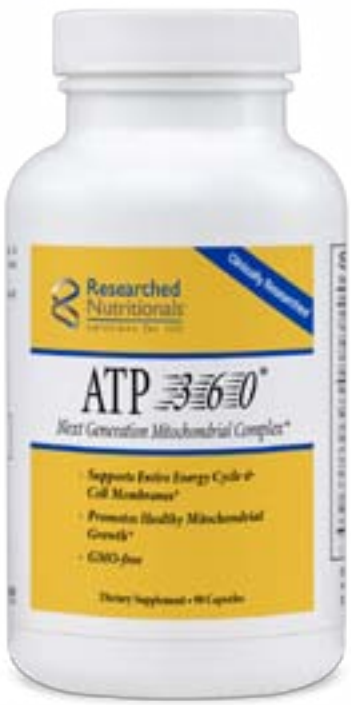


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# FCT®, ED, and Hormonal Upheavals in Men

## by Savely Yurkovsky, MD©

Perhaps another endangered species, men, have to be saved from joining the list as their famously dropping sperm count and now, erectile dysfunction (ED) buttress the membership. In a recent Italian study, 26% of men under 40 reported ED; and it is becoming more common even among men in their 20s, which the study sees as "a worrisome trend."[1] The lack of energy and exhaustion, even among the young, is not alien to the breed either. Certainly, "older men over 50" are 'expected' to have all of these problems, according to the chemical-pharmaceutical paradigm in both conventional and biological medicines, since the lab tests are unable to find the real causes of medical problems. Therefore, dumping these problems on age and low testosterone is 'logical'.

Following the low testosterone test, different pills are dispensed, including anti-ED boosters, with the promise to turn the involved apparatus into a construction crane. Testosterone often follows too. Under certain circumstances sex and adrenal, thyroid or growth hormone replacements for both sexes can be necessary and beneficial; yet under most, replacement must be avoided with better options. The reason for this is that no foreign hormone, call it "bioidentical" or synthetic, is perceived as "family" or recognized by the hormone receptors as one's own. Therefore, it is our innate hormones (testosterone, cortisol, estrogen, progesterone, growth etc.) that assure optimal sex, energy, antiaging, and other functions, or "the best return on the money."

**The advantage of skillful bioresonance testing is its ability to noninvasively identify underlying causes and treatment.**

Another shortcoming of the chemical-pharmaceutical approach is that lab tests cannot determine an optimal dose of hormonal replacements (HRT) as the prescribed doses might be too low or high. The latter leads to a suppression of one's own sex drive or energy by suppressing production of sex, cortisol, and other hormones and causes side effects. In the case of testosterone, it can even decrease sex drive because the testosterone receptors do not respond to the invader hormone that well, while it suppresses pituitary and hypothalamus stimulation of one's own. Lowered sperm count and fertility and enlarged prostate are the recognized side effects of testosterone administration. Indeed, when I shared with a pharmacist from a compounding pharmacy that neither its "bioidentical" nor synthetic testosterone are free of potentially suppressing sex drive and worsening ED, he admitted that he experienced this himself.

How to avoid the use of hormone replacement therapy, in the face of a medical condition or aging, for as long as possible? Obviously, by determining and addressing the exact causes of insufficient hormone production and properly addressing other major holes in chemical-pharmaceutical medicine. One of these holes is the inability to diagnose and address the treacherous interconnections and interdependencies between visible malfunctions and organs of the endocrine system. As an example, while the blame for ED usually falls on a low testicular production of testosterone, the adrenal glands also secrete testosterone that play a significant role in sex drive and erection. The important role of the thyroid in these is not to be forgotten, either. The testicles, adrenals, and thyroid are involved in the two-way feedback dependent loops with the hypothalamus and pituitary. To what degree these glands might be involved in hormonal upheaval, 'normal' lab tests usually cannot tell since the corresponding hormone levels are often, formally, in a normal range but which might be suboptimal for an individual patient. Adding to the biochemical confusion, that 'dirty' player, the liver, which can quietly ruin the libido of both men and women by overproducing a protein, sex hormone-binding globulin (SHBG) that will drop free, bio-available testosterone for its receptors. A malfunctioning liver can also fail to properly clear estrogen produced in men, leading to a low sex drive and ED.

Another and nonhormonal cause of ED can be a vascular problem without associated diabetes, due to a deposition of heavy metals spoiling the precious moments. A correlation between ED of vascular origin and heart disease has been reported, with both being victims of 'unknown' causes, which are written off as atherosclerosis or endothelial dysfunction.

When HRT is still necessary, how to prevent one's hormone receptors from either starving from too low or becoming drunk from too high of a dose? The general answers to all of these black holes, which concern all diseases, can be found in the obscure scientific literature, starting even with a statement of biochemist Nobel Laureate Albert Szent-Gyorgyi, PhD, pointing to physics, in the early 1960s. Later on, professor of materials science at Stanford University, William A. Tiller, PhD, stated the same that future medicine will be based on controlled energy fields, and more recently theoretical physicist Professor Hans-Peter Dürr, PhD, reiterated the same in the article "Are Biology and Medicine Only Physics?"[2] In a recent book[3] he and his colleagues emphasized, in more polite words than I have in previous articles,[4,5] that all of these "new discoveries" in molecular biology and biochemistry amount to pulling at straws because it is only through the physics of proper energetic diagnostics and therapeutics that one can intelligently understand their real value.[3]

FCT has been evolving these energetic approaches, bioresonance testing and energetic remedies, for decades and, based on this experience, has observed that the most rewarding results for hormonal problems and all diseases can be only achieved through properly addressing their main causes. Bypassing the main causes amounts to treating the body with unextracted bullets. The unique advantage of skillful bioresonance testing (BRT) is its ability to noninvasively tune into any organ to find its bullets and do the same with the connected organs. The main bullets are always heavy and other toxic metals, with mercury being their gang leader. This is simply because we all are born with many of these, and the pile grows as we live and age, while being incapable of metabolizing metals. Concerning the gang leader, one is to thank the genocidal dental practice of installing this poison by the tons annually, in the teeth of children and adults, that then gets passed down to the generations. Contaminated oceans, seafood, sea and mined salt, fluorescent light bulbs, and LCD screens add to the depth of poisoning. Mercury, estrogenic pesticides, Roundup, solvents, paints, formaldehyde, and other pollutants also affect the liver and its aforementioned hormone-related functions. Liver flushes or cleansing herbs and other 'detoxes' can do little against these powerful toxins.

Inevitably, once the main poisons result in immune suppression, more uninvited guests come to dinner; chronic infections affect the testicles, ovaries, and drain the body of energy – and fun. Addressing the removal of poisons, while protecting other organs and avoiding their spread throughout the body in the process, can be accomplished through energetic remedies (US patent, August 2020), which stimulate the release of toxins and minimize the chances for their uncontrollable shifting into other organs. Certainly, reducing the impact of ubiquitous electromagnetic fields in our environment, which act as magnets that block metals' release from the body, is crucial. This is done through proper environmental guidance and superb EMF-protecting Memon technology. It's not a coincidence that testicular cancer among police officers has been associated with their common practice of placing their electronic machinery on their laps, as other people do with their laptops. Similarly, frying our brains with smartphones, laptops, PCs, and TVs, which destroy the hypothalamus and pituitary, does not help the production of sex hormones down below. An association of cell phones with brain tumors has been reported by several studies that, like the new criminal 5G, are silenced by the media. Infections, likewise, are addressed through energetic remedies

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that, like vaccines, stimulate the immune system specifically against given sexually transmitted microbes, candida, parasites, Lyme, etc.

Among the documented successful cases is a more than a nine-fold increase – well into a normal range – of a prior, hardly present, sperm count in a 32-year-old man, who was managed by 'fertility specialists.' Almost a double increase of testosterone level, in a middle-aged man, was reported also. Also, a few good men in their 70s indicated their renewed ability of "going at it." None of them received testosterone, and one, not even DHEA.

The optimal doses of hormonal precursors, such as DHEA, wild yam, ginseng, and others, as well as the hormones themselves, if necessary, are determined by patients' own bodies through bioresonance testing. Better brands of hormone precursors and glandulars are selected through BRT, with these and hormones (sex, adrenals, thyroid) being tested for the selection of an optimal combination for an individual person. I use, among others, so called "bioidentical hormones," to offer patients' bodies more choices; but who and how exactly made these more bioidentical is a mystery, but the name is inspiring.

Synthetic hormones, brand names and generic all receive equal opportunity status; the cheapest generic often tests better than the rest. As the body, environment, degree of stress, pollution and re-poisoning, and even seasons change, so do the needs and combinations. These are reduced or discontinued when the desired goal – optimal organ function – is attained.

Speaking of HRT, last week a long-term FCT veteran, a female patient, who has never received HRT or any drugs, asked out of the blue, "Doctor, did you notice, I am 78, but I don't have any wrinkles?!" I looked carefully at her face, and she was right. My oversight.

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Savely Yurkovsky, MD, is board-certified in internal medicine and board-eligible in cardiovascular medicine. He undertook a particular interest in mercury toxicity as both its victim and a clinician managing a busy private practice. Shortly after moving to the US from the former Soviet Union, he received several silver amalgam fillings, which he recognized later as the cause of his mounting health problems. These problems persisted, despite removal of fillings that prompted him to explore various mercury detoxifying approaches: oral, intravenous, homeopathic. After observing their corresponding partial benefits, limitations, and aggravations on himself and his patients, he resorted to bioresonance testing and causative homeopathy, based on relevant knowledge from physics and toxicology to optimize benefits and safety of the detoxification. The guidance of his physics consultant, the Stanford University materials science professor William A. Tiller, PhD, was instrumental in enhancing diagnostic ability of bioresonance testing to address the known limitations of lab tests to detect the presence of toxicants in the internal organs. This testing also was used to draw a better comparative capacity between various mercury detoxifying treatments as well as to evolve a safer therapeutic strategy that minimizes the re-intoxication or dumping effect, which are common to these treatments. It also guides the optimization of the unlimited therapeutic potential of homeopathy that has a unique capacity to therapeutically connect with any organ and tissue, via specific signals, as no other treatment can.

His book, *Biological, Chemical, and Nuclear Warfare – Protecting Yourself and Your Loved Ones: The Power of Digital Medicine*, has been endorsed by Professor Emeritus William A. Tiller, PhD of Stanford University and MIT Physics Professor George Pugh, PhD. He presented this system at the Combating Bioterrorism Conference in 2005, sponsored by the Office of Homeland Security.

Dr. Yurkovsky founded a teaching organization, *SYY Integrated Health Systems, Ltd.*, in 1999, which is dedicated to training health practitioners in this biophysical system under the concept of FCT – Field Control Therapy®. He has lectured extensively in the US and Europe.

# Membrane Lipid Replacement with NTFactor Lipids® Reduces Pain, Fatigue, Gastrointestinal and Other Symptoms in Patients with Peripheral Pain

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

**Abstract**

We sought to determine if oral dietary wafers containing a combination of membrane glycerolphospholipids (NTFactor Lipids® wafers, 4-6 g per day) could reduce self-reported peripheral and widespread pain, fatigue, and gastrointestinal symptoms in chronic illness patients. This followed an open label clinical study where the membrane glycerolphospholipid supplement was tested in fibromyalgia patients who had widespread pain and suffered from chronic fatigue and other symptoms. In that clinical study middle-aged fibromyalgia patients showed significant reductions in self-reported pain, fatigue, and gastrointestinal symptoms, and improvements in quality of life (QOL) indicators within one week of taking 4.8 g per day NTFactor Lipids®. As we found in previous cross-over clinical studies, these improvements were dependent on patients' continuing to take the supplement. Increasing the dose of the membrane glycerolphospholipid supplement to approximately 6 g per day in patients with severe, intractable pain resulted in better resolution of pain and other signs and symptoms compared to lower daily doses, as long as patients continued to take the oral supplement.

**Introduction**

Membrane Lipid Replacement (MLR) using dietary NTFactor Lipids® results in the systemic replacement of damaged cellular membrane glycerolphospholipids with undamaged, unoxidized lipids to ensure the proper function of cellular membranes, including mitochondrial membranes.[1,2] By combining the glycerolphospholipids with antioxidants, MLR supplements have proven to be effective in reducing disease-associated symptom severity, age-associated loss of function, and providing organ support.[1-3] The MLR supplement NTFactor Lipids® has been utilized in several clinical studies that demonstrate that it significantly reduces fatigue in patients with chronic illnesses and in aged subjects with chronic fatigue and other symptoms.[4-7]

One of the most common clinical conditions marked by widespread pain and fatigue is fibromyalgia.[8,9] This condition is characterized by chronic, widespread pain, abnormal processing of pain, increased sensitivity to external stimuli, fatigue, gastrointestinal symptoms, and changes in memory, mood, and sleep.[8-10] Using this criteria it has been estimated that between 0.1-3.3% of the people in Western countries and 2.0% of the United States' population have fibromyalgia.[10] Higher incidence rates of fibromyalgia have been found in females compared to males, and this could be due to differences in hormonal status.[9,11]

**Dietary Supplements**

Dietary supplements have been used to reduce symptom severity in patients with fibromyalgia, chronic fatigue and other chronic conditions that have pain and/or fatigue as major symptoms.[1-7] Unfortunately, few if any, of these natural supplements have been considered effective in significantly reducing symptom severity, and in maintaining this reduction.[12] Some symptoms, such as fatigue and pain, also occur during normal aging, and they are important as secondary symptoms in many if not most chronic diseases.[13]

Using fibromyalgia patients who had been ill for periods of time greater than six months, we previously found that fatigue was reduced significantly when patients consumed dietary NTFactor

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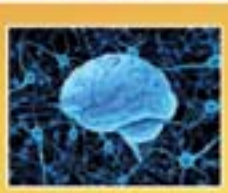

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*Rebecca Harder is the author of "Gastra Girl: Saving America One Colon at a Time,"* and owner of an immaculate and highly esteemed clinic in Portland, OR. She offers this well-researched comprehensive resource guide of holistic health information on topics such as environmental toxicity, vaccines, EMF, autism, hyperbaric oxygen, ozone therapy, colon hydrotherapy, far infrared saunas and much more.

Rebecca had come across the Relax Sauna at professional conferences many times before she decided to finally try it. She had been committed to wooden infrared saunas for 10 years at her respected clinic. Immediately after trying the Relax Sauna, she experienced instant dramatic positive healing results. She was so impressed with it that she dedicates an entire 8 pages to the Relax Sauna in the chapter "Why infrared Sauna is an absolute necessity for Everyone." She enthusiastically recommends the Relax Sauna to her clients and lets them know that it is the best way to rid the body of toxins and feel good.

Rebecca states in her book: "I realized the Relax Sauna was head and shoulders above all the rest to recommend."


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Lipids® (2-4 g per day) for 4-8 weeks.[4,5] For example, fibromyalgia patients that were placed on 4 g of NTFactor Lipids per day showed approximately 40% reductions in fatigue after eight weeks on NTFactor Lipids.[5] In these studies, pain and other symptoms were not recorded, but non-scientific feedback from patients in the study indicated that other symptoms (including pain reported by some patients) were also reduced along with fatigue.

Previously we found that a combination of low-dose controlled-release caffeine (184 mg per day) and 4.8 g per day of NTFactor Lipids® resulted in significant reductions in pain, fatigue, gastrointestinal and other symptoms in fibromyalgia patients within one week.[14] Since we found that the significant reductions in fibromyalgia pain and fatigue as well as gastrointestinal symptoms could be achieved with NTFactor Lipids® alone, without any caffeine, follow-on studies have employed only NTFactor Lipids®.[15]

**Case Reports**

Recently we published a brief case series that reported that patients with chronic, intractable pain benefited from daily oral supplementation with NTFactor Lipids® (Patented Energy™, NTFactor.com).[15] This case report was based on a series of patients who had intractable chronic pain but also had other symptoms as well. All of these patients had severe pain. Using an established fibromyalgia symptom severity scale patients scored their pain severity as 0 (no pain), 1 (slight or mild pain), 2 (moderate or considerable pain, often present at a moderate levels), or 3 (severe, continuous pain).[10]

*Case Report 1*.[15] This patient was a 51-year-old male veteran of the first Gulf War (1991). His symptoms at presentation included severe joint and muscle pain, disabling chronic fatigue, nausea, gastrointestinal symptoms (stomach pain, diarrhea, bloating), intermittent fevers, sleep problems, headaches, and short-term memory impairments that were similar to those of other Persian Gulf war veterans.[16,17] Since 1992 these symptoms persisted intermittently without resolution, even though he had been treated for post-traumatic stress disorder.[17] He had received diagnoses of chronic fatigue syndrome (CFS) and fibromyalgia in 2005 and had minor surgery in 2015 for benign skin lesions. No further treatments or procedures were conducted, and the patient refused follow-up consultations. Upon presentation in 2017 the patient complained of extreme fatigue, widespread severe musculoskeletal pain, gastrointestinal symptoms, including intermittent stomach pain, abdominal cramps, and bloating, intermittent headaches, sleep difficulties, and an inability to concentrate and retain information. His fibromyalgia symptoms score of 3 on the severity scale included widespread pain. He had stopped all pharmaceutical pain and psychotropic medications but continued to take vitamin and mineral supplements, and he maintained a largely vegetarian diet. Within one week of taking 4.8 g of NTFactor Lipids® wafers, the patient reported significant improvements in pain, fatigue, gastro-intestinal problems, headaches and sleep difficulties (score between 1 and 2). There were also patient-perceived improvements in cognition and short-term memory loss. These improvements have been sustained as long as the patient continues to take the oral glycerolphospholipids.

*Case Report 2*.[15] The patient presented as a 53-year-old female veteran with a congenital bicuspid aortic valve with moderate aortic regurgitation, as revealed by echocardiogram. Previously, an unrelated cardiac electrical issue had resolved with successful cardiac ablation for paroxysmal supra-ventricular tachycardia for A-V re-entry nodal arrythymia. The patient refused beta-blockers, and this part of her condition resolved within six months. In 2013 she began having sharp stabbing pain and numbness in her feet with tingling and electrical shocks, which progressed up to the thigh area with bilateral muscle weakness in her lower extremities. Cortisone injections failed to give any relief, and neuromas were ruled out with MRI. Sleeping became an issue because of foot pain and tingling sensations. She has maintained supplementation of her largely vegetarian diet with CoQ10, vitamins C, E and B-complex, fish oil, L-Carnitine, curcumin, lipoic acid, liposomal glutathione, and astaxanthin-lutein eye formula. In 2016 she was referred to a neurologist who performed a nerve conduction study and electromyelogram and suggested a spinal MRI, which was refused: diagnosis, idiopathic peripheral neuropathy. She also began having headaches starting at about 4 AM, but refused pharmacological remedies. In 2018 she was diagnosed with posterior vitreous detachment, which subsided after six months. In April 2018 at a fibromyalgia symptom severity score of 3, she started oral NTFactor Lipids® (approximately 2 g per day) wafers and continued the other nutraceuticals as before. Within 3-4 weeks her leg electrical surges/shocks and numbness and tingling had slowly diminished along with her peripheral pain, starting with the thigh area and extending with time down each leg. She continued on the same dose of NTFactor Lipids® for five months and realized that the recommended daily dose of NTFactor Lipids® for her condition was about twice the dose she had been taking, and she also noted that her symptoms would slowly return without the NTFactor Lipids®. After five months she increased the dose of NTFactor Lipids® to 6 g per day, and her condition continued to slowly improve (pain severity of 3 reduced to 1-2). As of 2019 she still had some numbness and very faint tingling in both feet; her chronic headaches are not as severe or frequent, and her sleep difficulties have largely resolved. She has now also added 3-5 mg of liquid melatonin sublingually as well as 20 mg of progesterone cream. Follow-up indicates that these improvements have been sustained, as long as she continues to take the NTFactor Lipids® (6 g per day).

*Case Report 3*.[15] A 68-year-old female had been shot point-blank in the abdomen and lower back with a

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12-gauge shotgun in 1978. At that time she sustained extensive damage to her large and small intestines that required partial large and small bowel resection. For decades she has suffered from unrelenting severe, chronic pain, fatigue, diarrhea and gastrointestinal symptoms (pain score of 3) that were unresolved with various treatments. She had been on narcotics and under the care of a pain management specialist, when she presented in 2015. Her pain specialist would only treat her pain with narcotics, and her fatigue and gastrointestinal symptoms were largely untreated. She discontinued narcotic pain treatment before presentation. At the time of her examination, she had severe pain (neck, mid-back, central-back and lower-back and left shoulder with limited range of motion), fatigue, and gastrointestinal distress with long-standing intractable diarrhea (fibromyalgia severity of 3). She received myofascal trigger point therapy with spinal manipulation and was placed on Propax™ with NTFactor Lipids® plus NTFactor Lipids® wafers for a total dose of approximately 5 g per day NTFactor Lipids®. After three days she reported her first solid bowel movement since her shotgun incident, and within three weeks she regained control over her bowel movements. Within three weeks her pain levels and fatigue levels improved substantially (1-2 pain scores), and her gastrointestinal symptoms had improved. She had more energy and stamina, and her chronic fatigue had almost resolved. She did not continue on the MLR with NTFactor Lipids®, and her symptom severity slowly returned to prior severe levels.

**Discussion**

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

Oral MLR supplements have been designed to reduce fatigue and protect cellular and especially mitochondrial membranes from damage.[1-5] By combining NTFactor Lipids® with vitamins and minerals (Propax™ with NTFactor Lipids®), cancer patients show reductions in the adverse effects of cancer therapy, such as chemotherapy-induced fatigue, nausea, vomiting and other side effects.[18] NTFactor Lipids® have also been used in other illnesses to reduce symptoms, especially fatigue.[2,3,5,7]

**Patient Consent**

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

**Acknowledgements and Disclosures**

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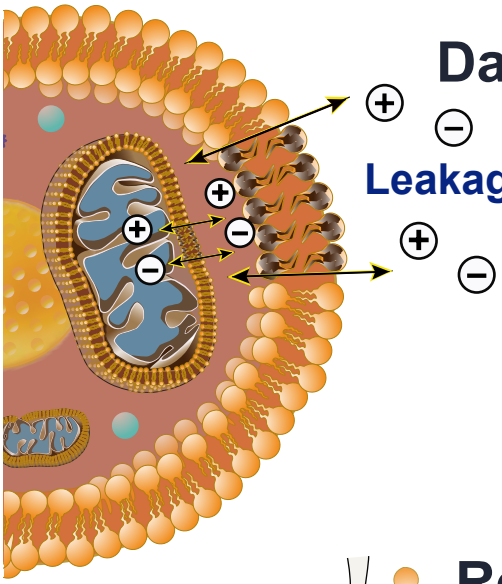


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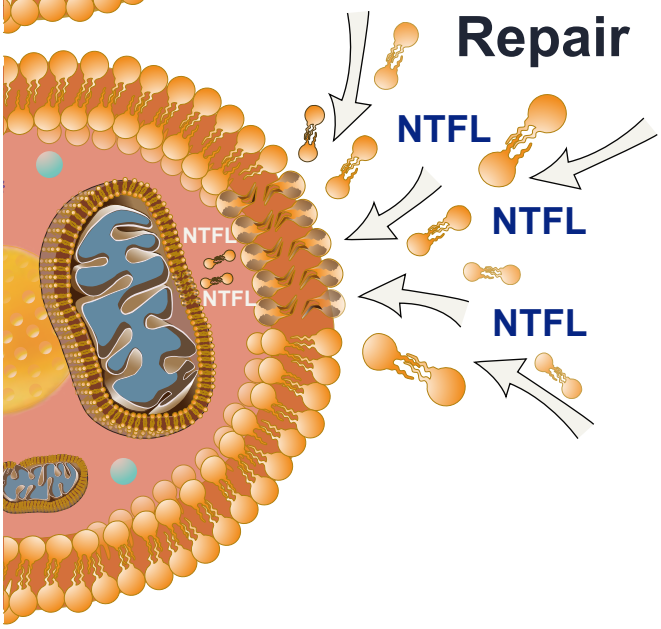
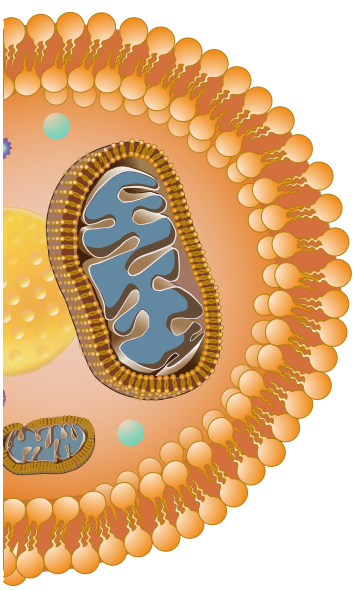



NTFL is researched and developed to be added as a functional ingredient to other nutrient formulas for the purpose of enhancing their effectiveness. NTFL restores function to damaged mitochondrial membranes and thus restores mitochondrial function in terms of cellular energy and other mitochondrial activities.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**briefed by Jule Klotter**
**jule@townsendletter.com**

**Influenza Vaccine and Coronavirus**

A January 2020 study by Greg G. Wolff looked at the possibility of viral interference in people who received influenza vaccination compared to those who did not. Although flu vaccines may provide some protection against that year's circulating viral strains, "vaccinated individuals may be at increased risk for other respiratory viruses because they do not receive the non-specific immunity associated with natural infection," according to Wolff. Wolff used data from the US Department of Defense Global Respiratory Pathogen Surveillance Program (DoDGRS) for the 2017-2018 flu season. DoDGRS contains vaccination status and results from multiplex PCR respiratory pathogen panels for DoD beneficiaries (active duty personnel, their spouses, children, retirees, and others); 6541 in the study were vaccinated and 2928 were not. In this retrospective study, Wolff excluded people with influenza and non-influenza coinfections, those who had multiple specimens taken over the season, and those who tested positive for bacterial infections (*Chlamydia pneumoniae*, *Mycoplasma pneumoniae*).

According to Table 5 in his study, a larger percentage of *unvaccinated* people (n=1299; 44%), compared to vaccinated (n=2050; 31.3%), tested positive for influenza viruses (Influenzas A, Hi1N1, H3N2, B, B Victoria, B Yamagata). The *vaccinated* population, however, were more likely to test positive for non-influenza virus (OR 1.15; 95% CI, 1.05, 1.27), coronavirus (1.36; 95% CI, 1.14, 1.63), and human metapneumovirus (OR 1.51; CI 95%, 1.20, 190).

The influenza vaccination is being highly promoted this year as a means of decreasing hospitalization rates in the coming season, during which many expect a resurgence of the coronavirus SARS-CoV-2. Noting that Wolff's findings "have triggered concern that influenza vaccination may detrimentally affect COVID-19 risk," Canadian researchers conducted their own retrospective study, using data from the community-based Canadian Sentinel Practitioner Surveillance Network that included specimens collected during the 2010-11 to 2016-17 flu seasons. They found "the adjusted OR (odds ratio) for influenza vaccination among coronavirus cases versus coronavirus test-negative controls was 1.4 (95% CI, .85-1.28)." The Canadian group also reported a "methodological problem" in Wolff's calculation of virus interference odds ratio for the 2017-2018 influenza season (Table 3). Although their study did not find evidence of viral interference, the Canadian researchers say, "population surveillance signals elsewhere suggesting cross-pathogen immunological interactions still warrant immune-epidemiological investigation."

One study that indicates viral interference is a 2012 double-blind randomized controlled trial, led by Benjamin J. Cowling. Although this study did not find an increased risk of coronavirus after vaccination, it did find increased risk of symptomatic non-influenza respiratory virus infections in children who received an inactivated trivalent influenza vaccine for the 2008-09 flu season: "participants who received [the vaccine] had higher risk of [acute respiratory illness] associated with confirmed non-influenza respiratory virus infection (RR, 4.40; 95% CI, 1.31-14.8)" – primarily rhinoviruses and coxsackie/echoviruses.

Both Wolff's study and the Canadian study used a test-negative design (TND). The Canadian researchers note that "random variation, bias, and confounding may influence TND findings." Wolff says this type of study is often used to calculate influenza vaccine effectiveness and the design is based on the assumption that a vaccine cannot affect the risk of other infections: "The virus interference phenomenon goes against the basic assumption of the test-negative vaccine effectiveness study that vaccination does not change the risk of infection with other respiratory illness, thus potentially biasing vaccine effectiveness results in the positive direction." Perhaps, other study designs should be used to evaluate the flu vaccine's ability to prevent illness?

Cowling BJ, et al. Increased Risk of Noninfluenza Respiratory Virus Infections Associated with Receipt of Inactivated Influenza Vaccine. *Clin Infect Dis.* 2012;54(12):1778-83.

Skowronski DM, et al. Influenza Vaccine Does Not Increase the Risk of Coronavirus or Other Noninfluenza Respiratory Viruses: Retrospective Analysis from Canada, 2010-2011 to 2016-2017. *Clin. Infect. Dis.* 2020.

Wolff GG. Influenza vaccination and respiratory virus interference among Department of Defense personnel during the 2017-2018 influenza season. *Vaccine*. January 2020; 38:350-354.

**Preventing Infectious Respiratory Illness with BCG Vaccine?**

Does the Bacillus Calmette-Guérin (BCG) vaccine prevent COVID-19? BCG, which contains live attenuated *Mycobacterium bovis*, is used to protect against *Mycobacterium tuberculosis* infection. A single dose, given to infants by intradermal injection or multiple puncture device, reduces the risk of tuberculosis (its primary target); but it also decreases the incidence of non-tuberculosis mycobacterial infections, like leprosy and Buruli ulcer, and respiratory tract infections, according to a review article by Kiddus Yitbarek and colleagues. They say the vaccine provides more protection when given to infants, age three months or younger, before (and not with) the diphtheria-tetanus-pertussis (DTP) vaccine. Yitbarek et al looked at nine studies (dated 2005-2020) that focused on the vaccine's effect on respiratory tract infections. BCG induces specific T-cell immune response against TB as well as adaptive immunity, which protects against other infections. BCG vaccination also appears to increase the removal of dead cells from the lungs by phagocytes.

While BCG is not on the US CDC vaccine schedule, it is (or was) a consistent part of vaccine programs in other countries for decades. Epidemiologists are reporting that countries with regular BCG vaccination have lower death rates from COVID-19. A study by Luis E. Escobar and colleagues looked at the evidence that BCG protects against severe COVID-19. They collected COVID-19 mortality data (as of April 22, 2020), BCG vaccination data, and potential confounding variables (i.e., income, population size, human density, urbanization, population's age structure, health and education services, and income). A "coarse analysis" found that percentage of population >65 years, urbanization, and higher Human Development Index (derived from life expectancy, education, and per capita income) "were consistently and positively associated with COVID-19 deaths" In addition, "countries with a strong BCG vaccination policy had significantly lower COVID-19 deaths per million."

To lessen the effect of confounding factors, Escobar et al performed another analysis that included 22 countries that met the following parameters: "at least one death per million inhabitants, ≥15% of population with an age of 65 y or more, >60% of population living in urban areas, >300 inhabitants per square kilometer, and an HDI of >0.7." Again, there was a statistically significant inverse association between BCG vaccination and COVID-19 mortality.

Germany provided particularly interesting data. Before unification, East and West Germany used different vaccine programs. East Germany, like other Eastern European countries, used BCG vaccine for decades. West Germany added BCG to its schedule later: "In West Germany, those 22 y to 59 y old today were vaccinated, while, in East Germany, those 45 y to 84 y old today received at least one dose of BCG." Average COVID-19 death rate in eastern German states, as of April 22, was 14.2 deaths per million. The average in western German states was 40.5 deaths per million – 2.9-times higher.

In another analysis that compared European countries that are socially similar, the author found "A highly significant linear correlation…between the BCG index and mortality during the first month of the pandemic ($r^2$=0.88; p=8 X $10^{-7}$); indicating that every 10% increase in the BCG index is associated with a 10.4% reduction in COVID-19 mortality."

Epidemiological evidence cannot prove cause and effect. A randomized double-blind, placebo-controlled clinical trial, with about 10,000 Australian healthcare workers, is being conducted now to see if BCG vaccination prevents severe COVID-19 in adults (NCT04327206). Primary completion is dated June 30, 2021. We can hope that SARS-CoV-2 has largely died out by then, but the clinical trial may provide evidence that BCG has unintended positive effects.

Escobar LE, Molina-Cruz A, Barillas-Mury C. BCG vaccine protection from severe coronavirus disease 2019 (COVID-19). *PNAS.* July 28, 2020.

Yitbarek K, et al. The effect of Bacillus Calmetter-Guérin (BCG) vaccination in preventing severe infectious respiratory diseases other than TB: Implications for the COVID-19 pandemic. *Vaccine*. 2020;38:6374-6380.

**Elderberry and Respiratory Infections**

A 2020 review of five randomized, double-blind controlled clinical studies, involving 936 participants, supports the use of elderberry (*Sambucus nigra*) preparations to reduce symptom severity and duration in cases of flu and/or common cold. The review authors evaluated the studies for risk of bias using the Cochrane Collaboration Risk of Bias tool. They noted concerns about treatment assignment in two studies, but low risk of bias otherwise. Three low-bias-risk trials (n=399) compared an elderberry extract product (Sambucol syrup in two studies, standardized extract capsules in one) to a placebo. In all three, elderberry treatment reduced illness duration (mean) by about 50%. A trial that compared an elderberry-echinacea product to oseltamivir (Tamiflu) reported similar recovery rates in the two groups and fewer adverse events in the herbal group. Data from the studies indicate that elderberry can reduce severity and duration of fever, headache, nasal congestion, and nasal mucus discharge when the treatment is started within the first 48 hours.

Australian researcher Golnoosh Torabian and colleagues discussed elderberry's known anti-influenza effects in a 2019 paper. In laboratory tests, Torabian et al showed that elderberry prevents influenza viruses from entering cells and replicating by deactivating viral HA glycoprotein spikes that permit the virus to attach to cell walls. Flavonoids in elderberry stimulate the immune system and production of cytokines, including IL-8, IL-6, and TNF. (There is no strong evidence, as of 2019, that shows elderberry can contribute to a cytokine storm, according to Harnett et al.) And polysaccharides in elderberries stimulate macrophage activity.

An elderberry product might be useful to have on hand during the cold/flu season.

Harnett J, et al. The effects of *Sambucus nigra* berry on acute respiratory viral infections: A rapid review of clinical studies. *Advances in Integrative Medicine.* 2019.

Torabian G. Anti-influenza activity of elderberry (*Sambucus nigra*). *J Functional Foods.* 2019;54:353-360.

**UC Flu Vaccine Mandate Lawsuit**

On July 31, 2020, former University of California System President Janet Napolitano issued an executive order

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mandating flu vaccination for all students, faculty, and employees by November 1, 2020. Failure to comply would result in job loss or removal from school. Faculty and staff can opt out if they work online; religious exemptions are also possible. Students were not given the same accommodations. The executive order affects 510,000 people. The rationale for the mandate is that the vaccine will reduce hospitalizations due to flu – leaving more beds for people with COVID-19. Several organizations, including Physicians for Informed Consent and A Voice for Choice Advocacy, have written to the Board of Regents and the current UC president, asking that they make flu vaccination a recommendation instead of a mandate.

On August 27, Richard Jaffe, Esq., Robert F. Kennedy, Jr., Esq., and Mary Holland, Esq. filed an injunction lawsuit against the Regents of the University of California and the UC president on behalf of two students, one employee, and two faculty members who do not want to be vaccinated. The faculty members are UCLA law professor Frances Olsen and Cindy Kiel, JD, an executive associate vice chancellor at UC-Davis. Kiel oversees research projects at UC-Davis, which includes oversight of ethical issues. The hearing is set for October 22 at the Hayward branch of the Alameda Superior Court.

The plaintiffs' team also filed a preliminary injunction on September 17 and pointed out the violation of students' equal protection and First Amendment rights since they were not given the same religious accommodations and online exemptions as faculty and staff. Days later, UC issued a revised executive order that permits online-only students to forgo vaccination and gives all students the ability to ask for religious exemption to the mandate. Rick Jaffe, in his October 1 blog at rickjaffesq.com, says, "The UC has apparently hired outside consultants to function as judges deciding on the bona fides of people seeking a religious accommodation to the flu shot." Criteria for religious exemption was unknown at that time.

In his September 17 blog, Jaffe has links to the statements being used to support the plaintiffs' case. I was very surprised to see names I recognized in the list, including international experts like Peter Gøtzsche, MD, co-founder of the Cochrane Collaboration; Thomas Jefferson, MD, the lead author of Cochrane's 2018 report on flu vaccination; and Peter Doshi, PhD, associate editor at *The BMJ* (*British Medical Journal*) who worked with Jefferson on the report. Jaffe's October 2 blog has links to the statements for the defense.

By the time you read this, the hearing will be over, and results should be in. I'm hoping the right to choose or forgo a medical intervention wins.

Jaffe R. Breaking News! UC Makes a Tactical Retreat with Its New Executive Order, and It's Good News for Students, (Albeit Temporary and Only for Some students). October 1, 2020.
Jaffe R. The High Priests of the Religion of Vaccinology Circle the Wagons Around the UC Flu Mandate and Recite Their Gospel. October 2, 2020.
Jaffe R. Preliminary Injunction Motion Filed in the UC Flu Mandate Case; Hearing Set for October 14 at 1:30 PM. September 17.
Jaffe R. UC Preliminary Injunction Hearing Now Set for October 22. October 13, 2020.

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# Literature Review & Commentary

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

**Does Eating Nuts Improve Male Fertility?**

One hundred six healthy Spanish men (aged 18-35 years; mean age, 25 years) consuming a Western-style diet were randomly assigned to consume 60 g per day of nuts (30 g of walnuts, 15 g each of almonds and hazelnuts) or no nuts (control group) for 14 weeks. Semen and blood samples were collected at baseline and at the end of the intervention. Compared with the control group, the group consuming nuts showed significant improvements in median values for total sperm count ($p = 0.002$), sperm vitality ($p = 0.003$), total motility ($p < 0.01$), progressive motility ($p < 0.04$), and morphology of sperm ($p < 0.01$). Participants in the nut group also showed a significant reduction in sperm DNA fragmentation.

Comment: In recent decades, human semen quality has declined in industrialized countries. Factors that have been hypothesized to contribute to this decline include environmental pollution and consumption of a Western-style diet. The results of the present study indicate that the inclusion of nuts in a Western-style diet can improve total sperm count and various parameters of sperm quality. These effects may be due in part to a reduction in the sperm DNA fragmentation. The mechanism of action of nuts is not clear, although they are rich in several nutrients that play a role in reproductive function.

Salas-Huetos A, et al. Effect of nut consumption on semen quality and functionality in healthy men consuming a Western-style diet: a randomized controlled trial. *Am J Clin Nutr*. 2018;108:953-962.

**Does High Fructose Intake Cause Gout?**

A meta-analysis was conducted on three prospective cohort studies (including a total of 154,289 subjects and 1,761 incident cases of gout) that investigated the relationship between consumption of foods high in fructose-containing sugars (mainly sucrose and high-fructose corn syrup) and risk of developing gout. Comparing the highest with the lowest categories of intake, the risk ratios (95% confidence intervals) were sugar-sweetened beverages, 2.08 (1.40-3.08); fruit juice, 1.77 (1.20 -2.61); and fruit, 0.85 (0.63-1.14).

Comment: Hyperuricemia is a risk factor for gout. Consumption of large amounts of fructose or sucrose (which consists of 50% fructose and 50% glucose) has been reported to increase serum uric acid levels. Sugar-sweetened beverages and fruit juices are major sources of dietary fructose. In the present study, there was a significant positive association between intake of sugar-sweetened beverages and fruit juices and risk of developing gout. The absence of such an association with respect to whole fruit could conceivably be related to the fact that it is much easier to consume excessive amounts of fructose from juice than from whole fruit. Other possible explanations for the absence of an association could be that the fiber in whole fruit slows the absorption of sugars, or that the fibrous portion of fruit contains compounds that influence uric acid metabolism.

Ayoub-Charette S, et al. Important food sources of fructose-containing sugars and incident gout: a systematic review and meta-analysis of prospective cohort studies. *BMJ Open*. 2019;9:e024171.

**Does High Sugar Intake Cause Cardiovascular Disease?**

The association between consumption of sugar-sweetened beverages (SSBs) and cardiovascular disease (CVD) was examined in a prospective cohort study of 106,178 women participating in the California Teachers Study who were free of CVD and diabetes at baseline in 1995. During a 20-year follow-up period, 8,848 cases of CVD were documented. After adjustment for potential confounding variables (including age, race/ethnicity, socioeconomic status, smoking, alcohol intake, family history of CVD, physical activity, history of hypertension, body mass index, and total energy intake), as compared with those who rarely or never consumed SSBs, those who consumed 1 or more servings per day had an increased risk of CVD (hazard ratio [HR] = 1.19; 95% confidence interval [CI], 1.06-1.34), revascularization (HR = 1.26; 95% CI, 1.04-1.54), and stroke (HR = 1.21; 95% CI, 1.04-1.41). ➤

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Comment: In the 1960s, when the prevailing view was that dietary cholesterol and saturated fat are the major dietary causes of CVD, John Yudkin was arguing that refined sugar may be at least as important as cholesterol and saturated fat in the causation of CVD. A growing body of research now suggests that Yudkin was correct. Numerous observational studies have found that higher intake of simple sugars is associated with a higher risk of developing CVD. In intervention trials, consumption of sucrose or high-fructose corn syrup has been reported to increase platelet aggregation, increase triglyceride levels, lower HDL-cholesterol levels, increase uric acid levels, increase blood pressure, increase body weight, and cause fasting hyperinsulinemia. Each of these changes would be expected to increase the risk of CVD. In addition, refined sugar contains virtually no micronutrients, so replacing healthful foods with high-sugar foods would decrease the intake of various cardioprotective nutrients such as magnesium, B vitamins, copper, and chromium.

Pacheco LS, et al. Sugar-sweetened beverage intake and cardiovascular disease risk in the California Teachers Study. *J Am Heart Assoc*. 2020;9:e014883.

**Can Cherries Prevent Gout Attacks?**

Eighty-four people with physician-confirmed gout were recruited through internet advertisements, social media, and clinic flyers. They were randomly assigned to receive cherry extract (3,600 mg per day) or dietitian-assisted diet modification for gout for nine months. The dosage of cherry extract was equivalent to 96 ounces per day of cherry juice or three pounds per day of cherries. All study outcomes were assessed via the internet and phone calls. In the cherry group, the number of gout flares per month decreased from 0.36 at baseline to 0.22 during the study ($p < 0.05$), and the proportion of participants who had at least one gout flare decreased from 98% to 56% ($p < 0.001$). The mean score on the Health Assessment Questionnaire also improved ($p = 0.001$). Improvements in these parameters were also seen in the diet group, but they tended to be less pronounced than in the cherry group.

Comment: In this study, treatment with a cherry extract for 9 months was associated with a significant decrease in the number of gout attacks and a significant improvement in overall health (as determined by a questionnaire). Some of these improvements may have been due to a placebo effect or to a "participation effect" (i.e., participation in a clinical trial is often associated with improvements in health). However, if these were the main driving factors, one would have expected at least as much improvement in the diet-modification group, since changing one's diet involves a greater amount of commitment and participation than simply taking a cherry extract. The fact that the improvement was greater in the cherry group than in the diet group suggests that the benefits of cherry extract were due to more than a placebo effect or participation effect.

Singh JA, et al. A randomized Internet-based pilot feasibility and planning study of cherry extract and diet modification in gout. *J Clin Rheumatol*. 2020;26:147-156.

**Intravenous Iron for COPD**

Forty-eight patients (mean age, 69 years) with chronic obstructive pulmonary disease (COPD) were randomly assigned to receive, in double-blind fashion, a single dose of intravenous iron (ferric carboxymaltose [FCM]; 15 mg per kg of body weight) or placebo (saline). At baseline, the mean serum ferritin level was 97 µg/L and mean transferrin saturation was 31.3%. The primary endpoint was peripheral oxygen saturation (SpO2) at rest after one week. Secondary endpoints included six-minute walking distance, severity of exercise-induced breathlessness, and exacerbation frequency. Compared with placebo, FCM had no significant effect on SpO2. Eight weeks after treatment, compared with placebo, mean walking distance increased by 12.6 meters in the FCM group ($p = 0.02$ for the difference in the change between groups). The proportion of patients who achieved at least a 40-meter increase in six-minute walking distance was significantly higher after one week (29.2% vs. 0%; $p < 0.01$) and nonsignificantly higher after eight weeks (45.8% vs. 27.3%; $p = 0.19$) in the FCM group than in the placebo group. The proportion of patients who experienced significant breathlessness on exertion (defined as a score of 2 or higher on the Medical Research Council Dyspnea Scale) was significantly lower after one week (33.3% vs. 66.7%; $p = 0.02$) and nonsignificantly lower after eight weeks (45.8% vs. 70.8%; $p = 0.08$) in the FCM group than in the placebo group. Some 91.7% of patients in the FCM group and 8.3% of those in the placebo group developed hypophosphatemia, which was asymptomatic in all cases and which resolved by week 8. Five patients had a serum phosphate level below 0.3 mmol/L at week 1 and were prescribed phosphate supplements according to clinical guidelines.

Comment: In this study of COPD patients who did not have iron deficiency, intravenous administration of FCM improved exercise capacity and breathlessness. However, hypophosphatemia occurred as a side effect in most of the patients. While hypophosphatemia did not cause any serious problems in this study, iron-induced hypophosphatemia has in rare cases been implicated as an apparent cause of osteomalacia. Hypophosphatemia is much less likely to occur when intravenous iron is given as iron isomaltoside than when it is given as FCM. In one study, 45.5% of patients given FCM, as compared with 4% of those given iron isomaltoside, developed hypophosphatemia.[1]

In the present study, the benefits of intravenous iron were clear after one week, but the effects had begun to fade by week 8. Therefore, repeated treatments would likely be needed to maintain the benefits. The potential adverse effects of repeated iron administration in patients who are not iron-deficient would include increased oxidative stress and impaired blood glucose regulation. Further research is needed to determine the risk-benefit ratio of giving intravenous iron to COPD patients who are not iron-deficient.

Santer P, et al. Intravenous iron and chronic obstructive pulmonary disease: a randomised controlled trial. *BMJ Open Respir Res*. 2020;7:e000577.

**Niacinamide for a Subcorneal Pustular Dermatosis**

A 62-year-old Japanese man presented with a one-year history of subcorneal pustular dermatosis, manifesting as pruritic scaly erythema with pustules in the groin and on the back. He failed to respond to topical treatment with a potent

glucocorticoid, a vitamin D analogue, and tacrolimus. Serum zinc was below normal, but he failed to improve after treatment with zinc-L-carnosine, despite normalization of the serum zinc level. He was subsequently treated with 1,500 mg per day of oral niacinamide. The lesions improved progressively and disappeared after two months. The lesions recurred within three months after niacinamide was discontinued, but they regressed rapidly after treatment was resumed at a dose of 1,000 mg per day. After an unspecified period of time, the dose was reduced to 500 mg per day and treatment was later stopped, without a recurrence of lesions.

Comment: Subcorneal pustular dermatosis is a rare pustular dermatosis that is difficult to treat. Niacinamide has demonstrated benefit against various dermatoses, including rosacea, acneiform eruptions, bullous pemphigoid, linear IgA bullous dermatosis, and now subcorneal pustular dermatosis. Niacinamide appears to work in part by exerting an anti-inflammatory effect.

Yamaguchi Y, et al. Successful treatment of recalcitrant subcorneal pustular dermatosis with oral nicotinamide. *J Dermatol*. 2019;46:e438-e440.

**Peppermint Oil for Irritable Bowel Syndrome**

One hundred ninety patients (mean age, 34 years) in the Netherlands who had irritable bowel syndrome (IBS) were randomly assigned to receive, in double-blind fashion, capsules containing 182 mg of small-intestinal-release peppermint oil, 182 mg of ileocolonic-release peppermint oil, or placebo for eight weeks. The dosage was one capsule, three times per day, 30 minutes before meals. A response was defined as at least a 30% decrease in the weekly average of worst daily abdominal pain compared with baseline in at least four of the eight weeks of treatment. The response rate (the primary outcome measure) was 46.8% with small-intestinal-release peppermint oil ($p = 0.17$ vs. placebo), 41.3% with ileocolonic-release peppermint oil ($p = 0.39$ vs. placebo), and 34.4% with placebo. The small-intestinal-release peppermint oil (but not the ileocolonic-release oil) produced greater improvements than placebo in secondary outcomes of abdominal pain ($p < 0.02$), discomfort ($p = 0.02$), and IBS severity ($p = 0.02$). Adverse events were mild but were more common in both peppermint oil groups than in the placebo group ($p < 0.005$).

Comment: This study showed that peppermint oil capsules formulated in such a way as to prevent release in the stomach but to promote release in the small intestine can improve various symptoms of IBS. A peppermint oil product designed to be released in the ileum or colon was less effective. Previous studies have found similar benefits of peppermint oil.[2] Small-intestinal-release products are commonly referred to as enteric-coated preparations. An enteric coating resists dissolution in the acid environment of the stomach but allows for dissolution at the higher pH of the duodenum. Peppermint oil should not be administered as a non-enteric-coated preparation because the release of peppermint oil directly into the stomach can cause heartburn and promote relaxation of the lower esophageal sphincter, potentially resulting in esophageal reflux. In addition, because enteric-coated peppermint oil may be released in a high-pH environment, it should not be taken during or shortly after meals (when gastric acid is being buffered by food) and it should not be given to patients with achlorhydria.

Weerts ZZ, et al. Efficacy and safety of peppermint oil in a randomized, double-blind trial of patients with irritable bowel syndrome. *Gastroenterology*. 2020;158:123-136.

**Vitamin C Treatment of a Patient with Acute Myeloid Leukemia**

A 42-year-old man was diagnosed with acute myeloid leukemia with mutations in TET2 and WT1. After he failed to respond to chemotherapy, he began treatment with intravenous vitamin C twice a week. The dose was gradually increased from 35 g to 95 g over one month. The treatments were reduced to every other week during the second year and to every three to four weeks in the third year. The patient maintained clinical and histological remission for 2.5 years. The disease subsequently recurred, and he died 10 months later.

Comment: In previous research, vitamin C inhibited the growth of some leukemic cells *in vitro*, but accelerated the growth of other leukemic cells.[3] That finding suggests that vitamin C therapy may be beneficial for some patients with leukemia but harmful to other leukemia patients. Pre-clinical evidence suggests that vitamin C may be beneficial for patients with acute myeloid leukemia who have mutations that affect the IDH1/2-TET2-WT1 pathway. The positive response to high-dose vitamin C in the patient described above supports that possibility.

Das AB, et al. Clinical remission following ascorbate treatment in a case of acute myeloid leukemia with mutations in TET2 and WT1. *Blood Cancer J*. 2019;9:82.

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1. Schaefer B, et al. Choice of high-dose intravenous iron preparation determines hypophosphatemia risk. *PLoS One*. 2016;11:e0167146.
2. Khanna R, et al. Peppermint oil for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. *J Clin Gastroenterol*. 2014;48:505-512.
3. Park CH, Kimler BF. Growth modulation of human leukemic, preleukemic, and myeloma progenitor cells by L-ascorbic acid. Am J Clin Nutr 1991;54:1241S-1246S.


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# Erectile Dysfunction: The Canary in the Cardiovascular Coal Mine?

## The role of endothelial function on tumescence – and beyond

by Erica Zelfand, ND

The stories I hear of men[1] with erectile dysfunction (ED) are strikingly similar: The issue begins insidiously and is initially treated at a "low T clinic" with gradually increasing doses of exogenous testosterone in regimens that yield varied but ultimately insufficient results.

A review of the lab work of these individuals reveals that they are typically overdosed on their prescription hormones, with total testosterone levels often above 1000 ng/dL. While supraphysiological levels of testosterone do, in fact, enhance the sexual desire and performance of some men, they come with significant health risks and pesky side effects like anxiety, irritability, and insomnia. Other men, however, find that even high doses of anabolic steroids fail to engender desired outcomes in the bedroom.

Erectile dysfunction (ED, impotence) is a fairly common medical condition, characterized by the inability to achieve and maintain a penile erection firm enough for satisfying sexual intercourse.[1] ED is also on the rise: While the condition affected an estimated 152 million males worldwide in 1995, that number is expected to swell (no pun intended) to over 320 million people by 2025.[2,3]

Just last week, a new patient shouted at his wit's end, "I'm taking testosterone, HCG [human chorionic gonadotropin], and anastrozole. I'm lifting more weight than the other guys at the gym. I look amazing. I have tons of energy – so much I can't fall asleep at night - but I after two years of playing with all my doses I still can't get hard. What the heck is wrong with me!? What are my other doctors missing? I really hope you can figure it out." [Note: This patient employed more expletives when expressing himself.]

Time and time again, I explain to exasperated fellows like this one that sex hormone levels are just one piece of the puzzle. The successful treatment of ED often also entails assessing the nervous system (including mental health), adrenal function, metabolic health, and endothelial integrity, with the latter being among the most overlooked aspects of sexual health.

Tumescence is a hemodynamic process characterized by enhanced penile arterial inflow and reduced venous outflow.[4,5] Because the physiology of tumescence (penile erection) requires that the penis engorges with blood, the integrity of the vascular system – and ergo the status of nitric oxide production – is of utmost importance to male sexual performance and satisfaction.[6]

**Nitric Oxide: The Endothelium Relaxer**

Our understanding of nitric oxide (NO) is relatively new: In 1998 three American pharmacologists received the Nobel Prize for their discovery of NO's effects as a signaling molecule within the cardiovascular system.[7]

This tiny gas molecule is produced in the blood vessels, nerves, and immune cells. Neuronal and endothelial NO causes relaxation of the surrounding smooth muscle, resulting in vasodilation.[8,9] With regard to male sexual health, NO triggers the relaxation of the cavernous smooth muscle of the penis, allowing for engorgement and subsequent erection.

NO production declines with age, however, placing males at increased risk of ED as they grow older.[10] It is now estimated that nearly half of men above the age of 40 have some degree of ED.[11]

Endothelial inflammation undermines NO production and is thus a significant determinant of ED and other vascular diseases.[12] It is also a culprit that can effectively be treated with naturopathic medicine.

**Erectile Dysfunction as Coronary Risk Marker**

Due to the relatively small size of the penile vasculature (on even the most well-endowed of individuals), ED may be understood as a warning sign of poor vascular function and impending coronary artery disease (CAD).[9,11,13,14] ED may present well before the observation of so much as an elevated blood pressure reading.[15] If left unchecked, the vascular inflammation and dysfunction associated with many cases of ED may lead to ischemic heart disease;[16] ED has thus been referred to as "penile angina."[17]

ED is such a strong predictor of cardiovascular disease in men,[3] in fact,

1. * Please Note: The terms "man" and "male" as used within this article refer specifically to individuals who were born with a penis. I acknowledge and honor that not all men were born with this anatomy, and that not all penis-owners identify as male.

that providers are now advised to assess the cardiovascular health of patients presenting with the condition.[16] While not all men with ED have cardiovascular problems, a significant percentage of males with angiographically demonstrated CAD have been observed to have ED.[13] ED was also shown in one study to precede CAD in a whopping 70% of male CAD patients.[13]

It is perhaps no surprise that ED and CAD go hand-in-hand, as they share many of the same risk factors, including sedentary lifestyle, obesity, diabetes, smoking, hypertension, dyslipidemia, metabolic syndrome, and declining NO activity.[9,11,18,19]

**Conventional Treatments of ED**

The first-line therapy for ED entails phosphodiesterase type 5 inhibitors (PDE5i) like sildenafil.[20] Although these drugs do not directly increase NO, they do augment NO-mediated pathways.[21]

When PDE5i's fail to improve symptoms, vacuum devices, intra-cavernous injections, and penile prosthesis implantation are considered second- and third-line therapies. Few patients are eager to try these interventions, however, which may not be too great of a tragedy, as none of these methods adequately addresses the underlying metabolic, neurological, hormonal, or endothelial aspects of ED.

Testosterone plays an important role in sexual function via several mechanisms, including the stimulation of NO release.[22] As more and more males become afflicted with ED, the increasing number of "low T" clinics that have cropped up over the years now comprise a multi-billion dollar industry.[23,24] Testosterone replacement therapy (TRT) does help many men with ED – though not all. In my experience and opinion, focusing on NO augmentation – either in lieu of or in addition to hormone prescription – may serve ED patients in both the short and long term.

**Two Pathways of Nitric Oxide Production**

There are two pathways by which NO is created in the body (see Figure 1).[25] One pathway entails the reduction of dietary nitrates to nitrite and then NO.[26] Another pathway depends upon the enzyme *nitric oxide synthase* (NOS) to convert L-arginine to NO.[27]

**Oral Hygiene**

In the NOS independent pathway of NO production, facultative oral microflora reduce dietary nitrates ($NO_3^-$) to nitrites ($NO_2^-$), which are then converted to NO in the acidic environment of the stomach.[26]

In this pathway, the presence of particular oral bacteria and the stomach's low pH are invaluable for NO production. These requisite conditions are undermined, however, by antiseptic mouthwashes, proton-pump inhibitors, and over-the-counter antacid medications – agents commonly used in industrialized societies.[28–30] Although restoring a patient's gastric acidity is a relatively straightforward task for the naturopathic physician, as of this writing there is no nutritional probiotic supplement that contains the oral bacteria essential for nitrate reduction. We may still, however, advise patients to avoid commercial mouthwash products.[26]

**Dark Leafy Greens and Beetroot**

Vegetable-rich diets have been shown to support heart health,[31,32] in part due to their nitrite and nitrate content. High nitrate diets lower the risks of hypertension heart attack, and stroke.[33-35]

Although dietary nitrites such as those naturally found in bacon have been vilified, nitrites and nitrates are actually naturally occurring molecules produced in the body that are important to health.[36,37] (The culprit in processed meats is likely not nitrite, but rather the carcinogenic compound nitrosamine.[38,39])

In addition to eating plenty of green, leafy vegetables, powdered greens products, beetroot (also known simply as "beets"), and beetroot products may all be used as supplemental sources of nitrates, antioxidants, and phenolic compounds pertinent to cardiovascular health.[40] Beetroot is a particularly rich source of nitrates and antioxidant compounds and has been observed to increase NO levels and lower blood pressure readings in both men and women of various ages.[41-43]

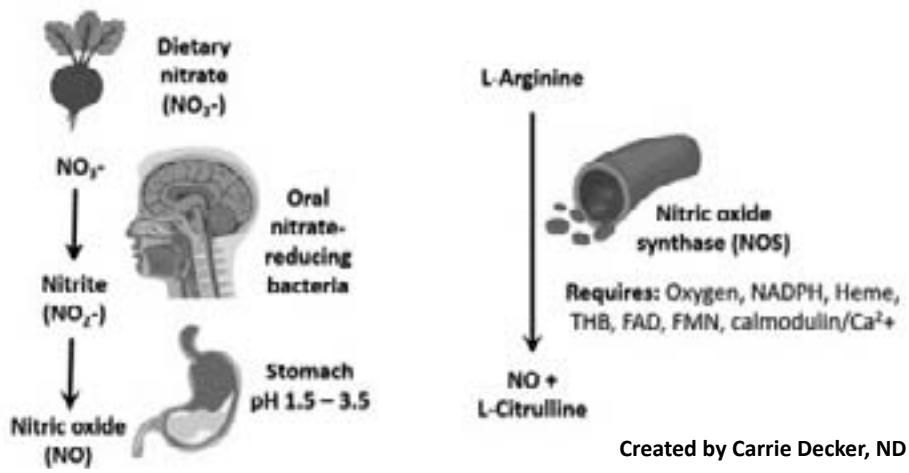
**Nitric oxide can improve sexual performance and protect vascular health.**

**L-Arginine and L-Citrulline**

L-Arginine may be acquired from nutritional supplements and/or endogenously derived from the amino acid L-citrulline, and serves as the source raw material from which the body produces NO via NOS (Figure 1).[44] Low serum levels of L-arginine have unsurprisingly been correlated with poor NO production.[45]

A significant percentage of ED patients have low L-arginine or L-citrulline levels, placing them at increased risk of disease.[45] Because of this and because the NOS-dependent route of NO production was the first pathway discovered, the nutraceutical product market is now replete with L-arginine-containing formulae.[46] ➤

**Figure 1. Pathways of nitric oxide production.**

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Although oral L-arginine supplementation may improve NO-mediated vasodilation and endothelial function, its effects as a monotherapy are transient due to the short duration of its presence in the circulation (on the order of milliseconds).[47] This may be why a review of L-arginine's efficacy in the treatment of ED reports that a minimum dosage of 3 g daily is necessary to achieve outcomes. Some studies have even dosed the amino acid at 5 g and higher.[48]

The efficacy of L-arginine may be improved by delivering it alongside N-acetylcysteine or glutathione (GSH), both of which contain sulfur residues or thiols. NO binds GSH, forming S-nitrosoglutathione. This molecule then transports and circulates NO, has a half-life of hours, and is just as vasoactive as NO.[49] Antioxidants like ascorbate also are able to cleave or release bound NO.[50] L-arginine also pairs particularly well with Pycnogenol, as is explored in the section below.

Unlike L-arginine, its precursor L-citrulline (named for the watermelon, or *Citrullus vulgaris*, from which it is derived[51]) evades presystemic metabolism, effectively increasing circulating NO levels.[45,52,53] This may make L-citrulline a more advantageous nutritional supplement than L-arginine in the treatment of ED, hypertension, and related vascular conditions.[54,55]

Although L-citrulline supplements are less effective than PDE5i's (at least in the short term), they are an effective adjuvant to PDE5i treatment.[54,56] L-citrulline has also been shown to be safe and psychologically well tolerated.[54]

What may be even more effective than L-arginine or L-citrulline monotherapy, however, is the administration of the two NOS substrates concurrently: Simultaneous oral supplementation of L-arginine and L-citrulline (1 gram of each) increased plasma L-arginine levels more than 2 g of either alone in a 2017 study.[57] (Note that because many viruses, including herpes simplex virus [HSV], are dependent upon the bioavailability of arginine,[58] L-arginine and L-citrulline supplements may be poorly tolerated by patients with frequent HSV outbreaks.)

In addition to augmenting the body's supply of L-arginine, it is also important to support conversion of the amino acid into NO.[38] This conversion is enhanced by oxygen, NADPH, heme, tetrahydrobiopterin (THB, also known as $BH_4$), and other coenzymes. Things as simple as checking oxygen saturation and ferritin levels may therefore prove advantageous.

**Pycnogenol**

A standardized extract from the bark of the French maritime pine, *Pinus pinaster* – or Pycnogenol, as it's known in the US by its patent name – can improve erectile function both as a stand-alone treatment and in combination with L-arginine.[59,60]

In a double-blind study of 21 males suffering from ED, patients received 120 mg of Pycnogenol or placebo daily. After three months, Pycnogenol significantly improved the symptoms of ED from moderate to mild stage. Perhaps more importantly, a significant increase in plasma antioxidant activity was noted among those who received Pycnogenol, while no such benefit was found in those who received placebo. The Pycnogenol group further enjoyed reductions in total cholesterol and LDL-cholesterol levels (from 5.41 to 4.98 mmol/L and from 3.44 to 2.78 mmol/L, respectively). (No significant changes in triglycerides or HDL were observed.) These findings suggest that Pycnogenol may not only treat ED but may also temper some of the more serious vascular changes that succeed it.[61]

In another study of 40 males, 25 to 45 years of age, a combination of L-arginine and Pycnogenol significantly outperformed Pycnogenol alone, helping 80% of men (and, after another month of the study, 92.5% of men) achieve a normal erection - as compared to only 5% of men who benefitted from Pycnogenol alone. Pycnogenol was given at a dose of 40 mg one to three times daily, with L-arginine at a dose of 1.7 g daily.[60] (It is worth noting that the minimum effective daily dosage of L-arginine as a standalone treatment of ED may be 3 g,[62] though this study suggests that lower doses may be used within the milieu of co-treatment with Pycnogeol.)

In a similar trial of 50 males, L-arginine (3 g/day) plus Pycnogenol (80 mg/day) restored normal erectile function after just one month of supplementation. Sperm quality improved in the men who took this combination and their testosterone levels increased significantly. The men also reported a doubling in their sexual intercourse frequency.[63]

**Glutathione and Other Antioxidants**

Supplementation with L-citrulline and GSH has also been shown to synergistically increase NO levels.[64]

In addition to providing thiols for the formation of S-nitrosoglutathione, GSH also affects the NOS enzyme function. In a GSH-depleted environment, NOS becomes uncoupled, resulting in the

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production of toxic superoxides instead of salubrious NO. Endothelial NOS (eNOS) uncoupling has been implicated in numerous conditions marked by vascular endothelial dysfunction, including heart failure, ischemia/reperfusion injury, hypertension, atherosclerosis, and diabetes.[65]

As the master antioxidant of the body, GSH strongly protects against the oxidative stress associated with endothelial dysfunction. Like other antioxidants, GSH may prevent eNOS uncoupling by scavenging free radicals, mitigating certain radical-generating pathways, maintaining the optimal ratio of reduced to oxidized glutathione, and protecting the endothelium against damage by toxic metabolites.[66]

GSH and other antioxidants can thus prevent oxidative stress, ameliorate vascular endothelial dysfunction, and stave off cardiovascular disease (among other chronic ailments).[66]

**DHEA**

The steroid hormone precursor dehydroepiandrosterone (DHEA) not only augments hormone production, but also positively affects eNOS. Supplementation with DHEA may thus further support endothelial health.[67] A systematic review of 38 trials found that DHEA improves various aspects of sexual health in both males and females, including sexual interest, sexual frequency, lubrication, arousal, pain, and orgasm.[68]

**Carnitine and Taurine**

Carnitine and taurine have been shown to support NO production and vascular health. Specifically, propionyl-L-carnitine (PLC) has been observed to stimulate NO production and facilitate the delivery of free fatty acids into the mitochondria.[69] When administered alongside acetyl-L-carnitine, PLC enhances the efficacy of sildenafil in treating the symptoms of ED in men who have undergone bilateral nerve-sparing prostatectomy.[70] Taurine also increases NO, likely by decreasing asymmetric dimethylarginine (ADMA), as an inhibitor of NO synthesis.[71,72]

**Meditation**

Beyond erectile function and blood pressure, NO's benefits include blood clot prevention, immune function enhancement, and nervous system support.[7] NO may also contribute to the relaxing effects of meditation and mindfulness practice – and mindfulness practice may likewise enhance NO production.[73] In one study, for example, experienced meditators were found to have lower levels of subjective stress and higher nitrate and nitrite levels.[9] This finding may be added to the long list of reasons to recommend meditation and other mindfulness-based practices to those with ED and other cardiovascular ailments.

**Exercise**

Sedentary lifestyle is a significant risk factor for both ED and cardiovascular disease.[9] Physical activity is known to increase vascular NO levels and improve vascular function,[74] which explains at least in part why exercise is hailed as the lifestyle factor most strongly correlated with erectile health.[74,75]

A 2018 systematic review of 10 studies concludes that moderate to vigorous aerobic exercise four times weekly for six months improves erectile function in men who have ED caused by sedentary lifestyle, obesity, hypertension, cardiovascular disease, and/or metabolic syndrome.[9] Considering that exercise helps with a wide array of other health conditions, physical activity should be a basic treatment guideline for just about every patient.

**Conclusion**

During sexual arousal, the vessels of the penis rely upon nitric oxide to help blood – and the oxygen and nutrients it carries – engorge the penis, resulting in tumescence. Erectile dysfunction may therefore represent poor endothelial health and a deficit of NO in many cases – and thus serve as a warning sign of more serious vascular ailments to come. Because there is no standard lab test for assessing NO levels,[76] it is important for healthcare providers to make astute clinical assessments of their patients' cardiovascular status when labs and imaging fall short.

Simple, natural strategies and supplements – like oral health, digestive hygiene, green vegetables and beetroot, L-arginine, L-citrulline, glutathione, DHEA, carnitine, Pycnogenol, meditation, and exercise – may well serve the men who suffer from erectile dysfunction. Even in the context of testosterone replacement and phosphodiesterase inhibitor prescription, nitric oxide support may further improve sexual performance and safeguard against more serious vascular disease. ◆

**References and full article are available online at www.townsendletter.com.**

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# Assessment and Treatment of Cognitive Impairment in Fatiguing Illnesses

by Craig Tanio, MD

**Introduction**

Cognitive impairment is a major component of fatiguing illnesses and a significant driver of disability and poor outcomes in these conditions. Cognitive impairment is part of the formal criteria in the 2015 National Academy of Medicine definition of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). A recent review of patients with ME/CFS showed self-reported issues with memory (80%), expressing thoughts (73%), attention (69%), slower thoughts (66%), and comprehension (55%). Other clinical frameworks used to define fatiguing illnesses such as chronic inflammatory response syndrome from water damaged buildings (CIRS-WDB), mast cell activation syndrome (MCAS), and multiple systemic infectious disease syndrome (MSIDS) all identify cognitive impairment as an important subset of symptoms.

Treatment of these issues should not occur outside of the context of treating the root cause and entire condition. However, specific interventions to assess and treat cognitive impairment as part of a comprehensive plan is likely to result in improved outcomes. We use the following approach to assess and support cognitive function:

- Assess current cognitive function using a three-pronged approach that incorporates subjective patient information, formal cognitive testing, and volumetric brain imaging.
- Assess and treat cognitive function with particular attention to brain perfusion, sleep/limbic system activation, pacing/glucose metabolism/nutrition, and neuroinflammation.
- Treat the overall fatiguing illness (out of scope for this article).

**Assess Cognitive Function with a Three-Pronged Approach**

The discerning clinician will notice signs of cognitive impairment from the moment the patient steps in the room. Common issues that may look like problems with adherence include forgetting instructions and suggestions from a prior visit, confusion with complex explanations, and trouble remembering medications. They may have delayed verbal responses to questions that worsen during the time of the visit. Patients may also report cognitive post-exertional malaise (PEM) that occurs in a similar pattern to physical PEM.

**Most patients with fatiguing illnesses will have some degree of neuroinflammation.**

We utilize a three-pronged approach to get an objective and practical assessment. The use of all three approaches can allow a clinician to confirm the location and degree of neurologic injury.

*Cognitive testing.* The use of validated brain testing software such as CNS Vitals™ is a straightforward way for the clinician to get objective measures of brain function within 30 minutes. Findings often seen include slowing of information processing speed, complex attention, and executive function, as well as changes in verbal and visual memory.

*Patient surveys***.** Detailed brain surveys such as the Brain Function Assessment Form™ are a practical way to correlate symptoms with specific neuroanatomic pathology. Survey information cannot be taken at face value but needs to be confirmed and further explored through the history.

*Volumetric imaging*. We utilize volumetric MRI imaging if patient survey and cognitive testing are positive. Volumetrics MRI imaging uses software such as NeuroQuant or NeuroReader to convert 2D segmented images into 3D volumes and compare the images to a control database with reports that show gray and white matter volumes reported out in percentiles. Larger volumetric sizes may reflect neuroinflammation with likely mechanisms including micro-interstitial edema related to incompletely regulated cell danger responses, failed autophagy, apoptosis, possible mast cell activation, and microglial cell activation. Smaller volumetric sizes may reflect neurodegenerative pathology resulting from chronic neuroinflammation, mitochondrial degeneration, reactive oxygen species damage, protein misfolding, and neuronal vascular injury. It is more accurate than a radiologist in assessing atrophy. Volumetric studies of patients with fatiguing illnesses have been plagued by independent small sample studies rather than a collective registry but the types of observations include the following:

- ME/CFS – The most consistent volumetric findings have been changes in the basal ganglia, including the caudate and putamen
- CIRS-WDB – Reported volumetric findings include increases in forebrain, hippocampus, and pallidum sizes and decreases in multiple grey matter areas,

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including caudate, forebrain, cortical matter

- MCAS – Mast cells can be present in the cerebellum, ventral diencephalon, caudate, putamen, and thalamus resulting in increased volumetric sizes

The use of volumetric imaging greatly helps patients who have often been told by previous clinicians that "it's in their head" to understand that there are clear biologic and neurologic issues. We will review patients' symptoms and correlate them with the location of their neurologic injury. Understanding the degree of neurologic injury can be motivating to patients at a time when they can take effective action. Finally, all three of these assessment methods can help to document clear improvement over time.

**Cerebral Perfusion**

The proper circulation of blood and delivery of oxygen, glucose, and other nutrients are critical for good neurologic performance.

Cognition can be readily impaired by cerebral perfusion deficits due to orthostatic intolerance (OI). OI and Postural Orthostatic Tachycardia Syndrome (POTS) can be practically demonstrated through a NASA 10-minute "lean test" that assesses postural changes in blood pressure, heart rate, and symptoms. Addressing orthostatic intolerance directly through electrolytes, hydration, compression stockings, and mineralocorticoids can often improve symptoms. At times, alpha-1 receptor agonists or low dose beta blockers may be required.



A recent study shows that patients with myalgic encephalomyelitis can have significant changes in cerebral blood flow even in the absence of hypotension or tachycardia. This may be mediated by changes in cytokines such as Vascular Endothelial Growth Factor (VEGF) with resulting changes in capillary perfusion. Physical examination can often show peripheral changes in capillary perfusion in hands and feet such as cold hands and feet that can be objectively measured by a laser thermometer. The use of hyperbaric oxygen can be a particularly helpful modality in these situations, where there can be clinical improvement in peripheral perfusion and neurologic symptoms evident after the first treatment.

If there is atrophy on the NeuroQuant, clinicians should look for evidence of coagulopathies as an additional contributor to diminished blood flow and oxygenation. Abnormal biomarkers can include antiphospholipid antibodies, elevated fibrinogen split products, elevated d-dimer, and abnormalities in von Willebrand Factor among others. These markers often improve with correction of the underlying inflammation.

**Sleep and Recovery**

Unrefreshing sleep is a hallmark of myalgic encephalomyelitis, and the most consistently reported symptom. This can include insomnia, sleep disturbances, daytime sleepiness, and irregular sleep cycles. Polysomnography often reveals abnormal sleep architecture with delayed onset of sleep, fragmented sleep, increased alpha waves, and decreased delta waves. The glymphatic system becomes much more active during sleep than during wakefulness in order to remove cellular debris. Therefore, restorative sleep is one of the most effective strategies to reduce neuroinflammation.

Good sleep hygiene such as avoiding caffeine, alcohol, and stimulants, avoiding brain-activating activities before bed, removal of electronics, use of blackout curtains, and a consistent sleep ritual is critical. Avoidance of pain amplification, sensory amplification and post exertional malaise can reduce disturbances of normal sleep. Magnesium threonate, L-theanine, taurine, 5-HTP, and valerian all have good safety profiles. Melatonin may be especially helpful for these patients as it has anti-inflammatory properties, preserves the blood brain barrier, and activates BDNF. Chronic use of pharmaceuticals for insomnia is discouraged due to their tolerance and dependence. Patients who do not respond to initial measures for sleep should have a sleep study to rule out sleep apnea. We find the use of biomonitors, such as the Biostrap and Oura ring, to be an excellent aid to track progress.

A significant subset of patients with unrefreshing sleep will also show signs of limbic system activation. This can range from signs of increased sympathetic activity such as anxiety, being easily startled, light sensitivity, tachycardia, or difficulty relaxing to signs of reduced parasympathetic activity such as dry eyes, dry mouth, or slow bowel movements. Patients can have a high score on the adverse childhood events score and show high volumetric sizes in their amygdala, hippocampus, cingulate, and thalamus. Their "flight or fight" response is consistently on.

While the literature on the efficacy of treatments for limbic system activation is not robust, in our experience it is a considerable roadblock for patients that needs to be overcome early in treatment. Interventions can range from mindfulness training, meditation, HeartMath, and ice baths to full limbic system retraining programs such as the Dynamic Neural Retraining System or the Gupta program. Herbs including baicalin, tribulus, and ginger can have salutary effects on reducing sympathetic activity. Measuring improvements in heart rate variability through the Apple Watch or other similar biometric devices along with surveys are a good way to monitor changes in a "N of 1" trial of such programs.

**Pacing, Sugar, and Nutrition**

The notion of cognitive pacing is similar to physical pacing for patients with ME/ CFS. Pacing is an individualized approach to managing physical, cognitive, and emotional energy within a patient's specific limits. Symptom journals and activity markers can help patients understand triggers of setbacks and where their tolerance limits are. Studies have shown that acute exercise can impair cognitive performance and affect brain function in ME/CFS patients as measured by functional MRI. Clinicians need to teach patients about how to pace and manage their energy envelopes and to not overdo it. Behavioral strategies to

manage cognitive impairment include selecting the best time of day to complete cognitive tasks, minimizing interruptions, and reducing sensory input to the brain through sound-reducing headphones and reducing screen glare.

Disorders in sugar and insulin metabolism can contribute to fluctuating cognitive performance, especially with changes in focus, concentration, and processing speed. With ideal blood sugar function, a patient's energy and mood are level between meals and this should be the target outcome. We favor a brain healthy diet based on the principles outlined in the Wahls protocol with an emphasis on high amounts of brightly colored vegetables, gluten-free, lower carbohydrate, low grains/vegetable oils, and brain-healthy fat. If patients have been on an unhealthy diet, often frequent meals are necessary until carbohydrate metabolism is improved. An evaluation for HPA-axis dysfunction, thyroid, sex hormone, insulin resistance, and reactive hypoglycemia can be necessary.

Given that there can be central nervous system issues with insulin resistance even without demonstrable peripheral insulin resistance, it is worthwhile to do a trial of intermittent fasting and ketosis for most patients in the course of their treatment once their metabolism can handle this challenge.

Even with a healthy diet, there can be relative nutrient deficiencies. Nutrients that are particularly important to brain function and where there are often clinical deficiencies with a healthy diet include vitamin D, choline, DHA, and butyrate. Another less recognized issue are patients who have a double variant of Transcobalamin 2 (TCN2), which is a gene for a protein that facilitates transportation of vitamin B12 into the cell, particularly in the brain and spinal fluid. These patients can have relative B12 deficiency in the brain with normal B12 levels. A trial of injectable B12 in these patients is warranted, if responsive they should continue on B12 replacement. The literature on the contribution of genomics variants to neurocognitive impairment is rapidly expanding and genomics testing can be helpful in select patients.

**Neuro-Inflammation**

Most patients with fatiguing illnesses will have some degree of neuroinflammation. At the root of neuroinflammation are microglial cell overactivation and chronic stimulation of the innate immune system. Increases in blood brain barrier permeability can continue to stimulate microglial cells through ongoing exposure to antigens, toxins, and mast cells. Blood brain barrier permeability can be increased by inflammatory cytokines such as MMP-9 and TGF-beta, which can create a vicious positive feedback loop.

Low dose naltrexone can be very useful in addressing microglia cell activation. It can block TLR 4 receptors from activation microglia, increase endogenous opioid growth factors, and decrease inflammatory cytokines, including TGF beta. The effects often can take one to two months. Palmitoylethanolamide (PEA) can take two to four weeks to fully realize anti-inflammatory effects.

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For patients who need a more rapid anti-inflammatory action, we will use a nasal spray compounded formula of Synapsin (ginsenoside RG3 and nicotinamide riboside), which can decrease microglial cell activated inflammation and neural cell apoptosis.

The combination of resveratrol and curcumin has been shown to increase NRF2 and to decrease TGF-Beta and MMP-9. Specialized pro-mediators, vitamin D, and bioflavonoids such as luteolin can also reduce neuro-inflammatory markers. Cytoquel® is a useful nutraceutical blend containing curcumin, resveratrol, tocotrienols, n-acetylcysteine, and epigallocatechin gallate, which has been associated with reduction of multiple inflammatory markers, including MMP-9 and fibrinogen.

In patients where toxins (e.g., mold, heavy metals) are a contributor, there can be clinical exacerbation of neurologic issues if there is a significant blood brain barrier permeability while they are being detoxified. Blood brain barrier permeability can be directly assessed through a serum S100B (available through Mayo Clinic Labs) or a Cyrex 20.

A common co-morbid contributor of neuro-inflammation that is often overlooked is iron overload, which can be measured with ferritin and iron/TIBC. In a study of patients with cognitive issues over the age of 60, more than 10% had iron overload issues. Therapeutic phlebotomy is effective at addressing this issue.

If patients are not responsive to treatments for neuroinflammation or the patient demonstrates concurrent psychiatric symptoms, a work-up for neurologic autoimmunity may be in order. Mayo Clinic Labs has very thorough autoimmune encephalopathy panels, and an alternate option is Cyrex 5. Neurologic antibodies themselves can be destructive to neurons unlike most autoimmune antibodies.

Neurodegeneration and atrophy are the cumulative result of neuroinflammation and mitochondrial insults (e.g., prolonged antibiotic treatments). Treatments to address hypometabolism and mitochondria efficiency will often get better results if other issues are addressed first. For example, the use of vasoactive intestinal peptide is reserved until the end of the Shoemaker protocol for CIRS. Other mitochondrial support protocols such as NADH and CoQ10 will usually get improved results if saved for the end.

**Conclusion**

Neurocognitive slowing, reduced executive function, cognitive fatigability, and cognitive post exertional malaise may be the most limiting aspects of fatiguing illnesses. It is a primary reason why patients with these conditions are unable to succeed in school or sustain employment. Specifically assessing and treating these impairments as part of a comprehensive plan for the fatiguing illness is likely to result in improved outcomes.

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# Introduction to Peptide Therapy: Effective, Safe, Natural Medicine

by Mitchell A. Fleisher, MD, DHt, DABFM, DcACBT

Peptide therapy is an evolving, cutting-edge, medical science in which specific, bio-identical, protein amino acid sequences called "peptides" are used to repair, regenerate, support, and improve the structure and function of different parts of the mind and body. Well-known examples of naturally occurring human peptides are insulin, ACTH, glucagon, growth hormone, and thyroid hormone.

Over 7,000 peptides that are naturally occurring in the body have thus far been identified, and over 60 medicinal peptides are currently used in clinical medicine.

Peptide therapy is becoming more popular with integrative medicine physicians because medicinal peptides are highly specific and very effective in their therapeutic action, typically very safe, and extremely well tolerated.

*It is very important to understand the difference between pharmaceutical drugs and medicinal peptides.*

With conventional, allopathic, pharmaceutical drugs, the mind and body will always have a "reaction" that unfortunately often includes unpleasant, potentially harmful, and sometimes lethal, adverse side effects. This is due to the fact that pharmaceutical drugs are foreign molecules unfamiliar to the body that biochemically 'force' changes and distortions upon the mind and body, which too often react badly.

In contrast, with bio-identical human medicinal peptides, the mind and body will always have a "response" that is very safe and virtually free of any adverse side effects when properly prescribed by a well-trained medical physician certified in peptide therapy. This is due to the fact that medicinal peptides are "messenger" molecules with which your mind and body are already familiar because they have been in you since you were born. These peptides are natural, human 'communication' molecules.

The cells in your mind and body use the innate, inborn, medicinal peptides to communicate with one another to tell them what to do or not to do. That is, they guide and balance all the metabolic and regenerative functions that serve to keep us healthy.

When *properly prescribed and administered by a specially trained physician*, medicinal peptides communicate with specific cells, tissues, and vital organs in the body by binding to peptide receptors on the cell surfaces, thereby signaling optimal, cellular messages for health improvement and potentially enhancing and optimizing the function of the entire body and mind.

Peptide therapy includes many new, potent, peptide medicines with amazing potential to promote greater health and well-being and a potentially longer, higher quality of life. Benefits of peptide therapy may include the following:

- Increased energy and stamina
- Better mental focus and memory
- Strengthened immune system defenses
- Improved recovery from illnesses and wounds
- Increased muscle mass and tone

## Over 60 medicinal peptides are currently used in clinical medicine.

- Increased bone density
- Improved skin elasticity
- Reduced wrinkled skin
- Fuller hair
- Decreased body fat and weight loss
- Lowered cholesterol and lipid levels
- Decreased joint and muscle pain
- Deeper, rejuvenating sleep
- Enhanced sex drive

Breakthroughs in modern medicine have shown the benefits of medicinal peptides to aid in the diagnosis and treatment of a wide number of both physical and mental disorders, as identified by the International Peptide Society (IPS). Peptide therapy may help with a broad range of health conditions:

- Anti-aging and regeneration of the entire body
- Tissue repair of bones, cartilage, ligaments, tendons, joints, muscles, and skin
- Balancing endocrine hormones
- Enhancing growth hormone production
- Hair regrowth and restoration
- Inflammatory diseases, both acute and chronic
- Arthritis, degenerative and rheumatoid
- Autoimmune disorders, e.g., lupus, MS, Sjogren's syndrome, etc.
- Cognitive, mood, and memory enhancement
- Cellular energy production, and enhanced vitality
- Cytoprotection from oxidative stress
- Alzheimer's disease and dementia
- Post-stroke recovery
- Obesity and weight management
- Osteopenia and osteoporosis
- Anxiety and stress disorders
- Depression
- Insomnia
- Improving sexual disorders, libido, and erectile dysfunction

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# Peptide Therapy

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**A Word of Caution**

Medicinal peptides should *only* be obtained from FDA-certified, 503A or 503B, US compounding pharmacies that provide peptides with greater than *99.8% purity and chemical integrity.* That is, you are receiving the highest quality, FDA-regulated, pharmaceutical grade, medicinal peptides by US law.

**Never** purchase peptides from online 'discount' websites, since they are **not** regulated and have been found to be adulterated, substandard, often fraudulent products that can potentially cause adverse effects and great harm. The principle of *caveat emptor* ("buyer beware") applies here.

Moreover, peptides are powerful medicines that should and must be carefully prescribed and individually managed by a specially trained, licensed, medical physician who understands the correct peptides and the dosages to be used for different health conditions. Peptide therapy requires expert medical guidance to experience and benefit from their exceptional therapeutic potential. For educational purpose, here are a few examples of the medicinal peptides.

**BPC-157**

BPC (Body Protection Compound) 157 is a pentadecapeptide (composed of 15 amino acids) that is naturally produced in the secretions of the gastrointestinal tract. The body uses it to protect and heal the gastrointestinal mucosal lining from inflammation and injury. BPC-157 stimulates the stem cells in the gut lining to promote healing and repair. Therefore, BPC-157 has been effectively prescribed for acid reflux, gastritis, GERD, eosinophilic esophagitis, peptic ulcers, intestinal hyperpermeability (leaky gut syndrome), celiac disease, food allergies, inflammatory bowel diseases, and, to improve digestive function, to help and protect the liver from toxic insults, and to generally protect and heal inflamed gastrointestinal epithelium. BPC-157 has also been shown to promote repair and regeneration of injured, inflamed tissues in the bones, cartilage, ligaments, tendons, joints, muscles, and blood vessels, as well as to protect and promote the healing of injured peripheral nerves and brain cells.

Benefits of BPC-157 may include the following:

- Potent, anti-inflammatory properties
- General digestive function improvement (IBS)
- Repair and maintenance of GI mucosal integrity
- Helps to prevent and heal gastric and duodenal ulcers
- Helps to protect and heal inflamed intestinal epithelium (leaky gut syndrome)
- Promotes healing in Inflammatory bowel disease (IBD), esp. in exacerbations/flareups
- Helps to protect and promote healing of liver from toxic insults (alcohol, antibiotics, etc.)
- Helps to promote tissue repair in the GI tract, brain, bone, ligaments, tendons, joints, muscles, etc.
- Helps to promote repair of damaged nerves and support healing of peripheral neuropathy
- Neuro-protective properties, specifically modulating the serotonergic and dopaminergic systems, which helps to improve memory and mood
- Effective treatment for traumatic brain injury (TBI) and post-concussion syndrome
- Promotion of angiogenesis and vasculogenesis (new, healthy blood vessel growth)

Specific target conditions for BPC-157 Peptide Therapy may include the following:

- Acute and chronic inflammatory conditions
- GI ulcers and inflammation
- Inflammatory bowel diseases
- Leaky gut syndrome
- *H. pylori* gastrointestinal infections
- Autoimmune diseases
- Chronic allergies
- Chemical sensitivity
- Lyme disease
- Chronic viral, bacterial and fungal infections with inflammation
- Chronic fatigue syndrome and fibromyalgia
- Cardiovascular and cerebrovascular disorders
- Heart rhythm irregularities (cardiac arrhythmias)
- Diabetes mellitus and associated chronic problems
- Post-surgical conditions
- Peripheral neuropathy
- Anti-aging and regeneration

**Cerebrolysin®**

Cerebrolysin® is a nootropic (cognitive enhancing), medicinal neuropeptide complex that possesses neuroprotective and neurotrophic (nerve regenerating) repair properties. It is a mixture of neuropeptides, including brain-derived neurotrophic factor (BDNF), glial cell line-derived neurotrophic factor (GDNF), nerve growth factor (NGF), ciliary neurotrophic factor (CNTF), and other neuropeptides. Neuropeptides are used by neurons to communicate with each other.

Cerebrolysin interacts with several pathways of intracellular signal communication. The cellular integration of these peptide signals results in the observed neuroprotective and neurorestorative effects. Cerebrolysin therapy is safe and well-tolerated by patients.

From a scientific perspective, these pathways regulate on a molecular level the cellular processes of neurogenesis, angiogenesis, dendrite arborization, axonal sprouting, myelination, and remodeling of the neurovascular unit, thereby supporting the maintenance and repair of the neuronal network in the brain.

Cerebrolysin has been proven to have a powerful, neurotrophic activity similar to nerve growth factors that promote peripheral and central neuronal stimulation. It improves efficiency within the brain's aerobic metabolic processes and enhances intracellular peptide synthesis. Cerebrolysin supports the brain's ability for self-repair by stimulating neuro-recovery.

The potent, neuroprotective properties of Cerebrolysin help to shield neurons from metabolic acidosis, to prevent the formation of free radicals and protect against oxidative stress in the central nervous system (brain) and peripheral nervous system, and to decrease the neurotoxic action of certain amino acids and other environmental toxins.

Research has shown that it may reduce the neurodegenerative pathology in Alzheimer's disease (AD), post-stroke, and post-acute traumatic brain injury. Significant improvement of the cognitive

function of patients on Cerebrolysin has been observed.

Cerebrolysin is used for the treatment of ischemic and hemorrhagic stroke, traumatic brain injuries (TBI), different forms of dementia (vascular dementia, Alzheimer's disease), and cognitive disorders, and to prevent cognitive decline after brain injuries. It prevents the formation of toxic protein aggregates (amyloidosis) and lowers the level of inflammatory processes in the brain, both linked to neurodegeneration.

Empirical observations by integrative medicine physicians using Cerebrolysin therapy for their patients with chronic pain syndromes have shown that it can provide significant, lasting, pain relief, when appropriately administered, for chronic pain due to arthritis, autoimmune disorders, peripheral neuropathy, and post-infectious, post-traumatic, and post-surgical injury to the nervous system.

Benefits of Cerebrolysin may include the following:

- Improved mental function and memory
- Protection of the brain from oxidative stress
- Protection of the brain from damage by toxins
- Helps repair the brain and nerves after injury
- Useful for treatment of different forms of dementia, cognitive disorders, stroke, TBI
- Prevention of cognitive decline after any brain injuries
- Helps relieve chronic pain in many different conditions: diabetic neuropathy, metabolic neuropathy, toxic and post-traumatic neuropathy

**Thymosin Alpha-1**

Thymic peptides, which are naturally produced in the thymus gland, promote physiological processes that include modulation of immune responses – i.e., both stimulation or suppression when needed – and can aid in the treatment of chronic, bacterial, viral, and fungal infections. They also help promote the regulation of cell motility, neuroplasticity (ability of the brain to form and reorganize neural synaptic connections, esp. in response to learning or experience or following injury), angiogenesis (new blood vessel growth), repair and remodeling of blood vessels, heart cells, and other injured tissues, as well as stem cell differentiation.

Benefits of thymosin alpha-1 may include the following:

- Increases immune cell activity
- Corrects immune system dysfunction
- Normalizes immune system balance and response
- Stimulates T-lymphocyte and natural killer cell production
- Promotes the development of B-lymphocytes into plasma cells
- Decreases production of pro-inflammatory cytokines
- Increases chemotactic response and phagocytosis by neutrophils
- Improves host defenses to infection
- Inhibits viral replication
- Improves tissue repair and healing
- Reduces and normalizes inflammation
- Improves stress tolerance
- Improves microcirculation
- Improves cancer defenses
- Increases antioxidant and glutathione production
- Reverses immunosuppression in chronic fatigue syndrome, fibromyalgia, and Lyme disease

Signs of low thymosin alpha-1 levels include the following:

- Chronic fatigue, physical exhaustion, tired appearance, lack of motivation, apathy
- Chronic infections (colds, herpes, hepatitis, shingles, Lyme, and other severe infections)
- Persistent illness, lack of full recovery, e.g., recurrent bouts of 'flu-like' symptoms, chronic fatigue immune deficiency syndrome (CFIDS)
- Easily injured joints, ligaments, tendons, and muscles with slow recovery
- Chronic pain and disability after musculoskeletal trauma
- Slow, difficult, and incomplete wound healing

**Thymosin Beta-4**

This is another thymic peptide, which naturally occurs in all human cells but is found in higher concentrations in areas of damaged tissues. It has potent, anti-inflammatory properties and helps to promote collagen repair and regeneration in the skin and soft tissues, as well as hair growth. It also works with thymosin alpha 1 to support the immune system.

Benefits of thymosin beta-4 may include the following:

- Potent, anti-inflammatory for wounds, involving the muscles, joints, and skin
- Helps to support stem cells to heal and regenerate injured tissues
- Helps to promote rapid wound healing with little to no scarring
- Enhances fibroblast cell activity and collagen deposition
- Helps to prevent the formation of adhesions and fibrous bands in injured tissues, esp. in muscles, ligaments, tendons, joints, and skin
- Protects and restores neurons in post-traumatic brain injury (TBI)
- Helps to reduce acute or chronic pain and inflammation
- Helps to promote improved flexibility of the body
- Promotes hair growth and darkening of gray hair

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# "Adrenal Fatigue": Does It Exist?

## by Alfred V. Zamm, MD

> "Despite the fact that the patient was seen by the best medical minds in Europe – he survived."
>
> Voltaire (1694-1778)

This is a single case report, a description of how dental mercury interfered with a patient's defense mechanism against an infection (primary atypical pneumonia) and permitted the infecting organism to persist as a lifelong intracellular denizen resulting in symptoms that would not be readily connected to the original infection, symptoms that included those of hypoadrenalism, yet without measurable adrenal failure. This report describes the measures taken to diagnose and mitigate this illness.

K had been lied to: He had been made ill as a result of egregious medical deceptions. The following is an account of K's medical odyssey, an adventure that involved a series of scientific medical reports, clinical observations, anamnesis, anecdotes, and conjectures describing how he was rescued from medical misinformation – and survived.

When K was 13, the first deception occurred: he received an "amalgam" dental filling (dental amalgam contains 50% mercury, a poison). As a result of K's constant exposure to the mercury emanating from this and later fillings and its bodily accumulation, he was sick for the rest of his life (allergies, asthma, migraine headaches, fatigue…). It took 30 years, more amalgam fillings, a variety of physicians, and his determination before the diagnosis of mercury poisoning was finally made.[1-7]

Not only is mercury poisonous directly to the metabolic process, it also combines with the essential trace element selenium, thus depriving the body of selenium and its function in the defense enzyme glutathione peroxidase (a defense against tissue hydrogen peroxide).

It defies credibility that licensed dental professionals, the dental and medical professional organizations, and the Food and Drug Administration (both dental and medical divisions) allow the prescribing of mercury, a known poison. This is a gross abrogation of responsibility by all of these professional organizations acting in unison as a cabal of professional miscreants foisting a toxic substance on a trusting public – a public that doesn't have the technical knowledge to defend itself – and telling them a poison is not a poison.

**Root Canals**

The next deception consisted of more professionally prescribed poison: the insertion of two "root canals" that further degraded K's health.

Root canals have at least three health problems: (1) they are very frequently (always?) infected, and hence a source of microbiologically derived cytotoxic and immune dysregulating substances; (2) they are endodontically executed using xenobiotic and cytotoxic substances that are potentially immune dysregulating; and (3) I question whether there has been adequate scientific proof (double blind crossover studies) of the safety of the materials used in the "root canal" (endodontic) procedure.[8-22]

**Trying to Help**

*Dental help*: I advised K to have the mercury-containing fillings removed and replaced with biologically inert materials, first with gold, which resulted in some improvement. The gold was then replaced with non-metallic, non-electrically conductive zirconium, when dental zirconium became available; zirconium provided further improvement. I additionally advised K to have his two "root canalled" teeth extracted and replaced with zirconium dental bridges. More improvement ensued but still not a restoration of his original health.

*Chemical help*: I advised K to take *inorganic* selenium in the form of sodium selenite solution (Allergy Research Group). Only the *inorganic* form of selenium and not the organic form has the chemical ability to substantially bind and inactivate mercury; this provided K with further benefit. Note: Regarding the ambient, unavoidable environmental pollution by cadmium, arsenic, and some other toxic heavy metals, selenium is also protective against these toxic metals.

Selenium also happens to be a nutritionally essential trace element whose only known enzyme function in the human body is its role in the detoxification process of glutathione peroxidase (*vide supra*).

A reader of the *Journal of the American Medical Association* asked: Since tuna, being predatory fish at the top of their food chain, and as a result have a high level of mercury in their tissues, why don't they get sick? The expert replied: In addition to accumulating mercury, tuna accumulate selenium in a molecular ratio of 1:1 with mercury, and this is an amount sufficient to negate mercury's ability to be toxic to the tuna.[23] (Nature figured out that selenium is safe and effective in protecting life against mercury poisoning.)

This inorganic form of selenium is innocuous and salubrious at a daily dose of 60 mcg. (micrograms) (1 ½ ml.) per day when taken on an empty stomach (*vide infra*) and is irreplaceable in its ability to benefit patients who have been poisoned by mercury. There is no equivalent substitute for it.[24-27] The sidebar contains

an instructional form that I have provided to patients in conjunction with my prescribing selenium. Readers are welcome to employ it.

*Infection as a Pernicious Force in K's Health.* K had contracted primary atypical (non-streptococcal) pneumonia in his mid-20s. Primary atypical pneumonia is commonly caused by intracellular organisms (e.g., viruses or Chlamydia) or extracellular organisms (e.g., Mycoplasma).

K's immune system had been weakened by mercury (mercury lowers the T-cell count).[28] Rather than completely vanquishing the invading microorganism, as might have happened with a healthy defense mechanism, K's impaired mercury-poisoned immune system could not prevent the infecting microorganism from establishing itself as a persistent subclinical intracellular lifelong troublemaking denizen.

K had objective evidence of a chronic subclinical infection: he had developed chronically swollen lymph nodes (lymph-adenopathy) after his encounter with primary atypical pneumonia.

More clues supporting a diagnosis of a chronic lifelong infection: Throughout his life, K had taken various antibiotics for miscellaneous infections, each episode of antibiotic consumption was followed by a temporary minimal improvement of his symptoms. Once, he received a smallpox vaccination, which was also followed by temporary minimal improvement of his symptoms. These therapies had two temporary benefits: (1) The antibiotics temporarily lowered the load on K's already microbiologically burdened immune system; and (2) The smallpox vaccination temporarily raised the activity of his immune system. Clinically, it appeared that a persistent subclinical residual infection was an operative force in K's lifelong illness and his symptoms of hypoadrenalism among other symptoms.

Intracellular microorganisms can hide behind a cell membrane and become invisible to the immune surveillance system, persist for the life of the victim, induce a pernicious inefficiency into cellular metabolism, and result in an elusive variety of protean clinical manifestations often not connected to the instigating surreptitious occult culprit. Some examples of this dynamic are the following:

1. Cardiovascular disease and microorganisms (viruses or bacteria)[29,30]
2. Diabetes II and Hepatitis C virus[31]
3. Hypothyroidism and Hepatitis C virus[2,33,34]
4. Cancer of the cervix and Human Papillomavirus[35]
5. Cancer of the oral cavity and Human Papillomavirus[35]
6. Crohn's disease and Herpes simplex virus I and II[36]
7. Food allergies[38]

The following essential digression is taken to share with the reader a remarkable revelation in regard to reference 36 in number 6, listed above, (U. Rüther et al) and intracellular organisms that have surprising clinical outcomes: the authors of this article recount how their patient was rescued from imminent perilous surgery for Crohn's disease and the induction of sustained subsequent benefit by prescribing a simple generic, inexpensive, readily available, anti-viral medication, acyclovir – a disease for which this medication is not a designated use. This article supplies an explanation for the mechanism by which acyclovir resulted in this remarkable and first recorded benefit for a Crohn's disease sufferer. I suspect that acyclovir may also be effective in ulcerative colitis and other diseases, associations yet to be revealed. (A trial of acyclovir with K was inconclusive, as K did not tolerate acyclovir and it had to be discontinued.)

Parenthetically (another digression), the essential amino acid L-lysine (not mentioned in the article) might have additionally benefited this patient with Crohn's disease, as it competitively inhibits arginine, an essential nutrient for the replication of herpes virus I and II.[37] (A trial of L-lysine with K was inconclusive.)

Infections from microorganisms can also play a role in *food allergies*.[38] It is conjectured that chronic infection reduces the magnitude of the electrical charge (voltage) on the secretory IgA molecule, which sits on the surface of the gastrointestinal membrane; this reduction in voltage will permit food allergens to gain entry into the body and induce the development of allergies.

*Nutrition*: K was prescribed a nutritional improvement program (foods, vitamins, minerals); some improvement ensued, yet his problems persisted.

*K's Environment*: His household environment was improved.[39] More benefit ensued, but recovery did not occur.

*Prophylactic Anti-inflammatory Therapy*: Aspirin (one-quarter of the standard 325 mg. tablet [approximately equal to 81 mg.]) was prescribed on a daily basis to mitigate inflammation from the conjectured chronic infection; the aspirin was substantially beneficial on a long-term basis. The frequency of this dose of aspirin, 81 mg., was raised to a daily dose from the less frequent dose mentioned in the referenced article, and the suggested addition of calcium carbonate for alkalization to mitigate the acidic effect of aspirin was found to be counterproductive and was eliminated because the aspirin was taken with a meal (the calcium carbonate's lowering of the stomach acid is deleterious to the digestive process).[40]

*Other Opinions*: In consideration of K's recalcitrant and unresolved affliction, I advised him to obtain more opinions by conferring with board-certified internists of professorial rank. These professors did fine investigations and all the findings were reported as being "within acceptable statistical range;" and there were no recommendations for treatment. The examinations and tests were "healthy"; the patient was not.

**A Big Clue**

K reported that he craved and was clinically benefited by ingesting green leafy vegetables (even though he employed a program of sufficient and salubrious foods, vitamins, and minerals). This craving wasn't just a minor craving; he bought pounds of all sorts of green leafy vegetables, used a kitchen blender to grind them into a slurry, which he then boiled down to a concentrate. This green super food worked: he felt remarkably improved – but why did it work?

**An Epiphany**

One day, while I was mulling over K's idiosyncratic green-leaf craving, a graphic picture of the chemical structure of chlorophyll vividly appeared in my

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## Adrenal Fatigue

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mind: a complex molecule assembled from four pentagons, and each pentagon was composed of carbon and nitrogen – all four of these structures were symmetrically arranged around a single central atom of magnesium, similar to the four sails of a windmill around a central point.

What if K was not craving chlorophyll *per se* but was craving the centerpiece of the chlorophyll molecule, the magnesium? Yes, he had had tests of his *serum* magnesium and his red blood cell magnesium (both of these are tests of *extracellular* magnesium); both results were "within a statistically acceptable range," but what did these results really mean? Was this another medical deception – more healthy test results about an unhealthy person – or did K really have an *intracellular* hypomagnesium state, a condition inside the cells that these tests could not measure? Were these *extracellular blood tests* accurate only about the outside of the cell but were misleading about the inside of the cell?

Interesting fact: Only 1% of the body's magnesium is *outside* of the cells – the rest (99%!) is inside the cells where it

# How and Why to Use Selenium

Some chemically sensitive and mercury-poisoned patients improve with the use of selenium. The response to the use of selenium can be divided into three clinical groups.

GROUP 1: They experience immediate benefit within the first few days. These patients feel better, stronger, and are more tolerant of xenobiotic chemicals.

GROUP 2: They improve slowly. These patients may not be aware of their slow progress until they realize that they can tolerate tobacco smoke and other xenobiotic exposures without deleterious results. Their symptoms decrease gradually in duration and magnitude.

GROUP 3: They initially react in an apparently *unfavorable* way. These patients are generally the most sensitive, the most debilitated, and those most in need of selenium; but they are initially unable to deal with it. It takes longer for these patients to receive benefit. It often can take these ultrasensitive patients up to six months of being free of their mercury fillings before they start to tolerate and benefit from selenium. At that point they find that they can begin to increase the amount of selenium they are taking. This may be because selenium combines with heavy metals, forming compounds that these sensitive patients may not tolerate.

Selenium is not a medicine. It is not a prescription item. It is an *essential nutrient* and is sold over the-counter. It is found in many over-the-counter vitamin preparations. The difference between taking selenium in a chemically pure liquid form and merely taking a selenium tablet or selenium mixed with other vitamins and minerals is that by taking selenium in solution, considerably more selenium is absorbed.

Selenium is needed in very small amounts. This means that other minerals, which are found in relatively huge quantities when compared with the amount of selenium present, "overwhelm" the absorption of the small amount of selenium, and the patient who takes selenium in a tablet form or in a vitamin-mineral mixture or with food is able to obtain very little of the selenium he swallowed.

Selenium must be taken on an *empty stomach.* Other substances found in foods bind to selenium and prevent its absorption.

*Selenium is essential for everyone, but it is especially important to patients who have difficulty dealing with environmental xenobiotics and are mercury-poisoned from dental fillings.*

1. Selenium binds with and neutralizes poisonous heavy metals found in the environment such as mercury, arsenic, and cadmium; this is especially helpful in regard to the mercury that leaches out of dental fillings.
2. Selenium is an essential part of the xenobiotic (harmful chemical) detoxification system:
   (a) Selenium is part of glutathione peroxidase, an important enzyme that the body uses to detoxify harmful chemicals.
   (b) Mercury leaching out from dental fillings produces another problem in addition to supplying mercury as a poison. *Mercury binds with selenium, thus depriving the patient of available selenium.* The patient becomes "selenium starved" and can no longer manufacture adequate amounts of glutathione peroxidase. Supplying selenium overcomes this problem.

**How to Take Selenium Solution**

*Remember: Always take selenium solution on an empty stomach!*

Transfer some selenium solution from the stock bottle you purchased at the pharmacy into the glass dropper bottle using a plastic funnel. Do not use a metal funnel, as it may react with the selenium.

For GROUPS 1 and 2: When you get up in the morning:

1. Dissolve the drop(s) (see below) in 2 oz. water
2. Drink the selenium solution before you swallow any food or take any vitamins or medication
3. By the time you are ready to have your breakfast (after 5-10 minutes) you will have absorbed a good deal of the selenium, without the interference or neutralization by any stomach contents.

**Suggested schedule for Groups I and 2 to take selenium**

Before Breakfast

| | |
|---|---|
| Day I | I drop |
| Day 2 | 2 drops |
| Day 3 | 4 drops |
| Day 4 | 7 drops |
| Day 5 | 9 drops |
| Day 6 | 11 drops |
| Day 7 | 13 drops |
| Day 8 | 15 drops |
| Day 9 | 17 drops |
| Day 10 | 20 drops |
| Day 11 | Before breakfast<br>Take 1/2 dropperful<br>+ 1/2 dropperful<br>+ 1/2 dropperful |

(A total of 1 1/2 droppers. Using 3 half droppersful is more practical than trying to fill a dropper completely, as the air trapped in the glass tube in the dropper may prevent complete filling.)

*On Day 12 and each morning thereafter*: Continue at this dose – you will have reached the daily maintenance dose.

For GROUP 3: The patients in Group 3 (the most sensitive patients), should increase the dose very slowly; it may take weeks to months to substantially increase the daily dose, and they may never achieve a full dose.

**Addendum**

Even on small doses of selenium, some patients with arthritis become symptom-free. (Veterinarians have used selenium to treat arthritis in dogs for years.)

Selenium is protective against cancer.

**Some references:**


Willett WC et al. Prediagnostic serum selenium and risk of cancer. *Lancet* Il. July 16, 1983; 130-4.

Shamberger RJ and Willis CE. Selenium Distribution and Human Cancer Mortality. *Critical Reviews in Laboratory Sciences*. June 1971; 2:211-21.

Shamberger, R. Relationship of Selenium to Cancer: Inhibiting Effect of Selenium on Carcinogenesis. *Journal of the National Cancer Institute*. April 1970; 44:931-36.

cannot be measured by tests available to the practitioner. Over 300 metabolic reactions depend on magnesium (magnesium is not only important, it is critical). To say "everything runs on magnesium" would be close to the truth.

Based on the magnitude of K's idiosyncratic green leaf cravings and despite his "healthy" tests for extracellular magnesium, I suspected that K really did have low *intracellular* magnesium, and I owed it to K to make a diagnosis one way or the other. Since we have established that I couldn't measure the magnesium level *inside* of K's cells, how was I to determine the truth of K's situation?

I prescribed a test of K's actual in vivo magnesium status, the so-called "therapeutic trial." This involved K taking magnesium in a controlled stepwise living test and observing what clinically occurred. K's health dramatically improved when he took magnesium; his green-leaf craving ceased, he stopped being a "chlorophyll chef," and another deception was revealed (the false assumption about his intracellular magnesium status based on conventional magnesium testing).

Note: The symptoms K had that are conventionally associated with hypoadrenalism (*vide infra*) became mitigated or disappeared when he continued taking magnesium – yes, magnesium is involved with everything (almost).

I suspected that the organism of K's conjectured intracellular infection, acquired via his primary atypical pneumonia episode, was the metabolic burden that was impeding his internal chemistry and inducing symptoms similar to those of hypoadrenalism (among other symptoms); the therapeutic addition of magnesium compensated for this microbial burden, thereby mitigating K's symptoms.

**How Magnesium Titration Was Done**

K was initially prescribed magnesium as magnesium gluconate starting with a daily dose of 50 mg of elemental magnesium b.i.d., p.c. Then the magnesium dose was incrementally raised every day by 50 mg. of elemental magnesium b.i.d., p.c. It wasn't until he received the daily dose of 400 mg. of elemental magnesium (200 mg. b.i.d., p.c.) that his health subjectively *started* to improve.

The magnesium titration is very safe when one follows this titration protocol; the end point is the dose that produces sufficient clinical benefit or the first appearance of slight diarrhea. At this point the practitioner should stop raising the daily dose, reduce the daily dose, and future dosage should be guided by ongoing clinical observations. Magnesium is connected to the absorption and metabolism of potassium (another element found in higher concentration *inside* the cell than outside the cell). K was prescribed 80 mg. of elemental potassium as potassium gluconate b.i.d., p.c. Magnesium is also connected to the absorption and metabolism of other minerals. (This connection between magnesium and other minerals is a story that I will have to leave for another article.)

**A Medical Detective Story**

I decided to move the investigation forward by collecting a list of clues, i.e., signs and symptoms, and to write them down in a manner of a detective collecting notes at a crime scene. Here are my crime scene notes.

*Clue #1, K's tan*: K's face had an unexplained "tan"; even in the winter, he would often be complimented on his healthy-appearing "winter tan" and would be asked if he had recently returned from a vacation in Florida or the Caribbean.

*Clue #2, Salt craving*: K reported that once, while eating a porkchop he, being distracted, had "breaded" the pork chop with a layer of salt so generous that the pork chop had acquired a saline carapace, a pork chop that he nevertheless enjoyed eating in its hypersalinated state. K enjoyed eating heavily salted foods; he was a salt craver.

*Clue #3, Low blood pressure*: K had low blood pressure. He would become *more* tired after he had laid down to rest (a drop in blood pressure) than he was before he had "rested" – counterintuitive. "Dizziness and unsteadiness" would occur if he arose rapidly from a supine position (orthostatic hypotension). His blood pressure measurements were always at the lower end of acceptability.

*Clue #4, Fatigue*: Easy fatiguability on exercise and chronic moderate fatigue

*Clue #5, Faulty glucose metabolism*: Episodes of hypoglycemia.

*Clue #6, Hypocholesterolemia*: Hypocholesterolemia can be found in true hypoadrenalism; K's cholesterol level was at the low margin of statistical acceptability.

Any third-year medical student would have said, "Mr. K, you have hypoadrenalism." The student would have been right (the symptoms) but wrong (the disease) – *vide infra*.

On the basis of these assembled clues, I referred K to a Harvard Medical School professor of endocrinology who specialized in and wrote definitive articles about adrenal disease. The professor did a fine comprehensive investigation, including the requisite standard test to measure how well his adrenal glands functioned: the provocative test of the adrenal glands using an ACTH-like substance, Cortrosyn (Organone Pharmaceuticals). Cortrosyn is the synthetic active portion of the adrenocorticotropic hormone (ACTH molecule) that is composed of 24 amino acids rather than the actual whole ACTH molecule, which is composed of 39 amino acids (this smaller molecule acts faster and is less allergenic). K's *bete noire* reappeared: the test result was reported as within the statistically acceptable range, the summation of the professor's evaluation was that K's overall health was without objective evidence of pathology, and once more K was not sick and sick at the same time.

Despite this excellent professorial investigation certifying K's objective good health, still K *did* have symptoms similar to those found in hypoadrenalism, and his illness had not been explained by this revered professor. My next step: Get another opinion about the first opinion. I sent him to another full professor of endocrinology at another prestigious medical school where K had another fine and erudite medical investigation, and he received another authoritative report confirming that the tests of his adrenal glands and all other tests were within the statistically acceptable range; he was once more without objective evidence of medical pathology.

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All of these fine physicians, their comprehensive tests, and their venerable academic analyses did not advance my knowledge of K's illness, but at least these investigations did rule out actual hypoadrenalism.

**A Microbial Hypothesis**

The etiology of K's *symptoms* of hypoadrenalism, "adrenal fatigue," appeared to have nothing to do with "adrenal," but rather appeared to be due to a metabolic defect induced by a chronic microbial intracellular denizen that resulted in some of the symptoms of hypoadrenalism but without actual hypoadrenalism. In this regard, one or more of the following three etiological possibilities help me to think about the etiology of K's condition:

1. An infection-induced defect in the cell's glucocorticoid receptor so that when cortisol alights upon it, an impaired signal is generated by the receptor that in turn distorts the targeted metabolic process.
2. An infection-induced epigenetic defect (a genetic lesion) that results in an impairment of the genetic control mechanism of cellular metabolism.
3. An infection-induced direct interference in metabolism.

**Summary of the Ameliorative Therapies That K Received**

The removal of poisons (mercury-containing amalgam dental fillings, root canals), the neutralizing of some of the residual mercury with selenium and selenium-aided repletion of glutathione peroxidase, a raising of K's intracellular magnesium and intracellular potassium to compensate for the infection-induced burden on K's metabolism, a nutritional program, an improvement of K's environment, and the use of prophylactic aspirin – altogether allowed K to at least deal with his apparent microbially induced metabolic inefficiency and permitted him to function substantially more efficiently.

The author reports that he does not have any conflicting interests.

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# Protecting Your Brain from Stress – Part 1


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**Abstract**

This two-part series focuses on integrative treatments that can bring improved regulation to the stressed brain. Concepts from stress research, i.e., allostasis, allostatic load, and allostatic overload, are defined and referred to within the article's chronic stress framework so as to enumerate treatments that mobilize allostatic systems to improve brain and psychological health, as well as physical health. The treatments advocated include natural health products to lower the intensity of emotional overwhelm and to reduce the pathophysiological harms to the brain and body. Other recommended treatments include diet, exercise, nature, meditation, sleep, the avoidance of substances, psychotherapy and/or social support, as well as an assortment of psychological and behavioral recommendations. The integrative approaches, such as those mentioned in this article, should serve as models of the kinds of interventions that can realistically and dramatically affect the course of chronic stress and prevalent medical diseases via allostatic brain mechanisms.


**Introduction**

When the brain is stressed, the limbic system (i.e, includes the amygdala, hippocampus and other brain structures) seems to dominate the prefrontal cortex (PFC). A functional disconnection between these brain areas ensue, such that the PFC cannot effectively modulate emotions and attenuate the resulting stress response.[1] When this becomes an enduring problem, as happens from chronic stress, many pathophysiological impacts result, including mental morbidity, psychiatric illness, and medical disease (Table 1 provides an explanation of the common terms used in this paper).[1]

Given the inherent challenges to working with chronically stressed patients, it is imperative that treatment aims to restore their biological regulation. First, a thorough clinical evaluation needs to be done to rule-out diseases that would continue to wreak havoc unless properly treated. Then, various therapeutic interventions should be used to mitigate the psychological and physical harms accrued from being chronically stressed. This article will describe numerous integrative treatments that target allostatic mechanisms within the brain, and also other physiological systems when needed, to increase patients' quality of life (i.e., healthspan), and maybe even longevity (i.e., lifespan).

**Using Natural Health Products to Lessen the Impacts of Chronic Stress**

The conventional approach involves pharmaceutical intervention, which can be extremely helpful and potentially lifesaving. In their article discussing stress- and allostasis-induced brain plasticity, McEwen and Gianaro stated the ➤

**Table 1: Definitions**

***Allostasis:*** Coined by Sterling and Eyer,[2] refers to biological adjustments that allow an individual to adapt to particular challenges that happen over the lifespan. Adapting to such challenges demands the synchronous though non-linear activation of many different physiological processes, such as neural, neuroendocrine, and neuroendocrine-immune mechanisms.[3] Allostasis begins with the brain and happens or is instigated by how an individual perceives and interprets any given situation. Allostasis is about adaptation, but the physiological adaptations may not ensure survival because they can become deleterious over time and cause irreversible damage.

***Homeostasis:*** Is about ensuring survival, and refers to "physiological parameters like blood oxygen and pH" that are "maintained within a narrow range" (p.37).[3]

***Chronic stress:*** Defined as "ongoing demands that threaten to exceed the resources of an individual in areas of life such as family, marriage, parenting, work, health, housing, and finances," p.638).[4] In physiological terms, chronic stress refers to a "pathological state that is caused by prolonged activation of the normal acute physiological stress response, which can wreak havoc on immune, metabolic, and cardiovascular systems" (p.56).[5] When an individual is faced with chronic stress, which is common among most psychologically distressed patients, it may seem enduring and without a clear ending.

***Allostatic load (AL), and allostatic overload* (AO):** AL represents body degradation that results from repeated allostatic responses during stressful situations.[6] This results when an allostatic system fails to habituate to the recurrence of the same stressor, fails to shut off following overwhelming stress, and/or whose response is deficient resulting in heightened activation of other, normal counter-regulatory systems.[3,7] AO is thus an extension of AL, which often results in irreversible damage to body organ systems, and/or mental illness. Thus, unmitigated chronic stress that results in AL and AO will typically cause all sorts of psychological distress signals, especially among individuals vulnerable to mental illness.

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following in reference to pharmaceutical interventions:

> Sleeping pills, anxiolytics, beta blockers, and antidepressants are all used to counteract problems associated with allostatic overload. Likewise, drugs that reduce oxidative stress or inflammation, block cholesterol synthesis or absorption, and treat insulin resistance or chronic pain can help deal with the metabolic and neurological consequences of chronically stressful experiences. All of these agents have value, but each one has side effects and limitations that are based in part on the fact that all of the systems that are dysregulated in allostatic overload interact with each other and perform normal functions when properly regulated (pp.439-440).[8]

Similar to pharmaceutical interventions, natural health products (NHPs) can be used to attenuate AL and AO. They are often of great importance to patients because they typically possess fewer adverse effects compared to pharmaceutical interventions. Many NHPs can be safely integrated with standard approaches or can sometimes be used as an alternative. NHPs can be used to modulate the activity of the PFC and/or limbic system to presumably improve the functional connection of these brain circuits, thereby, assisting the PFC with improved top-down control and processing, and/or attenuating limbic activity to dampen bottom-up control. NHPs can also mitigate pathophysiological harms from AL and AO, such as high blood pressure, insulin resistance, and other medical problems.

Information known about pharmaceutical interventions can be extremely helpful when postulating how NHPs assist with improving PFC and limbic functionality and connectivity. The essential aim of a modern treatment strategy is to deconstruct the psychiatric illness in question, then consider a treatment or set of treatments that hypothetically improves or attenuates malfunctioning neurocircuitry by targeting specific neurotransmitters in that circuit, which then relieves symptoms and improves overall functionality.[9] Antidepressant medications are good examples of pharmaceutical interventions that possess specific pharmacological effects to modulate implicated neurocircuits. They can increase the availability of serotonin and other monoamines between the synapses of neurons. The release of serotonin at target neurons, for example, activates receptors that are widely expressed in the hippocampus, amygdala, and PFC, and which mediate fear, anxiety, stress, and cognitive function.[10]

Antidepressants also increase brain-derived neurotrophic factor (BDNF) expression, which is believed to be responsible for the time lag prior to an antidepressant response, since it takes several weeks for the pharmacological actions to augment the expression of BDNF.[11] Antidepressants may help to compensate for the levels of BDNF in specific brain areas (i.e., the PFC and hippocampus) that are presumed to be insufficient as a consequence of chronic stress.[11]

Depression is also associated with perceiving social cues as more negative, including the tendency to focus on more aversive information, and even recalling more "negative than positive information about oneself" (p.4).[11] Antidepressants can reverse this core psychological process, known as ***negative affective bias***, by increasing the processing of positive affective information.[11]

**Table 2. NHPs that putatively possess therapeutic effects similar to antidepressant medication**

| *Treatment* | *Suggested Daily Dose* | *References* |
|---|---|---|
| 5-HTP (timed- or sustained-release formulations) | 400-1200 mg | 13,14 |
| Acetyl-L-carnitine | 1000-4000 mg | 15,16 |
| Chamomile extract (1.2% apigenin) | 500-1500 mg | 17,18 |
| Curcumin extract (BCM-95) | 1000 mg | 19,20 |
| *Rhodiola rosea* extract (3% rosavins and 1% salidroside) | 300-1360 mg | 21-23 |
| Saffron extract | 30-100 mg | 21,24 |
| SAMe | 1600-3200 mg | 25,26 |
| St. John's wort extract (0.3% hypericin) | 900-1800 mg | 27,28 |
| Theanine | 200-400 mg | 29,30 |

The chronic stress of depression is also related to an increased amount of extracellular glutamate within the brain, which contributes to excitotoxic damage.[11] There is reason to believe that antidepressant treatment can act as glutamatergic modulators and attenuate excitotoxic damage though more studies are certainly needed.[12]

Overall, these specific effects resulting from antidepressant use should be capable of modulating the implicated brain circuits to reduce symptoms of emotional overwhelm, improve functionality, and lessen the pathophysiological effects of AL and AO. The same logic about antidepressants can also be extended to specific NHPs (Table 2) that possess mechanisms of action that: (1) augment serotonin or other monoamine neurotransmitters; (2) augment BDNF expression; (3) increase the processing of positive affective information; and/or (4) attenuate glutamatergic excitotoxicity. The majority of the published data on these specific NHPs were derived from clinical trials, though some systematic reviews and meta-analyses were also referenced. All of these NHPs have an adverse effect profile that is superior to antidepressants. Extracts of St. John's wort and *Rhodiola rosea* should not be combined with antidepressant medication. Though it is sometimes clinically valuable, ongoing clinical vigilance is advised when combining 5-hydroxytryptophan (5-HTP) or S-adenosylmethionine (SAMe) with antidepressants.

Anxiety or anxious feelings are other target areas of pharmaceutical interventions that differ from antidepressants. Reducing anxiety is an obvious and helpful component when mitigating the AL and AO that accompanies chronic stress. Commonly prescribed treatments are the benzodiazepines that should be reserved for short-term use, but are taken chronically by numerous anxious patients. All benzodiazepines target the benzodiazepine-binding site in the brain located on the chloride channel. They boost the effects of gamma-aminobutyric acid (GABA) on the frequency of the opening of the chloride channel, culminating in a hyperpolarization of the target cell, a decrease in the firing rate of these neurons, and pharmacological effects that include muscle relaxation, lowered arousal, and sedation.[31] Benzodiazepines also modulate the

activity of the HPA axis by mitigating the effects of CRH,[32] and reduce the limbic response to anxiety.[33]

The problems with taking benzodiazepines long-term are well known, and include dependence, withdrawal-associated problems, and addiction. They also prevent the brain from creating new pathways of growth, which undermines a patient's ability to effectively manage and/or overcome their anxiety.[34] There are published reports, for example, that have documented reduced effectiveness of exposure-based treatment when patients are taking benzodiazepines, and clinical benefits from exposure-based treatment when patients are not taking them.[34] When a patient comes off benzodiazepine treatment, they will almost always re-experience the same anxiety that they had when they first initiated treatment because the cumulative benefits from treatment are very limited. This class of medication can, however, be beneficial when used as needed and very judiciously, or for brief durations of time (i.e., 2-4 weeks).

Given what has been noted about benzodiazepines, it makes sense to consider specific NHPs (Table 3) as alternative treatments since they have mechanisms of action that interface with the benzodiazepine-binding site and/or the GABA system, but without serious adverse effects and problems of addiction, dependence, and withdrawal. Moreover, these specific NHPs likely reduce HPA axis activation, and assist with top-down PFC processing by attenuating the limbic response to anxiety. Though they can be combined with benzodiazepines, these NHPs will potentiate the clinical effects of benzodiazepines, and in some cases may be contraindicated because of too much sedation. All the published data on these specific NHPs involve clinical trials and/or aggregated datasets involving large numbers of patients (i.e., more than several hundred), except for niacinamide, which only has lower quality evidence in the form of published case reports discussing its benzodiazepine-like effects.

The final component involves the clinical use of NHPs (Table 4) that work similarly to pharmaceutical interventions used to mitigate AO represented by high cholesterol (i.e., an abnormal cholesterol profile), metabolic-based diseases (e.g., insulin resistance and obesity), oxidative stress, inflammation, and/or chronic pain. All of these medical problems contribute immeasurably to the burdens of chronic stress and should be managed aggressively. Specific NHPs will be highlighted here though clinicians are certainly encouraged to consider many more NHPs when attempting to lessen the pathophysiological effects associated with AO, and the consequential increased morbidity and premature mortality that normally follows. These NHPs have a superior adverse effect profile compared to commonly prescribed pharmaceutical interventions (e.g., statins and metformin), but several of them (i.e., berberine, curcumin extract, and resveratrol) can sometimes cause symptoms such as gastrointestinal upset, flatulence, constipation, and/or nausea. The published data is strongest for berberine, pantethine, and palmitoylethanolamide, while both curcumin extract and resveratrol require more clinical trials, systematic reviews, and meta-analysis to better support the indications listed in the table.

**Using Lifestyle Modifications to Lessen the Impacts of Chronic Stress**

In this section, I will review numerous lifestyle modifications that can be recommended to patients suffering from the deleterious effects of chronic stress. All of these lifestyle modifications do not have to be done in their entirety to improve enduring problems associated with AL and AO, but certainly several of them can become part of a comprehensive plan aimed at lessening the biological and psychological impacts resulting from chronic stress. This won't be an exhaustive review but will instead highlight salient research linking lifestyle modifications with reduced stress, increased psychological and physical health, and when possible, implicated brain mechanisms.

*Diet.* There should be no dispute about the enduring and negative health impacts from nutrient-poor and carbohydrate-rich diets, which are notably high in energy density, contain too much sugar and saturated fat, are low in fiber, and are abundantly processed. This type of diet has contributed to the exponential rise in obesity and associated metabolic diseases like type 2 diabetes mellitus and non-alcoholic fatty liver disease.[83,84] Type 2 diabetes mellitus is also associated with psychiatric illnesses, such as depression, since they both likely have the same underlying inflammatory pathophysiology.[83] A high-fat diet has been associated with anxiety and anhedonic behaviors due to cascading effects that adversely impact synaptic plasticity and insulin signaling/glucose homeostasis, which result in increased cortisol levels and inflammatory cytokines.[85] Unhealthy eating in an adult population was shown to be associated with an increased prevalence of anxiety, depression, and stress.[86] In that same study, the data showed that an excessive intake of sweets and low consumption of dairy products was particularly associated with a higher prevalence of psychological and sleep disturbances.[86]

Based on what has been noted, it is rather obvious as to what constitutes a healthier diet. Recommending well-balanced meals that are rich in fruits, vegetables, and fiber, with adequate protein, healthy fats, low levels of sugar ➤

**Table 3. NHPs that putatively possess therapeutic effects that interface with the benzodiazepine-binding site and/or the GABA system**

| *Treatment* | *Suggested Daily Dose* | *References* |
|---|---|---|
| Ashwagandha extract (2.5-5% withanolides) | 1000-1800 mg (providing approx. 45-50 mg of withanolides) | 35-38 |
| Broad-Spectrum Micronutrients | 2-15 pills daily (depending on the recommended NHP) | 39-41 |
| Chamomile extract (1.2% apigenin) | 500-1500 mg | 42-44 |
| Holy Basil | 1000-1200 mg | 45,46 |
| Lavender extract | 80 mg or 160 mg | 47-50 |
| Niacinamide/Nicotinamide (i.e., amide form of vitamin B3) | 500-2500 mg | 51,52 |
| Passion Flower extract | 425-1275 mg | 53,54 |
| *Rhodiola rosea* extract (3% rosavins and 1% salidroside | 400-600 mg | 55-57 |
| Valerian root extract (0.8% valerenic acids) | 500-1500 mg | 58-61 |
| Theanine | 200-400 mg | 62-64 |

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and carbohydrates (i.e., limiting foods with a high glycemic index), and lower amounts of food (i.e., meaning calories), is something that should be advocated to all patients.[85] In terms of a specific dietary approach, a clinical trial used a ***modified Mediterranean diet*** to treat patients with major depressive disorder (MDD), and the results showed remission among 32% of the treated patients and an impressive number needed to treat of 4.1.[87] A less rigorous evaluation showed that an increased consumption of plant foods consistent with a Mediterranean diet were positively associated with physical function and general health, and with reductions in trait anxiety, depression, and perceived stress.[88]

Even though there isn't just one dietary approach that would ideally help all patients with chronic stress, recommending a dietary approach that is similar to a Mediterranean diet seems to be the best one to approximate. Of course, compliance will always remain an issue, but it possesses broad health benefits that appear to additionally improve mental health symptoms. With respect to brain changes, adopting a Mediterranean diet has not specifically been linked to changes in brain morphology though in one cited study positive effects were observed in plasma BDNF levels among a subset of participants (i.e., it attenuated reductions in plasma BDNF levels).[89] In a couple of systematic reviews and meta-analysis on adults, the Mediterranean diet was shown to improve a variety of cognitive parameters known as cognitive domain composites (i.e., global cognition, memory, and frontal cognitive domains),[89] and cognitive functions (i.e., delayed recall, working memory and global cognition).[90] Mechanistically, its benefits are likely attributed to anti-inflammatory, antioxidant, microbiome effects, the lowering of the glycemic load and advanced glycation endproducts, and increasing dietary fiber and specific micronutrients (e.g., omega-3 essential fatty acids and polyphenols).[89]

*Exercise.* Recommending regular exercise to all chronically stressed patients makes logical sense. It is certainly preferable that patients have some type of planned exercise each week to overcome the psychological and biological burdens associated with being sedentary and/or bored. There is published data demonstrating specific mental health benefits from exercise in being able to attenuate mental health symptoms, improve social connectedness and functionality, and augment personal empowerment. In a systematic review that evaluated the impact of regular exercise among people with severe mental illness, the results showed improvements that included mood, alertness, concentration, sleep patterns and even psychotic symptoms. Unsurprisingly, the data revealed that exercise contributed to improved quality of life "through social interaction, meaningful use of time, purposeful activity and empowerment" (p.48).[91] A comprehensive literature review also showed that a broad range of exercise types was associated with different outcomes, such as reduced mental health symptoms, improved functionality, and/or better concentration.[92]

The biological factors associated with the improvements from regular exercise include increased levels of monoamine neurotransmitters, beta-endorphins, opioids, endocannabinoids, neurotrophic factors, and even specific (yet helpful) pro-inflammatory processes.[92] Specifically, exercise induces the following neurochemical alterations: increased serotonin levels decrease anxiety; increased norepinephrine levels increase alertness; increased dopamine levels increase pleasure; and increased levels of opioids and endocannabinoids

***Table 4. NHPs that mitigate AO represented by high cholesterol, metabolic-based disease, oxidative stress, inflammation and/or chronic pain***

| Treatment | Primary Indication | Pharmacologic mechanisms of action | Suggested Daily Dose | References |
|---|---|---|---|---|
| Berberine | Cholesterol modification and insulin resistance | Insulin sensitization; increases glucose uptake; enhances glucose metabolism; stabilizes LDL receptor mRNA; and inhibits lipid synthesis within hepatocytes | 500-1500 mg | 65-68 |
| Curcumin extract (80-95% curcuminoids) | Chronic pain (i.e., joint arthritis), inflammation, oxidative stress, and insulin resistance | Down-regulates nuclear factor-kappa B; modifies proinflammatory cytokines such as interleukin production, phospholipase A2, cyclooxygenase-2, and 5-lipoxygenase; reduces tumor necrosis factor; reduces inducible nitric oxide synthase; protects against advanced glycation as well as collagen crosslinking; and inhibits osteoclastogenesis | 1000 mg | 69-73 |
| Pantethine | Cholesterol modification | Increases coenzyme A levels in cells; inhibits acetyl-CoA carboxylase and HMG-CoA reductase; and favorably modifies lipoprotein metabolism | 900 mg | 74,75 |
| Palmitoylethanolamide | Chronic pain (irrespective of etiology) | Acts as a congener of the endocannabinoid anandamide; agonism of peroxisome proliferator-activated receptor-α; inhibits the release of proinflammatory mediators such as cyclooxygenase, and inducible and endothelial nitric oxide synthase; reduces mast cell migration and degranulation; and reduces over-activation of astrocytes and glial cells | 1200 mg | 76-78 |
| Resveratrol | Inflammation, oxidative stress, and insulin resistance | Too numerous to note, but includes interactions with a large number of receptors, kinases, and other enzymes; and stimulates the activities of sirtuin 1 and adenosine monophosphate-activated protein kinase | 1000 mg | 79-82 |

increase euphoria and decrease anxiety. Additionally, neurotrophic factors such as BDNF and insulin-like growth factor-1 increase from regular exercise, and contribute to its experienced and durable benefits over time. Exercise also causes pro-inflammatory processes associated with durable benefits related to neurogenesis, angiogenesis and synaptogenesis.

Another biological model that explains the benefits from exercise involve a hypothesized mechanism known as ***transient hypofrontality***.[92] When a person exercises, the ensuing blood flow and energetic resources are diverted from the brain to motor activities. In doing so, there would be a transient hypofrontality because the brain's metabolic demands have been rightfully shifted. This has the net effect of attenuating psychiatric symptoms by temporarily deactivating involvement of the PFC (i.e., less hyperawareness, vigilance and attention), which then reduces the ensuing amygdala activation, resulting in less mental distress.

Psychologically, regular exercise can induce a variety of positive states of being that reduce symptoms of mental distress.[92] Exercise can result in a state known as ***flow,*** which is related to focused concentration, being in the moment, and experiencing feelings of reward. ***Self-efficacy*** is another benefit from regular exercise, and relates to feeling a sense of accomplishment. Exercise also increases social interaction, which is known to assuage mental distress.

Different types of exercise have been studied (e.g., yoga, walking, weight-lifting, and running), and all of them produce benefits when they are done consistently, and for adequate durations of time (i.e., at least 90 minutes each week).[92] Exercise that is of moderate to high-intensity has been shown to produce greater therapeutic effects at attenuating psychiatric symptoms.[92]

With respect to specific brain changes, it is known that the volumes of the hippocampus and medial temporal lobes are larger in adults with a high level of fitness, and that exercise increases hippocampal perfusion.[93] In a randomized clinical trial, 6 months of regular aerobic exercise was shown to increase the size of the anterior hippocampus, resulting in spatial memory improvements.[93] Specifically, exercise increased hippocampal volume by 2%, which reversed age-related loss in volume by 1-2 years. The increased hippocampal volume was also associated with increased serum levels of BDNF.

**Many natural health products can be safely integrated with standard approaches or can sometimes be used as an alternative.**

*Nature.* An obvious lifestyle treatment that enhances mental health is that of ***nature experiences***, which "includes individuals' perceptions and/or interactions with stimuli from the natural world (from potted plants and private gardens to more expansive public green spaces and wilderness, weather, and the movements of the sun) through a variety of sensory modalities (sight, hearing, taste, touch, and smell)" and that "can occur through conditions of 'real' (in situ) contact, window views, representations (e.g., landscape photographs), or simulations (e.g., virtual reality; p.2)."[94] Evidence supports enhanced psychological well-being, positive affect, increased happiness, positive social interactions, improved sleep, increased meaning and purpose in life, and reductions in stress (i.e., as per self-reported improvements, and/or improvements in various physiological measurements and biomarkers of acute and chronic stress) when engaging in nature experiences.[94] Other published data has shown improvements in working memory, cognitive flexibility, and attention control when being exposed to nature experiences.[95] Being in nature also increases ***hedonic well-being*** (i.e., feeling good and experiencing a sense of satisfaction), and ***eudaimonic well-being*** (i.e., meaning, autonomy, vitality, and feelings of transcendence).[96]

Several hypotheses have been proposed to explain the benefits of nature experiences and include the ***biophilia hypothesis*** (that we have an innate drive to be in nature), the ***stress reduction hypothesis*** (that there is a resultant physiological response that reduces stress levels), and the ***attention restoration theory*** (that nature reloads cognitive resources and re-establishes the capacity to concentrate and pay attention).[96]

Even though no direct published research was cited about nature experiences and brain mechanisms, it seems likely that increasing these types of exposures would enhance the functional connectivity between the cortico-limbic systems. Nature experiences should therefore be capable of providing protection against chronic stress by preventing (or moderating) decoupling between the PFC, amygdala, and hippocampus. ◆

**References and article are available 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.*

# Neural Therapy: Part of a Comprehensive Approach to Pain

by Jeff Harris, ND; Perry M. Perretz, DO; and Carolina Stephany Gonzalez, MD

*"Given the importance of the autonomic nervous system in health and disease, it is surprising how little attention it receives in medical education and practice. When the ANS is overreacting or underreacting, the question, 'Why?' is seldom asked."*

*Robert Kidd, MD*

Neural therapy classically involves the injection of local anesthetics into autonomic ganglia, peripheral nerves, scars, glands, trigger points, acupuncture points, and other tissues with the goal of balancing the autonomic nervous system. It takes advantage of the body's inherent electrical nature to relieve chronic pain and stress. Neural therapy is an important approach to the treatment of pain and many other conditions. This article will attempt to explain some the fundamental concepts of neural therapy, it's history, and application in the treatment of painful conditions. A quick clinical vignette may help introduce the subject.

A.N. hated doctors, with good reason. She'd had over twenty surgeries in her life, for everything from trigger finger to ulcerative colitis. appendectomy, hysterectomy, and cholecystectomy, among others. Her surgeons had all done admirable work, but she was riddled with pain throughout her body, and no one could find a way to relieve it with medications or exercise. During her first examination it was clear that her scars were acting as "interference fields" that limited her body's neurological equilibrium. The treatment of choice was neural therapy. After intradermal injections of her scars with 1% buffered procaine she nearly floated off the table with relief. Ranges of motion that had been limited for years returned almost instantly. Her pain was so greatly reduced that she changed her opinion of her doctors.

**History**

Neural therapy was first developed by the Huneke brothers, in Germany, during the first half of the twentieth century. As the story goes, their sister came to the office one day in 1925 with a migraine headache. They tried a new treatment on her with two products, one for intramuscular injection and another for intravenous delivery. Accidentally, they put the IM product (procaine) into the vein and the migraine went away! Only later did they realize what they had done. Frustrated that their intended intravenous medicine hadn't worked for other patients, they finally found their mistake; that the solution they used for their sister was the procaine that had originally been intended only for numbing the site of the intramuscular injection! At the time it was thought that injecting procaine into the vein was dangerous, but their error had serendipitously proven it to be safe, and very effective.

With this understanding of procaine, the Huneke brothers advanced neural therapy by studying the past, and by practicing what they had learned. They found that in 1906, Spiess discovered that wounds and inflammatory processes subside more quickly, and with fewer complications, after local anesthetic. Then, in 1931, it was discovered that post-operative pain disappeared immediately after procaine infiltration of the surgical scar. They found that injecting procaine intradermally over painful areas treated the pain effectively, regardless of the location. Back pain, abdominal pain, joint pain… anywhere in the body. In 1940, they discovered what came to be known as the Huneke phenomenon, or "lightning reaction," by injecting a scar on the lower leg with procaine, only to find an instantaneous release of otherwise chronic, intractable pain in the patient's shoulder.

How does that work? Procaine is a local anesthetic that has some interesting properties. It is a vasodilator, which in the case of migraines is important, as the blood vessels are constricted in areas of pain. It is also numbing, of course, which takes away pain instantly. It is short acting, with a half-life of roughly 20 minutes, so the expectation is that the pain relief should not last longer than the anesthetic effect. But clinically, the effects are often found to be much longer! Why? This may require a little discussion of pathophysiology. Injured tissue loses the integrity of its resting membrane

potential, causing its threshold for firing to decrease. As an anesthetic, procaine works to restore a normal resting membrane potential. While the anesthetic effect may be temporary, the restoration of normal resting potential may permanently influence the local tissue's peripheral communication with the central nervous system.

More than one session may be needed to break a well-established dysfunctional chain of signals such as those responsible for migraines or cluster headaches, but an experienced practitioner will learn to interpret feedback from the autonomic nervous system to help unravel a coherent program of treatment.

**The Interference Field**

The key to applying neural therapy is finding the "interference field," or "focus," which is the region that presents a dysfunctional signal to the autonomic nervous system. All connective tissues are semi-conductors of electricity—most notably, nerves. There are electrically conducted reflexes that travel through the nerves, from the skin to the organs (somato-visceral) and back again (viscero-somatic). In fact, 80% of the sympathetic nerve fibers in the body course through, or near, the skin, making it a potent area for treatment. In neural therapy, we use the surface of the skin and subcutaneous tissues over the painful areas when treating all types of pain, and we utilize the somato-visceral and viscero-somatic relationships to help influence deeper structures. These "segmental" treatments are determined by the level of dermatomal, sclerotomal, or myotomal relationships to the affected areas. In this way, gastritis might be treated with segmental injections over the thoracic nerve roots from T5-T9. Sciatic nerve pain might be treated with segmental therapy to the nerve roots from T12-S2. Segmental therapy is a good option for pain that presents anywhere on the body. Not only does segmental therapy help directly with pain, but it increases the circulation of the treated area, so you get increased uptake of any medications used, and more effective removal of the waste products of inflammation associated with the pain.

**Finding the Interference Field**

The best way to uncover an interference field is by doing a careful history. Patients will almost always reveal something significant as they tell their stories. The most basic neural therapy question is, "What happened to you just before you had the pain?" If the answer is not immediately forthcoming, the question will often jog the patient's memory at just the opportune moment to allow for a breakthrough.

Sometimes, the interference field presents itself during the physical exam, as inspection, palpation, and intuition take over. The application of autonomic response testing, using muscle testing, has become almost indispensable in the practice of neural therapy, helping to quickly identify sources of neurologic dysfunction. This method can also be used to identify the sequence of sites to be treated, cooperating with the patient's autonomic system in a way that is more likely to contribute grace and ease to the healing process.

Some indicators that an interference field is causing the present(ing) illness are the following:

1. The illness is not responding to other therapies.
2. Another type of treatment has made the illness unexpectedly worse.
3. All symptoms are located only on one side of the body. (From Klinghardt, 1993.)

Some chronic problems are tied to specific interference fields that are common enough to be approached empirically. Acupuncturists will understand the relationship between an appendectomy scar or a hernia scar and chronic problems with ipsilateral hips or knees because the fascial plane of the stomach meridian has been interrupted in the surgical process. Similar understandings are achieved with regard to sciatic pain and interference fields on the legs – or migraines and issues with tonsils or teeth.

**How Is an Interference Field Created?**

Imagine what happens to the conduction of nerve impulses when there is an adhesion in the connective tissues, such as a scar. It is remarkable how often scars are tied to chronic pain, and how frequently they are overlooked by physicians who treat pain. Relieving the irritated nerves at the site of scarring has body-wide effects. A simple intra-cutaneous injection of procaine into the scar can make a world of difference.

**An interference field is the region that presents a dysfunctional signal to the autonomic nervous system.**

What causes a scar to become an interference field? It could be from a terrifying event, like an automobile crash, or a surgery that was emotionally traumatizing. An emergency C-section, for instance, for an expectant mother who is shocked to find out that her baby's life may be at risk. Maybe there is a complication, like poor wound healing from a post-surgical infection, or a retained suture that doesn't dissolve. In this way, a scar is a more obvious site for an interference field, but interference fields can be triggered by almost any physiologic disturbance. Vaccination sites can become interference fields. Insect bites can cause interference fields. Dental issues can become interference fields.

Perry Perretz, DO: *A patient in my practice was infected with Chikungunya virus that presented as a painful frozen left shoulder. It persisted weeks longer than would be expected from such an infection. This was relieved with a combination of local procaine injection to the site of the bite, and a "segmental" injection over the C6 nerve root.*

*Another patient had erroneously been diagnosed with rheumatoid arthritis, despite negative CCP and RF labs. He had swelling of knees, ankles, elbows, and wrists that added almost fifty pounds of weight to his body. An interference field in a root canal tooth*

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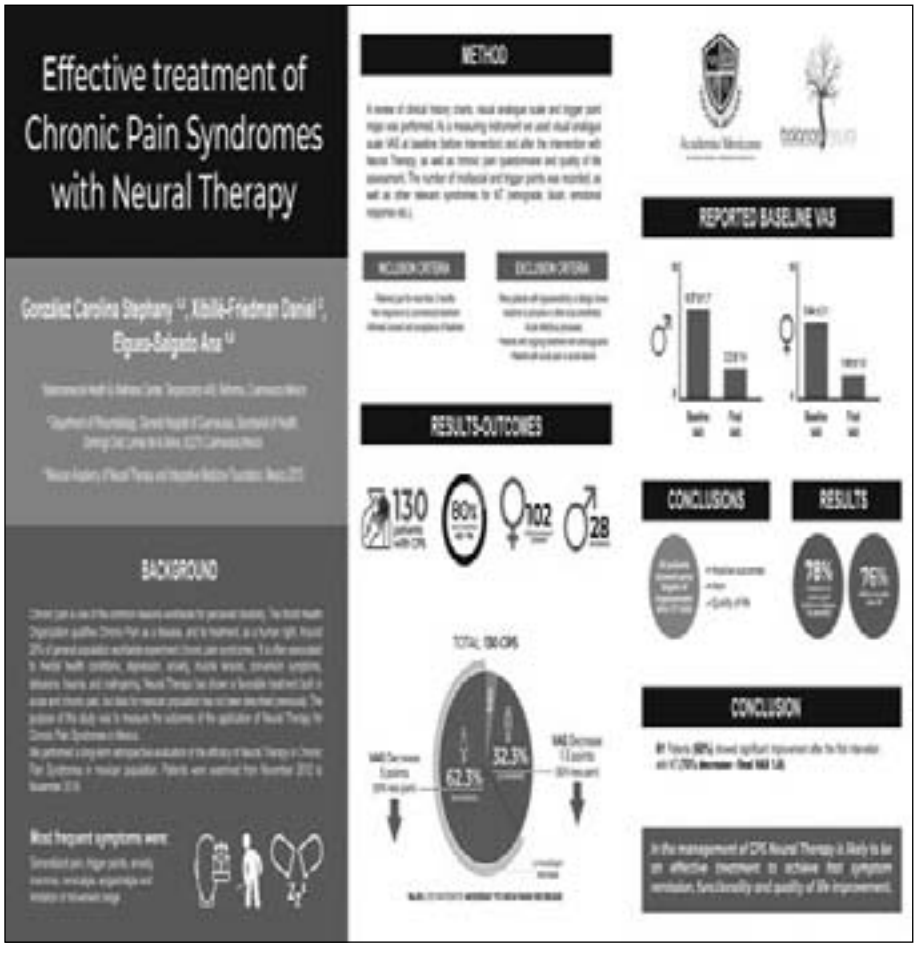
*was identified. I considered giving him a diagnostic injection of procaine to determine its importance, but he was already motivated to get rid of the tooth. Once the tooth was extracted his rheumatoid symptoms disappeared overnight, and he lost almost forty pounds within the week.*

Emotions create powerful interference fields. In the October 2017 issue of the *Townsend Letter,* our colleague Michael Gurevich, MD, wrote an excellent article on the use of neural therapy in psychiatry. Clearly, we have begun to understand more about the effects of trauma upon the central nervous system. Other avenues of study have helped us understand more about post-traumatic stress and the induction of autonomic responses that are triggered by the engagement of a traumatic memory.

Jeff Harris, ND: *I have worked with many soldiers who have had very severe pain and PTSD. Their pain medications weren't helping. They were losing their relationships, or already had lost them. They hadn't been able to sleep for days on end and they were desperate for help, knowing that many of their friends in the same situation had committed suicide. At first, I was nervous to treat them, but neural therapy has been almost magical for them. The very first one I saw had a bomb go off right in front of him while wearing an ordinance disposal suit. He was a star on a military athletic team, a family man with children. He suffered with chest pain and high blood pressure. I first treated the circumference of his head and the area over the left side of his chest, where most of the explosive impact had been absorbed. Immediately following this treatment, he asked if he could leave the office to sleep in his truck. I asked him to come back before he drove off so I could evaluate him. Four hours later, he came back and hugged me! He hadn't slept for many days before, but he reported that he felt normal for the first time since the explosion. More importantly, he had hope for his future. He has seen me a number of times over the last few years, as he has needed additional treatment, but he says that the PTSD and pain have never returned to the level he felt prior to our first office visit. He has told his medical team on the military base about the treatments he received. He asked them to have me come and talk with them, but so far, they haven't invited me.*




**COVID-19 and the "Long-Haulers"**

Extreme stress can bring back the memory of trauma. The COVID-19 pandemic represents just such a trauma for some of those who have been infected. As this is a novel coronavirus, we are still struggling to understand the severity of its course for many different populations. We know that it is extremely contagious and that no one is naturally immune. Those infected have been forced to confront their diagnoses much the same as any terminally ill patient. Is this going to kill me? How badly will I suffer? Do I need to say good-bye to my kids? Change my will? Change my medical directives? Will I die alone? There is a subset of COVID-19 survivors who have endured the acute infection, only to find themselves exhibiting symptoms far beyond their "recovery." They are referred to as "long-haulers."

Perretz: *Recently, I evaluated a long-hauler, infected in March 2020, still suffering symptoms of her viral illness in July, though she had tested negative since April. Her symptoms were pain, heaviness, and tightness in the chest, shortness of breath, and heart palpitations. X-rays, ECG, and labs were all negative. Surgical history included appendectomy, C-section, and breast implants. On physical exam, the lung reflexes were dysfunctional bilaterally, and the heart rhythm reflex was found to be positive. There were trigger points in the bilateral infraspinatus muscles known as the Infraspinatus Respiratory Reflex (IRR), the discovery of which is attributed to the late Dr. Henry Philibert, MD. Scars,*

*in this situation, were not found to be neurologically active. Treatment was delivered with intradermal injections of procaine to the acupuncture points, Lung 1, bilaterally, CV15, for the heart reflex, and Governing Vessel 18. The IRR was injected with procaine, and a touch of Kenalog to increase respiratory ease. Osteopathic manipulation was employed to release the ribs, which had been restricted by coughing. Emotional Freedom Technique was also employed to address trauma. Immediate ease came to her breathing, and by the next day she was symptom-free.*

Our colleague, Dr. Stephany Gonzalez, performed a seven-year (2012-2019) retrospective evaluation of neural therapy's efficacy for chronic pain syndromes in 130 patients. All patients in the study reported pain greater than three months' duration that had failed to respond to conventional treatment.

Results showed that ALL patients receiving neural therapy treatment reported some improvement after an average of 1.7 visits. Ninety-four point six percent (94.6%) reported decreases in pain by Visual Analog Scale. Sixty-two point three percent (62.3%) reported VAS decreases of 5 levels, or greater. In total, 76% of surveyed patients achieved remission or near-remission of chronic pain with neural therapy treatment.

In summary, neural therapy's chief application has come as a treatment for chronic pain and illness, and one of its greatest values is that it represents a comprehensive approach to physiology, avoiding some of the reductionistic traps of Western diagnosis. An aspect of its attractiveness is that it can be appreciated by professionals from a wide range of trainings, and it provides the perfect blend of Eastern and Western medicine. A typical Western-trained medical doctor can easily understand the use of anesthetics to neutralize dysfunctions of the autonomic nervous system, but might be surprised at how the application of this model tends to "teach" us how a patient compensates, as an individual, to the experiences of life. A naturopath might be excited to exploit neural therapy's ability to determine root causes of illness and pain and treat them using the least possible force. An acupuncturist might see neural therapy as a form of medically applied acupuncture, and the dentists will be pleased to see how neural therapy recognizes the influence of the teeth and oral cavity on the health of the entire individual.

Neural therapy is practiced more in Europe and South America than in North America, but it is gaining traction here. Much of the earlier literature is in German, but translations in English and Spanish have been available for years now. Many of us in North America owe a great debt to Dr. Dietrich Klinghardt for his teaching. Within the last three years, a North American Academy of Neural Therapy has been created to encourage leadership and training for professionals of various disciplines. Membership and continuing education opportunities are available through its website, www.NAANT.org.

**Resources**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Jeff Harris, ND, is a teacher of neural therapy internationally. He has been practicing neural therapy since 1993 in Seattle, Washington. He is the vice president of NAANT, the North American Academy of Neural Therapy.

Perry M. Perretz, DO, is the current president of the North American Academy of Neural Therapy (NAANT). Dr. Perretz first entered medical school after eight years of practice as an acupuncturist. As a practitioner of Eastern medicine, he saw that many patients were falling through the cracks in our health care system. Inspired to serve people better as part of a medical team, he graduated from the University of New England College of Osteopathic Medicine in 1999 and completed his PM&R residency at Schwab/ University of Chicago in 2003. His private practice, called Advanced Pain Solutions (Redding, Connecticut), is dedicated to the treatment of musculoskeletal pain, featuring an eclectic mix of osteopathy, prolotherapy, acupuncture, and neural therapy.

# Facts About Gums and Thickeners

## by Betty Wedman-St Louis, PhD

Gums and thickeners in processed foods are problematic for individuals with digestive issues. Different gums are used throughout the food and pharmaceutical industries. Studies have shown that gums are structurally and molecularly similar to common foods, so cross reactions can lead to sensitivities and inflammatory damage. Food additives, including emulsifiers, stabilizers or bulking agents, are present throughout the Western diet; and consumption is increasing.

*Carrageenan* is commonly used in dairy products and milk-alternative beverages like almond milk and coconut milk. Studies over the past 25 years have linked carrageenan to gastrointestinal disorders even though the FDA, US National Organics Standards Board, and FAC/WHO consider it a safe food additive.[1-4]

*Karaya Gum* is produced from the Sterculia tree. The sap material from the tree grown in India is used as medicine (laxative, aphrodisiac). As a thickener, it is in dental adhesives**,** cosmetics, and medications like stool softeners (it thickens in the gut to produce bulk). Use of this gum can reduce how medications are absorbed so it needs to be avoided or used only when medications are not consumed.[5] As a gum, it is used as an emulsifying, gelling and textural agent in bakery products.[6]

*Locust Bean Gum* is also known as carob bean gum since it is made from the seeds of the carob tree. It causes gas and abdominal discomfort, so it needs to be avoided by individuals suffering from SIBO (small intestinal bacteria overgrowth). It is widely used as an additive in food, pharmaceuticals, paper, textiles, and cosmetics.[7]

*Tara Gum* is derived from legumes and interest in galactomannans as a functional health supplement have increased its use.[8] It increases water absorption and is used in food and medical products.

*Gellan Gum* is produced from bacteria fermentation and used as a bulking agent in foods and medications. It is used in soy protein isolate gel products for improved texture.[9]

*Gum Arabic* is from the sap of the acacia tree and is frequently used as an edible coating on fruits – mango, blueberries – to increase shelf life by serving as a barrier to gas and vapor properties.[10] Fruit-flavored yogurts and coconut products use it as an emulsifier to improve flavor distribution and stability.[11]

*Guar Gum* is from Guar beans in India and Pakistan. It is frequently called galactomannan on labels and is used widely throughout the food industry – ice cream, yogurt, salad dressing, gluten-free foods, gravies, sauces, kefir, almond milk, coconut milk. In addition it is used as a laxative or for treating diarrhea in IBS (irritable bowel disease).[12] It is a thickener and stabilizer in foods, as well as a binding agent in making tablets in addition to being a thickener in lotions and creams. Guar can cause increased abdominal discomfort and gas if SIBO is a problem.

*Xanthan Gum* is a frequent food additive in bakery products to make the dough stickier. It is derived from the bacteria *Xanthomonas campestris* in a fermentation process.[13] This bacteria strain is the same one that causes black mold on broccoli, cauliflower, and leafy vegetables resulting in a slimy coating on these foods. Bloating and gas are frequent complaints when consuming foods containing xanthan gum, such as ice cream, egg substitutes (egg beaters) and salad dressings.

*Maltodextrin* is a thickener produced from enzymatically treated corn, rice, wheat, or potato starch to make a white powder that is found in shake mixes, sugar-free sweeteners and diet products. It has been shown to increase blood glucose causing increased *E. coli* adhesion in the gut and allergic reactions.[14] It provides no nutritional benefit and needs to be avoided because it suppresses antimicrobial defenses in the gut and promotes salmonella survival while causing diarrhea and gas.

**FODMAP Diet**

Individuals on a low FODMAP (fermentable oligo-di-monosaccharides and polyols) diet need to consume unprocessed foods to avoid these carbohydrate sources. Ingesting the above-mentioned gums and thickeners plus carbohydrates found in sugar, cereal grains, and legumes leads to gastrointestinal symptoms: gas, bloating, pain and irregular bowel movements. Oligosaccharides, disaccharides, monosaccharides, and polyols are poorly absorbed and can lead to bacteria and yeast overgrowth. Excess mucus secretions and inflammation damage the intestinal lining, which

causes the irritable bowel symptoms.

Oligosaccharides include fructose (high fructose fruits) and galactose (wheat, rye, onions, legumes, cruciferous vegetables like broccoli, cabbage, kale, Brussels sprouts and cauliflower). Some prebiotic/probiotic dietary supplements can also contain oligosaccharides like inulin and gum arabic.

Disaccharides are two-linked sugars found in dairy products, including whey protein.

Monosaccharides are sweet foods like honey, beet sugar and cane sugar. High fructose fruits (pineapple, watermelon, mangos, papaya and grapes) need to be consumed in small portions.

Polyols are also called "sugar alcohols" that occur naturally and in processed foods. They are predominately listed in packaged food ingredients as sorbitol, mannitol, xylitol, erythritol, lactitol, and isomalt. Sugar-free foods like gum, ice cream, candy and dried fruit like apples and prunes have polyols.

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# The Science Behind NMN – A Stable, Reliable NAD+ Activator and Anti-Aging Molecule

## by Christopher Shade, PhD

In June of 2018, the World Health Organization (WHO) released the 11th edition of its *International Classification of Diseases,* and for the first time added aging.[1] The classification of aging as a disease paves the way for new research into novel therapeutics to delay or reverse age-related illnesses such as cancer, cardiovascular and metabolic disease, and neurodegeneration.[2,3] Nutrient sensing systems have been an intense focus of investigation, including mTOR (the mammalian target of rapamycin) for regulating protein synthesis and cell growth; AMPK (activated protein kinase) for sensing low energy states; and sirtuins, a family of seven proteins critical to DNA expression and aging, which can only function in conjunction with NAD+ (nicotinamide adenine dinucleotide), a coenzyme present in all living cells.[4]

Across the kingdom of life, an increase in intracellular levels of NAD+ triggers shifts that enhance survival, including boosting energy production and upregulating cellular repair.[5] In fact, the slow, ineluctable process of aging has been described as a "cascade of robustness breakdown triggered by a decrease in systemic NAD+ biosynthesis and the resultant functional defects in susceptible organs and tissues."[6] Aging is marked by epigenetic shifts, genomic instability, altered nutrient sensing ability, telomere attrition, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and dysregulated intercellular communication.[7,8]

By middle age, our NAD+ levels have plummeted to half that of our youth.[9] Numerous studies have demonstrated that boosting NAD+ levels increases insulin sensitivity, reverses mitochondrial dysfunction, and extends lifespan.[10,11] NAD+ levels can be increased by activating enzymes that stimulate synthesis of NAD+, by inhibiting an enzyme (CD38) that degrades NAD+, and by supplementing with NAD precursors, including nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN).[12,13] A conceptual framework called NAD World, formulated over the last decade by developmental biologist Shin-ichiro Imai, MD, PhD, of Washington University School of Medicine, posits NMN as a critical, systemic signaling molecule that maintains biological robustness of the communication network supporting NAD+.[6]

Taken orally, NMN is rapidly absorbed and converted to NAD+.[14] In numerous studies, supplementation with NMN has increased NAD+ biosynthesis, suppressed age-related adipose tissue inflammation, enhanced insulin secretion and insulin action, improved mitochondrial function, improved neuronal function in the brain, and more. Here, we look at the science behind NMN, its stability, possible pharmacokinetics, transport, function, and ability to induce biosynthesis of NAD+.[15] Supplementing NMN may be an effective nutraceutical anti-aging intervention, with beneficial effects on a wide array of physiological functions.[16]

**Pathways to NMN in the Human Body**

A veritable symphony of interlocking transformations allows NAD+ to be both synthesized and regulated in the body. It is well known that vitamin B3 is a building block for nicotinamide adenine dinucleotide (NAD+). It is also widely recognized that NMN is a potent precursor for NAD+. Though NMN is naturally found in small amounts in fruits and vegetables such as avocados, broccoli, cabbage, edamame, and cucumbers,[17] in mammals most NMN is synthesized from vitamin B3 in the form of nicotinamide. At the center is nicotinamide phosphoribosyltransferase (NAMPT), an essential rate-limiting enzyme that catalyzes the conversion from nicotinamide to NMN, which exists in both an intracellular (iNAMPT) and extracellular form (eNAMPT).[18] The extracellular form has higher enzymatic activity than the intracellular form and has been found in blood plasma, seminal plasma and cerebrospinal fluid in humans.[19,20] In addition, eNAMPT appears to be produced by a wide array of cell types—including fat (adipocytes), liver (hepatocytes), white blood cells (leukocytes and monocytes), and heart and brain cells (cardiomyocytes and glia cells).[21] Like NAD+ and NMN, eNAMPT declines with age. Both white and brown adipocytes actively secrete eNAMPT, suggesting that fatty tissue may be a modulator

of NAD+ biosynthesis.[6] Adipose tissue actively secretes extracellular vesicles (EVs) that are enriched with NMN and can circulate through the plasma. EVs are membrane-derived particles surrounded by a phospholipid bilayer that are released by cells in the human body.[22] These EVs not only protect their cargo, they can deposit their payload where needed.[23]

NMN and nicotinamide riboside (NR) dance together. NMN can be converted by the body to NR, which then enters cells, and is converted back to NMN by an enzyme called nicotinamide riboside kinase (NRK). More recently, an "elusive' transporter was discovered, which can transport NMN directly into cells.[24] NMN is transported across cell membranes directly into the cytoplasm of the cell, by an enzyme called Slc12a8. Uptake pathways of NMN vary with tissue types, and interestingly, Slc12a8 expression is about 100-fold times higher in the small intestine of mice than the brain or adipose tissue. Researchers speculate that the gut microbiome and certain resident bacteria within it may produce NMN.[25]

NMN levels fall with age, and aging itself has also been shown to significantly compromise the body's conversion of NMN to NAD+.[26]

**Abundant Evidence for Anti-Aging and Health-Enhancing Effects of NMN**

In numerous mouse models of disease and aging, NMN has demonstrated a wide array of remarkable effects, benefitting conditions ranging from diabetes to Alzheimer's disease to ischemia.[27] Orally administered NMN is quickly synthesized into NAD+ in tissues in mice. NMN has been able to suppress age-associated weight gain, enhance energy metabolism and physical activity, improve insulin sensitivity, improve eye function, improve mitochondrial metabolism, and prevent age-linked changes in gene expression.[28] In mice bred to be diabetic or obese, NMN improved both the action and secretion of insulin.[29] NMN also protected the mouse heart from ischemia and/or reperfusion injury.[30] It has restored skeletal muscle in aged mice,[31] and slowed cognitive decline in a mouse model of Alzheimer's disease by improving the survival of neurons, improving energy metabolism, and reducing reactive oxygen species.[32] It may help maintain the integrity of the blood brain barrier.[33] NMN is likely a good candidate to suppress inflammaging—the increase in inflammation associated with aging—since studies show it lowers adipose tissue inflammation associated with age. In fact, older mice appear to be more responsive to NMN, in comparison with young mice.

NMN appears to be stable in water; in one study 93%–99% of NMN was maintained intact in drinking water at room temperature for 7–10 days. NMN also appears to be rapidly absorbed. When given to mice by oral gavage, there was a steep increase of plasma NMN in a mere two and a half minutes, with further increases at 5-10 minutes. Plasma levels then declined to baseline,

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suggesting rapid absorption in the gut.[29] Long-term (1 year) NMN given orally, in doses of up to 300 mg/kg, was found to be safe and well tolerated in normal mice.[29]

**Looking Forward: NMN and Human Health**

NMN is clearly a murine fountain of youth. But what about humans? Shin-ichiro Imai has said that NMN may improve adult human metabolism, rendering it more like that of someone ten or twenty years younger.[34] His team is now studying NMN in humans. David Sinclair, Harvard University's noted anti-aging researcher, whose research on resveratrol, NAD+, and sirtuins is world renowned, is also conducting human trials. He is taking NMN himself; he has said his lipid profile has improved dramatically and he feels more energetic and that his blood markers, at nearly 60 years old, are closer to those of a 31-year-old.[35,36]

An interesting question is the delivery system for oral NMN: the EVs that transport the molecule through plasma in the body are liposomes. A liposomal version of NMN may well mimic the body's own transport system, enhancing uptake and delivery, as science advances its understanding of the holy grail of reversing aging.

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# Environmental Medicine Update

**by Marianne Marchese, ND**
**www.drmarchese.com**

## Wildfires and Their Health Effects

**Introduction**

Every year the number of wildfires burning across the US increases as does the proximity to major cities and towns. Some wildfires are man-made, both accidental and on purpose, and others are due to forces of nature like a lightning strike. Global warming and climate change also play a role in the increase in wildfires. Numerous toxic chemicals are released into the air when fires rage through forests, fields, and towns. The health effects of the first responders is well documented but not as much attention is paid to the effect on those living or working nearby. It's important for physicians and health care providers to understand what chemicals are released when a wildfire burns. These toxicants can travel through the air, contributing to respiratory conditions in vulnerable populations. Identifying the health effects of wildfires and how to treat these patients is imperative as wildfires are expected to increase each year.

As the world warms up it has the potential to burn. While wildfires are a normal part of our landscape, across the US and the globe the number of fires each season is increasing and wildfire seasons are longer each year. Climate change is considered a driving force behind the increase. According to the National Interagency Fire Center, from January 1, 2020 to August 10, 2020, there were 33,917 wildfires in the US compared with 28,821 wildfires in the same period in 2019. About 2.3 million acres have burned in the 2020 so far, compared with 3.6 million acres in 2019. California has been especially hit hard in 2020 seeing a 68% increase in wildfires from January 1, 2020 to August 20, 2020, compared to the same period in 2019. California is an easy example of climate change with warmer temperature and precipitation. Climate change raises the risk of wildfires several ways; longer periods of draught, warmer temperatures, less rain or snow pack, and drying out vegetation.[1] Warmer temperature cause the atmosphere to create more thunderstorms and lightning strikes, which contribute to more wildfires. Man-made fires, whether on purpose or accidental, will easily spread in such warm and dry conditions.[1]

**What's Burning?**

A wildfire can rip through forests, grasslands, buildings, and homes that stands in its path. Numerous toxicants that are known carcinogens, immunotoxins, endocrine-disrupting compounds are released into the air and can affect the pulmonary and cardiovascular system. Both firefighters and residents near fires are exposed to these chemicals. Toxicants travel through the

air to neighboring towns, cities and even other states. A 2004 publication in the *Journal of Occupational and Environmental Hygiene* identified some of these harmful chemicals. They include acrolein, anthracene, benzene, benzo(a)anthracene, benzo(a)pyrene, benzo(b)fluoranthene, benzo(k)fluoranthene, carbon monoxide (CO), chrysene fluoranthene, formaldehyde, indeno(1,2,3-cd)pyrene, particulate matter (fine particles smaller than 10 μm), phenanthrene, and pyrene.[2] Most of these are known to disrupt the endocrine, neurological, immune and cardiopulmonary system—even in healthy individuals without underlying conditions.[3]

In 2013 the US Department of Agriculture released a report that outlined additional harmful chemicals emitted from wildfires and forest fires, including carbon monoxide, aldehydes, particulate matter, crystalline silica, and polycyclic aromatic hydrocarbons. Again, many of these are known carcinogen and respiratory irritants.[3] When vegetation burns, it emits carbon monoxide, sulphur dioxide, particulate matter, aldehydes, benzene, and acrolin.[3] It will emit pesticides or herbicides if the area has been sprayed, such as agriculture or farmland.

As fires move toward urban areas and homes, buildings and structures are burned and the contents inside them. Additional chemicals are released, such as pesticides, arsenic, lead, mercury, solvents, paints, cleaning solutions, plastics and their chemical compounds, defluorinated chemicals, volatile organic compounds, and more.[4] The adverse health effects span multiple organ systems. As firefighters move in to extinguish the flames, chemical suppressants and foams are used and have a host of health effects as well.[5] The make-up of these wildfire suppression chemicals allows firefighters to contain the fire while also protecting physical structures and homes. There are two major types of wildfire suppression chemicals: foams and flame retardants, which are often what the average person sees on the evening news being sprayed from planes flying over a wildfire. These can also have detrimental health effects especially to firefighters who are in close contact with these chemical suppressants.[5] These foams and flame retardants can also travel in the air, affecting people nearby.

**Health Effects**

As wildfires are becoming more prevalent near towns and cities, emitting harmful chemicals into the air, health care providers need to consider the health impact on those living nearby. Certain populations are more vulnerable to chemicals released from wildfires. These populations include children, the elderly, and pregnant woman.[6-8] People with underlying conditions are predisposed to the effects of toxicants from wildfires, and those conditions include asthma, COPD, diabetes, cardiovascular diseases, and cystic fibrosis.[6-8] Even people who are younger and without any underlying conditions may experience symptoms related to wildfires. Short-term effects range from shortness of breath, wheezing, coughing, sore eyes and throats, runny nose, and sinus issues, to headaches, fatigue, heart palpitations, and chest pain. Longer term effects include increases in asthma-related hospitalizations, chronic and acute respiratory and cardiovascular health outcomes, and even premature death.[9,10] People with these health effects should seek medical attention, especially asthmatic patients, as the use of a steroid inhaler, home oxygen, and other medication may be needed in the short term.

As fires burn nearby and flame retardants are sprayed from above, it is important people take measures to protect themselves from the exposures to toxicants released in the air. Recommendations include the following:

- Stay indoors with the windows closed.
- Use a HEPA-type air filter in the home and at work.
- Wear an N-95 mask indoors and outdoors.
- Roll up your car window when driving.
- Seek out a health care provider trained in environmental medicine to help mitigate the effects of toxicant exposure.

If someone is experiencing acute cardiac or pulmonary concerns, immediate medical attention may be required at an emergency room or urgent care center. Advanced pulmonary function testing and cardiac tests will help evaluate if there is long-term damage to the lungs or heart. Once acute concerns are addressed and they are stable, then seeking out the guidance from an environmental medicine doctor to address the toxicant exposure from wildfires will help overall health. Most people exposed to chemicals emitted from wildfires experience only mild symptoms such as ear, nose and throat irritation, coughing, shortness of breath or wheezing. But over time these toxicants can produce chronic health issues.

**Mitigate the Health Effects of Wildfires**

Many of the chemicals inhaled during a wildfire can directly damage lung tissue, cause inflammation in respiratory passageways, create oxidative stress and free radicals, cause macrophage cytotoxicity, and deplete glutathione, which is the most important antioxidant in the body.[11] These mechanisms of damage underlie the changes in respiratory symptoms and why people seek out healthcare after a wildfire event. To mitigate some of the effects, restoring glutathione levels, offsetting free radical production with antioxidants, and trying to decrease body burden of toxicant exposure are key methods in treating or preventing health effects from wildfire smoke. Most of the research done in this area is on people living in areas of high air pollution and on firefighters who as frontline workers face the highest level of exposure and health effects from wildfires.

Air pollution contains chemicals found in wildfire smoke, including particulate matter, carbon monoxide and sulfur dioxide and benzene. Carotenoids, vitamin D, and vitamin E help protect against pollution damage, which can trigger asthma and COPD.[12] Vitamin C, curcumin, and omega-3 fatty acids also help mitigate the harmful effects.[12] N-acetylcysteine (NAC) is a major antioxidant in the body and precursor to glutathione. NAC has long been used for supporting lung function in conditions such as COPD and chronic bronchitis. Studies show it is beneficial in patients with inhalational smoke-induced lung injury.[13] Glutathione is beneficial for patients with asthma, COPD and bronchitis. Supplementation can help mitigate the effects on the lung of inhaled smoke.[14]

Sauna therapy has been used for years for numerous cardiovascular and pulmonary conditions. *Mayo Clinic Proceedings* published an excellent review showing sauna bathing can reduce the risk of high blood pressure, cardiovascular

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disease, neurocognitive diseases, and pulmonary diseases.[15] Sauna is being utilized by firefighters as a method to treat the damage induced by wildfire smoke. A study just completed by researchers at the University of Arizona demonstrated sauna therapy lowered the urinary level of polyaromatic hydrocarbons PAHs of firefighters.[16]

Sauna therapy, vitamins, minerals and antioxidants are not only important for lung function and pulmonary conditions but also to support liver metabolism of toxicants. As stated above, wildfire smoke emits numerous chemicals into the air including lead, mercury, arsenic, pesticides, solvents and polyaromatic hydrocarbons. An environmental medicine approach can be useful in assessing and addressing health concerns due to wildfire smoke. An in-depth history and intake, testing for toxicants, and treatments including sauna therapy, vitamins and minerals are important steps in mitigating effects from wildfires.

**Case**

At the end of May 2020, a man-made fire broke out in Cave Creek, Arizona, a town just a few miles north of Phoenix. It was called the Ocotillo fire and located between popular recreation hiking spots Cave Creek Regional Park and Spur Cross Ranch Conservation Area. Hundreds had to evacuate, and numerous structures and homes were burned. A 45-year-old woman who lived near the fire and had to evacuate began experiencing shortness of breath, dry cough, and fatigue a few days after returning home. She had a history of seasonal allergies and was currently receiving allergy shots every other week at her allergist office and used Flonase and Allegra-d as needed. She was on no other medication and was otherwise healthy. She took Vitamin D (2,000 iu a day), a probiotic, and fish oil (1,500 mg a day). She initially went to her PCP who did an appointment via telemedicine and prescribed a steroid inhaler, which didn't help. After a week she wasn't better and came to my office (June 2020).

Her exam was unremarkable: lungs clear, oxygen saturation 99%, peak flow meter 420, 440, 440, regular heart rate and rhythm, and no signs of distress. She did not cough once while in the office but says she has a dry cough and shortness of breath on exertion and in the evening. The intake reveals every Spring when her allergies flare, she has the same symptoms as well as during the summer monsoon season when the wind blows dust throughout her area. She had Valley Fever five years prior, like many living in Arizona. Many patients who have had Valley Fever and recovered tend to have comprised lung function. Environmental history was unremarkable except she lives on a golf course where pesticides are sprayed. CBC, CMP, TSH, ESR, CRP-hs all within normal limit.

The initial treatment consisted of the following:

1. HEPA air filter to run 24 hours a day
2. N-Acetylcysteine 600 mg twice a day
3. Supplement to provide vitamin and mineral co-factors for liver phase one and two metabolism (four a day). The cofactor support product contained vitamin A, vitamin D3, vitamin K1, vitamin B1, vitamin B2, vitamin B3, vitamin B5, vitamin B6, vitamin B12 (as methylcobalamine), vitamin C, vitamin E, biotin, folate (5-methyl-tetrahydrofolate), calcium, chromium, copper, iodine, magnesium, manganese, molybdenum, potassium, selenium, zinc, choline, inositol, boron, vanadium, green tea extract, turmeric.
4. Liver herbal supplement (2 a day); it contained milk thistle, beet root, dandelion, burdock and artichoke.
5. Sauna therapy two times a week for eight weeks. This was done as 7-10 minutes in the heat then 30-second cold shower, repeat five times and end on cold.
6. Rumex 200C (3 pellets under the tongue in the evening for 2 weeks).

After four weeks she returns and reported her energy, cough and shortness of breath all improved significantly and she was feeling better.

**Summary**

The past few years have shown an increase in wildfires across the US and around the world. This is in-part due to global warming and changes in our climate. Even man-made fires, both on purpose or accidental, are spreading like never before due to warmer, drier conditions. As vegetation, forests, structures, and homes burn, numerous toxicants are released posing health risk for both firefighters and those living and working nearby. It is important health care providers understand the toxicants emitted from wildfires and the flame retardants used to manage fires, and their effects on health. Educating patients on measures to protect themselves during the fire and providing treatments for managing the health effects are a key part of integrated care.

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# Steak and Potatoes: Metabolic Typing on the Gonzalez Program

## by Mary Swander

"You need to go out and have a steak and a baked potato," Dr. Nicholas Gonzalez said to me the first time I saw him as a patient in 1994 in New York City. He held my chart in his hands and strode me down the long hall from his waiting room to his office, his shoes clicking on the hard wood. "And you've had a serious neck injury. We need to address that because it is keeping your body from functioning correctly."

I was simultaneously stunned and pleased. I had come to Dr. Gonzalez filled with fibroid tumors with excessive bleeding and anemia, hypothyroidism, fatigue, multiple food and chemical sensitivities, and widespread severe pain from a couple of car accidents. In the Midwest where I live, I had been hospitalized, in and out of physical therapy. I'd had a myelogram, x-rays, and had been put in traction and a variety of neck, shoulder, and back braces. I had made the rounds of medical model physicians to no avail. I then sought out acupuncturists, homeopaths, naturopaths, and chiropractors who managed to keep most of my symptoms at bay but made no real advance in my overall condition.

I was totally self-supporting and had a rising literary career, so I was intent on retaining my academic job, keeping my health insurance, and finding a way to live a functional and fulfilling life. I read and researched. I spent weekends in the medical library. In the days before the internet, it was harder than one might now expect to search out non-pharmaceutical treatments, so I began to travel wider distances to seek out more renowned alternative physicians. They, in turn, then placed me on rotation diets, high protein protocols, then a vegetarian macrobiotic diet. I took herbs, supplements and desensitization drops. Nothing made much of a dent.

**Dr. Gonzalez used 10 different diets with 90 different variations with his patients.**

Then in my early forties when I was heading into perimenopause, this thumb-in-the-dyke approach collapsed. I was so weak and exhausted that I could barely work. Again, I made the rounds of allopathic doctors – nine general practitioners and gynecologists in total from my internist to the head of the ob-gyn department at a nearby teaching hospital – who simply shook their collective heads, offering no treatment or course of action, and said, "Well, you don't have cancer."

No, I didn't have cancer; but through word-of-mouth and more research, I had found my way to Dr. Gonzalez who treated cancer but had also begun to take on patients with immune system disorders. This man knows how to shrink tumors, I told myself, and at that time, my fibroids were my most threatening problem. And here he was telling me to start eating meat to improve my condition.

"A macrobiotic diet is a disaster for you," Dr. Gonzalez scoffed, seating himself behind his large oak desk. "You need to eat meat, meat, meat."

I had never liked being a vegetarian. On the diet, I immediately gained weight and felt bloated. Beans and rice gave me terrible gas pains. Even as a child, I never liked salad or leafy greens. I loved other vegetables, from broccoli to potatoes, but could live without lettuce, sprouts, arugula or any of the other things that were touted as health foods. But I was trying to be a compliant patient to the doctor who had recommended the macrobiotic diet.

"You're not an Inuit, but almost," Dr. Gonzalez had said. "Your genes indicate a metabolic type that originally comes from an area just below the Arctic circle."

Dr. Gonzalez' treatment program was gleaned from years of studying with the dentist William Kelley, who in turn, synthesized the research of biologist John Beard with neurophysiologists Francis Pottenger, Ernst Gelhorn, and nutritional anthropologists like Weston A. Price. Kelley arrested his own pancreatic cancer and eventually the cancers of scores of patients through a combination of diet and supplementation based on metabolic typing, pancreatic enzymes, and detoxification.

Dr. Gonzalez used 10 different diets with 90 different variations with his patients. The diets ranged from

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vegetarian, to balanced, to carnivorous, each a reflection of the sympathetic and parasympathetic dominance of a patient's autonomic nervous system. In general, the closer your genetic make-up to cultures who lived close to the equator, the more likely you are to sympathetic dominance with an acid pH, and so function best on a vegetarian diet. The farther your genetic make-up to cultures who lived far from the equator, the more likely you were to be parasympathetic dominant with an alkaline pH, and so function best with a carnivorous diet.

According to Dr. Gonzalez' tests, I was alkaline, very alkaline.

"You're a moderate carnivore," Dr. Gonzalez explained with instructions to eat poultry or fish once a day, and red meat at least once daily. To my joy, I could eliminate leafy greens and eat all other vegetables with an emphasis on root vegetables like potatoes, turnips, beets, and carrots. All foods had to be organic. I bought beef from my Amish neighbors while I planted rows of root vegetables and other crops: broccoli, carrots, onions, garlic, peas, beans, squash, asparagus, eggplant, and peppers in my garden.

Right away, I felt stronger, my blood count rising from 6 to 14. My recovery took longer than Dr. Gonzalez had expected; but over the course of the next year, my fibroids began to dissolve, and the bleeding stopped. I had regular check-ups with my gynecologist at home, and she verified my progress. Then another bad automobile accident caused more major neurological problems, and my metabolic typing was pushed even further toward the alkaline end of the scale.

"I'm shifting you to an extreme carnivore diet," Dr. Gonzalez told me during one of our six-month appointments. This adjustment meant stepping up the red meat even more, with two to three 8-ounce servings daily. The vegetables remained in the same varieties and quantities as the past, but grains were now diminished, and all fruits were eliminated. Again, I immediately felt a huge improvement on this new dietary program, with even more energy and improvement of symptoms.

And an extreme carnivore is where I've stayed as I've remained on the Gonzalez program now for 23 years, my health stabilizing.

One day for curiosity sake, I decided to send away for my DNA testing. I thought I had my DNA fairly well in mind. My mother's family was 100 percent from the British Isles, from families who had been in Ireland and England for hundreds of years. My maternal grandmother's family had been British and "Black Irish," from the small minority of Irish people with dark skin and dark hair. My maternal grandfather had been fair, from the Lynch clan, a group who had originated in France, and had settled in Ireland during the Norman Conquest. Others on that side of the family were very fair, with clear Viking connections, an invading tribe who had pillaged the west coast of Ireland.

My paternal grandfather's family was originally from Switzerland, of Amish-Mennonite descent. My paternal grandmother's family was from Prussian Pomerania on the Baltic Sea. Again, both sides of this lineage had lived in their respective locations for at least a couple hundred years.

With this mix of genetics, I had always guessed that I had a fair amount of Viking blood in me from both the Irish and the Pomeranian sides. At one time in history, a part of Pomerania had even been under Swedish control. The Pomeranian side of the family also had a history of terrible allergies, and I fit right into that framework, a parasympathetic dominant characteristic in the Gonzalez schema.

The Black Irish were thought to be related to the Basques from northern Spain and southern France. A seafaring people, the Basques were known to have traded with the Irish. Ireland and Spain have had a long history of cooperation. The Basque genes would explain my mother's dark hair and complexion. I thought it might also help explain her sympathetic dominant metabolism. She died of breast cancer, which according to Dr. Gonzalez, is almost always a sympathetic dominant condition. Recent research has also linked Sardinian genes with the Irish. And again, this Mediterranean group would most often be closer to the balanced or sympathetic dominant side of the spectrum.

So, in the fall of 2017, I swabbed my mouth with a Q-Tip and sent it into the GPS Origins Ancestry Test at HomeDNA. A few months later, they emailed me these results:

#1 Fennoscandia 23.2 %
Origin: Peaks in Iceland and Norway and declines in Finland, England and France.

#2 Orkney Islands 14.5 %
Origin: Peaks in Orkney Islands and declines in England, France, Germany, Belarus, and Poland.

#3 Southern France 14.2 %
Origin: Peaks in south France and declines in north France, England, Orkney Islands, and Scandinavia.

#4 Sardinia 12.9%
Origin: Peaks in Sardinia and declines in Italy, Greece, Albania, and the Balkans.

#5 Western Siberia 11%
Origin: Peaks in Krasnoyarsk and declines towards east Russia.

#6 Basque Country 8.1%
Origin: Peaks in France and Spain Basque regions and declines in Spain, France, and Germany.

#7 Tuva 6.8%
Origin: Peaks in south Siberia (Russians: Tuvinian) and declines in North Mongolia.

#8 Southeastern India 6.4%
Origin: Endemic to southeastern India with residues in Pakistan.

#9 Northern India 2.5%
Origin: Peaks in North India (Dharkars, Kanjars) and declines in Pakistan.

#10 Western South America 0.2%
Origin: Peaks in Peru, Mexico, and North America and declines in Eastern Russia.

#11 West Africa 0.2 %
Origin: Peaks in Senegal and Gambia and declines in Algeria and Morocco.

For the most part, my intuition was on target about my gene pool, although I have no way of knowing how accurate these DNA tests really are. Perhaps most Americans of Northern European origin would get similar results. But this GPS Origins Ancestry DNA test suggested that the largest percentage of my DNA originated in Scandinavia, near or just below the Arctic Circle, confirming Dr. Gonzalez' analysis. The next highest DNA percentages – Orkney Islands, just north of Scotland, and Southern France – appear to have an overlap with the range of the Fennoscandia gene pool. The Vikings raided the Orkney Islands before they headed south to Ireland. As expected, I found the Basque and Sardinia DNA in my profile, but the surprise came in the percentage of Western Siberian and Tuva DNA.

All these percentages seem to support the profile of a moderate to extreme carnivore. For comparison sake, I also sent away for a DNA test with Ancestry DNA. After a wait of a few months, I received these results:

**Europe West** ..... 25%
**Ireland/Scotland/Wales** ..... 24%
**Connacht, Ireland**
**Great Britain** ..... 24%
**Scandinavia** ..... 16%

Low Confidence Regions
**Europe South** ..... 5%
**Iberian Peninsula** ..... 4%
**Europe East** ..... 2%

The two DNA tests appear to match up fairly well on the top ethnic categories, those that would suggest parasympathetic dominant genetics. Variations in locations and percentages occur in the lower ethnic categories. Notice that the lower categories tend to be ethnicities that often suggest sympathetic dominant types. The DNA data, with its Northern European emphasis, appears to back-up my metabolic typing on the Gonzalez program.

I was fascinated to have my DNA results, but ultimately, the data that most intrigued me about my ancestry and the link to diet was an ethnographic study conducted on Inishbofin and Inishark Islands in 1893 by Charles R. Browne, MD. My mother's family had come from Claddaghduff on the Aughrus Peninsula in Connemara, County Galway, a remote fishing village on the west coast of Ireland. Family genealogy shows that they intermarried with the people of Inishbofin Island in the Atlantic Ocean, just seven miles from Claddaghduff.

"Your mother was clearly sympathetic dominant," Dr. Gonzalez had once told me. "But most of the Irish tend to be parasympathetic dominant."

I have dual American-Irish citizenship and go to Ireland often, staying on Inishbofin for at least a week each summer. To my delight, the Irish diet matches my extreme carnivore routine. Those large Irish breakfasts complete with sausage, bacon, eggs and blood pudding are a great way for me to begin the day. Meat, fish (including salmon and mackerel), root vegetables, and some dairy are the staples of the Irish diet. If the Irish eat a salad, it's usually coleslaw. Leafy greens, pastas, grains, and sweets are not emphasized, if present at all.

"If you are hungry for a salad, have coleslaw," Dr. Gonzalez had once told me.

Of course, the Irish didn't always have the luxury of eating coleslaw. Dr. Brown documented the Inishbofin people who lived in poverty, went through frequent famines, and derived

## Gonzalez Program

their sustenance entirely from their own farming and fishing. In 1893, their diet consisted of:

- Breakfast: Tea and homemade bread.
- Lunch: Fish, or eggs and potatoes.
- Dinner: Tea and homemade bread.

Small amounts of red meat, usually mutton, were eaten on special occasions, and poultry and geese were also added to the diet sporadically. Fish was the staple of the diet with fresh fish eaten from spring through fall, then dried fish providing food throughout the winter. On first glance, the diet doesn't sound at all healthy, with no vegetables but potatoes, no dairy, and no variety. One would imagine the islanders having all sorts of health problems, especially given the fact that the population was isolated and in-bred. Yet, Browne also included a medical report in his article[1] that documented the health of the islanders, courtesy of Dr. P.T. Hart, the medical officer of the Inishbofin.

> The islanders were of sound mental health, with no signs of **insanity, idiocy and imbecility. Epilepsy** was not common. Two cases were known. One of these patients stated that "after a fit he believed he'd been with the fairies on the mainland." Deaf mutism had not been known for years but for a case of temporary mutism on Inishark in 1892. Blindness was equally rare, but for one man who had lost his sight over the age of sixty. In contrast, the Inishbofin people

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were known for their keen eye sight. Malformations were rare. Hernias, though, were on the rise with the increase of heavy weight lifting in the building of fish-curing stations, piers, and other relief work.

**Measles and scarlet fever** had not been seen for some time, although some years before, there had been an outbreak of typhoid, resulting in a couple of deaths. Phthisis was uncommon, but did occur from time-to-time. Strumous affections, abscesses, etc. were not numerous, especially noteworthy given the unhygienic condition of most houses, and the lack of regard for general sanitary laws.

**Malignancies** were unknown **Lumbago** was common, but the more acute form of **rheumatism** was not. **Bronchitis** was common as was **pneumonia** in the winter. Dietetic disease, mostly flatulence and constipation, were the most frequent complaints of the islanders, which Dr. Hart ascribed to the large amount of tea drinking by the population. And ento-parasites from fish in the diet were the most common of all troubles.

The islanders' **teeth** were usually very even and white, and seemed to last well. Even men over sixty years of age have good incisors, although many complain of toothache. But dental abscesses were not common. **Skin issues** were often due to rough clothing and fishing ropes. **Ringworm** was common. **Uterine problems** were not. And **venereal diseases** were basically unknown. Accidents were numerous, resulting in burns and abrasions. Fractures and contusions from falls were also common. Cuts from reaping hooks and injuries from livestock were also frequent.

**In temperament**, the islanders were shy, but once they dropped their reserve to strangers, they were kindly, communicative and courteous. Among themselves, they were social, given to gossip, loved dancing and music, and playing the concertina and melodeon. They were fair and honest with each other and crime was non-existent with the exception of small quarrels among neighbors. Begging was unknown and **drunkenness**, as a habit, did not exist. The islanders were religiously observant and looked to their clergy for leadership and spiritual guidance. They were also observant of sexual norms and mores and illegitimacy was virtually unknown. The islanders generally lived into a ripe old age in the eighties.

Note that Dr. P.T. Hart makes little to no mention of cancer, heart disease, diabetes, lupus, infant mortality, alcoholism, depression or anxiety or any of the other common maladies and degenerative diseases of the twentieth and twenty-first centuries. Today, even with greatly improved sanitation, the islanders suffer these afflictions as do those on the mainland. A wide variety of foods, both whole and processed are available. Fish and potatoes remain the foundation of the islanders' fare, but a nutritionist would easily say that the islanders' diet has greatly improved, with the addition of more meat, vegetables and variety. Yet sugar, white flour, modern processed vegetable oil, and alcohol consumption have also increased. And, based on Browne's ethnographic study, in general, the islanders were much healthier in 1893 than they are in 2020.

Does diet account for the total decline in health? What other changes have been made? With the influx of tourism, the islanders are exposed to more contagious diseases. There is no longer a resident priest on the island and strict religious observance has dropped off. The population has declined from 243 inhabitants in 1893 to 180 permanent residents in 2020. Currently, the school enrolls under 10 children. With improved transportation, the islanders make many more trips to the mainland and are connected to the internet and regular use of cell phones. Television sets are plentiful and automobiles, although not abundant, have cut down on the amount of walking done on Inishbofin. To some extent, exercise has declined, and the tight social bonds of the nineteenth century have loosened.

The Browne study appears to have identified an isolated culture, eating a local diet and enjoying good health, a culture that seems to have walked right out of the pages of Weston Price's 1939 book *Nutrition and Physical Degeneration.* In this volume, Price presented his research drawn from his world travels arguing that as healthy non-Western groups abandoned indigenous diets and took up Western eating habits, they developed typical Western diseases, from cavities and over-crowding of teeth, to tuberculosis.[2]

Dr. Gonzalez' dietary recommendations for me included both a return to my genetic indigenous diet – meat, fish, poultry and root vegetables – and the removal of any trace of Western dietary influences. For close to thirty years, I've eaten no sugar, white flour, processed vegetable oils, additives and preservatives including GMOs, hormones and herbicides and pesticides. I have returned to stable, good health without any dental problems and a nearly complete resolution of all the symptoms that first brought me to Dr. Gonzalez' office. A steak and small baked potato is now a normal dinner for me. Every bite is a tribute to my metabolically adapted ancestors who ate what they had, and who enjoyed excellent health into their elderly years.

Mary Swander is the co-founder and executive director of AgArts, a non-profit designed to imagine and promote healthy food systems through the arts. She is also the artistic director of Swander Woman Productions, a theatre company that tours plays about agriculture and the wider rural environment. Swander is an award-winning author of poetry, non-fiction and drama, and is best known for her books Driving the Body Back, Out of this World, and The Desert Pilgrim. She has published widely in such places as The Nation, The New York Times Magazine, The New Republic, and Poetry Magazine. Swander lives in an old Amish one-room schoolhouse, and raises sheep, goats, and a large organic garden. www.maryswander.com, www.agarts.org.

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# *The Maverick M.D. – Dr. Nicholas Gonzalez and His Fight for a New Cancer Treatment*

## The Authorized Biography by Mary Swande

"Babies calling Babies," Nick dialed Mary Beth on the phone at the end of the day on September 4, 2008. Both Nick and Mary Beth referred to each other by the nickname "Babies," and he always called her just before he was about to go out the door of his office and depart for home – often as late as 8:00 or 9:00 P.M. When Mary Beth received the call, she started steaming vegetables for their dinner, and as soon as he arrived, they would sit down to eat together.

Immediately, on the other end of the line, Mary Beth could tell that Nick was upset, more upset than usual in these long grueling years of the clinical trial. "What's wrong?"

"It's over," he said.

"The trial?"

"The trial, my research, my practice, my career. Take your pick."

"What happened?"

"Tell you when I get there."

Briefcase in hand, Nick walked up Fifth Avenue toward his apartment building as he did most nights, his shoes clicking the pavement of the sidewalk. Past Saks Fifth Avenue, Tiffany's, and Trump Tower, Nick got angrier and more worried with each step. The trial had already done damage to his reputation. The word was out about the purported results and his numbers of new patients were down. His expenses were up. The cost of his office suite climbed every year as did his malpractice insurance. His apartment, too, wasn't cheap. But most of all, his twenty years of research were over. Tanked.

And scores of cancer patients could potentially be denied a therapy that might save their lives. Science. He believed in the tenets of sound science with each molecule of his being. But was this clinical trial science? Or biased manipulation of the facts? Oh, yes, he knew what he was in for before he even hung out his shingle. He'd seen what Kelley had suffered. He'd churned it over and over again in his mind throughout the years. Kelley was an eccentric dentist in Texas. Nick was an Ivy League-trained physician in New York City. A world of difference.

Nick loved and had the upmost respect for the medical field. He was part of the establishment. He wanted nothing more than to be a researcher at Sloan Kettering right now. Twice, not once but twice, Sloan Kettering had offered him that job that he so desired. But there were strings attached, always the same strings. He could only research conventional treatments, not this nutty Kelley thing that included coffee enemas. Oh, no, no, no, not enemas, heaven forbid! Tell that to Florence Nightingale. Nick had turned down the plush Sloan Kettering jobs to do his Kelley research. How could the medical world be so blocked that they would have no interest in a protocol that is saving lives? How could the medical world, the reputable, distinguished scientists behave this way? How could any human beings, period, behave this way?

With each step up Fifth Avenue, Nick was falling into a darker and darker mood, a mood that only Dr. Hans Moolenburgh had been able to address in the past. Yes, maybe he would try to call Hans tonight … On second thought, maybe he would just fold his practice right now. Call it quits for good. What was the use? Here he was left to fend for himself, to try to do his own research. How did he pay his bills? Not through the support of a grand institution with health insurance and benefits, labs and assistants, but through a private practice, a demanding practice filled with very ill patients who flew in to New York from all over the world. Here he was working day and night, every weekend and most holidays, to try to advance science. He just wanted a chance to prove his theory in a conventional way, through a clinical trial, through the rigors of the medical model. Then he wanted some free time, please God, just a couple of hours a day of free time to write about his program and get the word out to the public.

Mary Beth met him at the door with the "Babies dance," but she knew that as much as he loved the greeting, this time it wasn't working to elevate his mood. Nick slumped down at the kitchen table, and he and Mary Beth ate organic roasted chicken and steamed vegetables. He told her about Dr. Andreason's short response that he had received that afternoon.

"The OHRP has closed their case. There is no more recourse," Nick said. Mary Beth knew full well the implications of the actions of the OHRP. This was the final appeal. The final bundle of documents supporting his case had been sent long ago. Now Nick could no longer throw himself into writing rebuttals. His work at the computer had been a stress release as well as a necessary defense. Now what?

After their meal was finished, Mary Beth thought a little television would take his mind off of work. She knew not to suggest they watch a movie as she didn't have anything on hand that she had pre-screened. So she clicked on Fox News. They sat together on the sofa and watched, but Nick soon became irritated and yelled at Bill O'Reilly on the TV set.

"What in the world are you saying?" he shouted. Nick, a Reagan Republican, thought the party had recently taken a wrong turn. He walked out of the room, leaving Mary Beth to click off the set.

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## The Maverick M.D.

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It was too late to call Hans – still in the middle of the night in the Netherlands. So Nick sat in his study and took solace in his Bible, reading favorite passages that tended to calm him. The Psalms were usually his first stop. His Bible open on his lap, he let the words sink down into his body and his soul.

*I want you to trust in times of trouble, so I can rescue you and you will give glory to me*. (Psalm 50:15).

At last it was time for bed. Tomorrow was a busy day with patients, and he knew he needed his rest. Mary Beth was already in bed, so he sat on the edge of the mattress and pulled out a stack of letters from the bedside table, cards of appreciation and letters of acknowledgement, thanking him for what he had done, from patients and colleagues.

*Dear Dr. Gonzalez:*
*Thank you so much for your brilliance and guidance throughout my illness. I'm so thankful to be on the other side of it now…*

*Dear Nick:*
*Thank you for your dedication and hard work. You've done brilliant work in cancer research and deserve the Nobel Prize…*

On and on the letters went. Nick read through the whole stack, fingering their pages. He read some of them a second time. He smoothed the sheets and pressed the letters back into their envelopes. He arranged them in a pile, larger envelopes on the bottom, smaller ones on top. Finally breathing more deeply, he slipped under the covers next to his wife, as if he were folding himself into a sealed and secure space, drifting off to sleep.

A few weeks later, the stock market crashed on September 29, 2008, and an air of panic spread through New York City. Consumers all over the United States worried about their savings, their pensions, their mortgages, their jobs, and how they could make ends meet. People doubled up on housing. Young adults lived in their parents' basements. More homeless appeared on the streets. People everywhere tightened their belts and spent less. Many who had wanted to become Gonzalez patients, held off, due to the out-of-pocket expense. Once again, Nick thought he might just have to close his office.

But Congressman Burton wouldn't let Nick nor the case rest. on October 31, 2008, Burton, dissatisfied with the progress of the government investigations thus far, wrote to the Inspector General Daniel R. Levinson of the Department of Health and Human Services, the official with the power to authorize investigations of institutions and individuals engaged in government-sponsored research. Burton summarized the history of the study, then requested the IG open a formal evaluation of the trial's management.

In the meantime, fired up again, Nick arranged a meeting with Dr. Josephine Briggs, the new director of NCCAM in Bethesda, and a date was set for December 12, 2008. Nick hoped to brief her on all the many snafus in the trial, the OHRP report, and the managerial problems that had derailed the study. Nick also asked to bring along his patient in the Washington, DC, area who had accompanied him to the meeting with Senator Harkin.

# Letters to the Editor

## Azithromycin COVID Treatment

I understand why Dr. Gaby may believe that the use of hydroxychloroquine as a treatment for COVID-19 was mishandled, especially, unlike most drugs, the cost of administration is low; however, his conclusion of recommending hydrochloroquine in conjunction with azithromycin, has no basis. No where does he show any studies of the combo of these two drugs as being effective. That omission alone leads me to question the validity of his research and conclusions.

I was given azithromycin as a preventative antibiotic and developed an adverse reaction to the drug. I was poisoned by Zpack (as it is known). My liver enzymes skyrocketed, my bilirubin was off the charts, and my liver and gall bladder shut down from the poisoning. This is relatively uncommon in the population, but it does occur. As this was a poisoning and not an allergic reaction, no antihistamine could help. In fact, there was no treatment. I was seen by the head of the liver transplant team at Columbia/Cornell Weill as, if I did not heal on my own, the only option was liver transplant.

Rhona Stanley, DDS, MPH, LicAcup, RD

## Request for Kruesi Paper

My late father, Oscar R. Kruesi, MD, gave a presentation at an American Biologics Conference on the island of Malta in the late 1990s to early 2000s. He wrote a paper titled "Histamine as a determinant of human behavior," published in the Conference Proceedings. The book was the size of a Sears catalog, white paper cover with light blue AB logo on the front.

I am asking readers of the *Townsend Letter* if they attended that conference or know someone who did. If so, if they still have a copy of the Proceedings, my family would greatly appreciate a photocopy of the paper by Dr. Kruesi. We are happy to reimburse the expenses for photocopy, postage, etc.

Thank you very much for making this request known to your audience.

William K. Kruesi, DVM (retired)
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While preparing for the Briggs meeting, Nick received a letter from Dr. Dahlberg, the director of the Office of Research Integrity, a division of the US Department of Health & Human Services to whom he had appealed in 2006. The ORI reported that Nick's concerns about the consent process, the changes in protocol, and the conflict of interest did not fall within the department's legal jurisdiction. Nick shook his head. He couldn't understand what he was reading. Where else was he supposed to go with these concerns?

*Tap, tap, tap*. Nick began again, drafting a 16-page letter to Dr. Dahlberg. Once more, Nick outlined, then carefully documented all the areas of concern, from the Columbia team's attempt to publish the article about the trial, to Dr. Chabot's false statements in the article that Nick had withdrawn from the study, to Dr. Chabot's inappropriate down-staging of five nutritional patients. Nick bundled up the material and sent them off to Dahlberg, settling down for what he assumed would be another long wait.

On December 12, 2008, Nick, accompanied by his patient, pulled open the heavy glass door to the NCCAM headquarters, located on the sprawling NIH campus in Bethesda.

"I was not aware of all these issues in your clinical trial," Dr. Briggs told Nick, sitting across from him at the table. Dressed in a smart dark suit, her blond hair parted on the side, gold earrings accenting her rounded face, Dr. Briggs was a pleasant, open-minded person who graciously discussed Nick's problems with the study. "No, I'm afraid I haven't been debriefed about your study. But I hope that we can all look forward instead of backwards from now on."

Nick explained out the basic protocol of the study, and Dr. Briggs did agree that clinical studies investigating nutritionally based treatments for disease required a more flexible design.

"I don't think a simplistic comparison of Drug A to Drug B format would be suitable for evaluating your program."

Briggs then became intrigued by Nick's patient's story. She listened carefully to his tale of recovery from cancer through the Gonzalez program.

After forty minutes, Briggs concluded the session by turning to Nick and saying, "I hope that you will be willing to share your experiences with others at NCCAM and NIH, so that we might all learn from the mistakes made during your eight-year effort."

Several days later Nick wrote to Dr. Briggs thanking her for the meeting and enlarging on some of the points they had discussed. On December 30, 2008 she wrote back, thanking him for coming down to Bethesda:

> *I very much enjoyed our conversation. It is clear to me that you have a deep commitment to your patients and to exploring innovative methods to help with this terrible disease.*

She then said that NCCAM was beginning its strategic planning process, and in the future, she would invite Nick to come and share his thoughts on how they might conduct clinical trials more effectively.

Nick replied that he was most willing to return to NCCAM and share his experiences with her staff.

But he never heard from Dr. Briggs again.

In late January of 2009, Inspector General Levinson wrote to Congressperson Burton. Levinson informed Burton that he had referred the concerns about the clinical trial to their Office of Investigations. Burton's staff told Nick that she thought this a good sign as the Office of Investigations, with limited funding, only pursued a small number of complaints.

Dr. Dahlberg's letter came next on February 2, 2009, responding to Nick's 16-page letter and supporting documents:

> *The Division of Investigative Oversight (DIO) within the Office of Research Integrity (ORI) has received your letter of November 24, 2008. While your letter contains information that could lead to an inquiry into research misconduct, that inquiry and the related fact finding must be conducted by the institution.*

So now we're going around in circles again, Nick thought. I'm to go back to Columbia? Columbia who was supposed to have investigated the trial for the OHRP? Columbia whom Nick hadn't heard from in two years? Even after he had written to them about the aborted attempt to publish the *JAMA* article?

"Babies," he said to Mary Beth that evening. "Babies, Babies, Babies. I've been sent on another wild goose chase."

After dinner and mulling over Dahlberg's letter for a while, he finally decided no, he wasn't going back to try to appeal to Columbia. He would leave the matter in the hands of the Inspector General.

Nick slumped down in front of the television set and yelled at Bill O'Reilly. ◆

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

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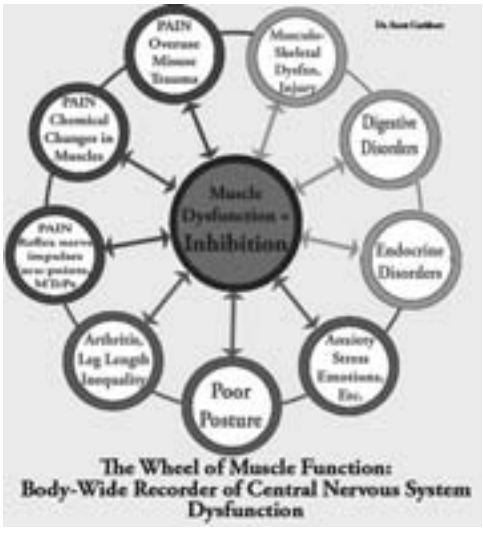
# Print Edition: *Introduction to the History of PAK Around the World, Part 1*

**The history of Professional Applied Kinesiology is available online at www.townsendletter.com.**



The Wheel of Muscle Function: Body-Wide Recorder of Central Nervous System Dysfunction

In this long-awaited history about the growth and spread of Professional Applied Kinesiology (PAK) around the world, thirteen contributing authors and teachers of this manual diagnostic technique tell the story of PAK's growth on each of the continents of the world and its penetration into allied natural health care fields. This story documents the detailed, colorful journey of the permeation of AK manual muscle testing (MMT) methods and philosophy into the daily practice of hundreds of thousands of clinicians. Illustrated throughout with historical pictures covering over five decades, this is the first comprehensive history of PAK.

Dr. George J. Goodheart, Jr., the founder of Applied Kinesiology®, showed how the muscle system is the most exposed part of the nervous system. Diagnosing neuromuscular problems with manual muscle testing has proven to offer a great appeal to clinicians from all the healing disciplines, as evidenced by the fact that there are today an estimated 1 million clinicians who use some or all of Goodheart's PAK method. From the chiropractic colleges in the United States, to the osteopathic and chiropractic colleges across Europe and Australasia, to massage and acupuncture and naturopathic colleges, PAK methods have been uniquely successful in reaching health care professionals and their patients around the world today.

Applied Kinesiology has looked beyond the chiropractic profession to the fields of biomedicine, osteopathy, naturopathy, physiotherapy, acupuncture, dentistry, nutrition, biochemistry, and others for methods to increase the health and well-being of patients based on using the body itself as a diagnostic tool.

This history details the intimate whys and the hows of a single chiropractic and alternative health care technique's journey across the world and answers the question about why it has been taken up by physicians from a great number of healing disciplines. PAK is a microcosm of the entirety of alternative and complementary medicine (a grassroots rebellion against hospital-based and allopathic medicine). It's a true romance and an intense social-political story unique in the history of the healing arts.

Dr. Scott Cuthbert is a chiropractic specialist at Intercare Chiropractic Clinics (Makati Manila, Philippines). He is the author of *Whiplash Dynamics and Manual Muscle Testing* (2020), *Applied Kinesiology Essentials: The Missing Link in Health Care* (2018), and *Applied Kinesiology: Clinical Techniques for Lower Body Dysfunctions* (2013) Dr. Cuthbert is a 1997 graduate of Palmer Chiropractic College (Davenport, Iowa) and practices in Makati Manila, Philippines. He has published 15 Index Medicus clinical outcome studies and literature reviews, and 50 peer-reviewed articles on chiropractic approaches.

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# The Censorship Pandemic

Over the past few years, I have noticed a marked increase in tactics that limit access to medical information that challenges the pharmaceutical-corporate status quo. Research studies about vaccine safety have been withdrawn from publication,[1,2] a researcher who studies aluminum neurotoxicity was defunded,[2] and Google has developed algorithms that hide non-pharmaceutical treatments.[3] During the 2020 pandemic, censorship has heightened. Suppression of information that does not concur with official views has taken many forms.

Back in March, respected Stanford professor John Ioannidis, a researcher in statistics and biomedicine, was castigated in the press for questioning the models that predicted a 3-4% death rate from COVID-19.[4,5] His opinion that lockdown measures would cause more harm than the virus itself – an opinion consistent with his "longstanding body of work" on the harms caused by medical interventions – was widely disparaged in media.[5] A few weeks later, he published a study with 16 co-authors, using real data from Santa Clara county, California; the study estimated an infection fatality rate of 0.12-0.2%, which is slightly lower than estimates from other studies.[5] This study was heavily criticized and discounted as being part of a political agenda.

Minnesota state senator and practicing family physician Scott Jensen was reported, anonymously, to the state medical board for "spreading misinformation on a regional tv station…claiming that the Minnesota Department of Health instructed providers to list COVID-19 as the cause of death on death certificates regardless of whether a patient died of COVID-19."[6] During the TV news report, Jensen explained that the Minnesota Department of Health (MDH) had sent an email to physicians, such as himself, that said "COVID-19 should be reported for all decedents where COVID-19 caused, is assumed to have caused, or contributed to death." The MDH email also provided a link to a CDC seven-page document that said "it is acceptable to report COVID-19 as the cause of death without laboratory confirmation if the circumstances are 'within a reasonable degree of certainty.'" In his response to the medical board, Jensen wrote: "…the initiating disease in the train of events leading to death has long been the basis for data and statistical compilation so as to inform public health policy, legislation, and even funding for disease control initiatives….I was alarmed that the nature of the April 3 MDH email seemed to 'coach physicians' to complete death certificates in a manner outside standard practices and protocols."[6] The medical board dismissed this complaint. Six weeks later, Jensen received notice of yet another anonymous complaint to the medical board for making "misleading" statements about COVID-19 in another video.[7]

While mainstream media have closely followed government officials' call for social distancing, mask wearing, and lockdowns until a vaccine becomes available, possible treatments have been censored and/or discredited. Reporters ignored reports about MATH+, an integrative protocol developed by critical care clinicians (https:flaccc.net) – even though one of the doctors, Dr. Pierre Kory, testified about its effectiveness in treating hospitalized patients before the US Senate Committee for Homeland Security and Government Affairs on May 6, 2020.[8]

US Federal Trade Commission ordered David Brownstein, MD, "to stop making any statements about… treatment protocols of Vitamins A, C and D as well as nutritional IV's, iodine, ozone and nebulization to support the immune system with respect to Coronavirus Diseases 2019 (COVID-19)."[9] As a result, Dr. Brownstein posted on his website, "What this means is that I will not be able to blog, post, tweet, email, etc. for awhile."[9]

In July 2020, America's Frontline Doctors, a group founded by Simone Gold, MD, JD, faced censorship and smears after holding press conferences in which practicing physicians related their experiences when using hydroxychloroquine to treat COVID-19 patients.[10] The group also videotaped a two-day White Coat Summit during which practicing physicians related their experiences and concerns about official COVID policies. Facebook and YouTube removed the press conference video, seen by over 15 million people. Twitter "forced" them to remove physicians' video testimonials.[11] Squarespace, the group's web host, removed their entire website; the group had to re-build on another site. The doctors were smeared across corporate and social media as conspiracy theorists and for providing "medical misinformation." Simone Gold, who has served as an emergency room doctor for 20 years, was fired from her job for appearing at the White Coat Summit. She has hired a lawyer.

In September, a group of Philippine doctors who have used inexpensive treatments to treat early stage COVID tried to publicize the available treatment resources and the terrible economic and health consequences from the ongoing lockdown of their citizens.[12] Like America's Frontline Doctors, the Philippine practitioners were smeared and threatened with criminal lawsuits, according to integrative physician Homer Lim, MD. Media failed to report about the treatment options. Andrew W. Saul, PhD, was unable to share Dr. Lim's report on Facebook: "When I (AWS) posted Dr. Lim's protocol on Facebook, I was immediately banned by

Facebook from further posting of any kind for 30 days."

I have come to believe that censorship and the smear campaigns against the doctors and researchers who question the prevailing COVID-19 narrative is far more dangerous to our health than the virus. If the only permitted response to a health crisis is the one espoused by government agencies (and their corporate allies), we can expect to lose access to any form of alternative or integrative care. The doctor-patient relationship will be overseen by bureaucrats that follow agency laws. Moreover, real-world observations by practicing doctors – which have historically been a primary source for improvements in medical care – will be squashed. Doctors who dare to step outside the prescribed guidelines in order to offer individualized care will be called before medical boards and lose their licenses. California has already passed a law (SB 276) that limits the number of medical vaccination exemptions that a doctor can write without attracting medical board attention.

Censorship, smear campaigns, job loss, medical board complaints, retaliation from government regulators – these are deterrents that produce the greatest threat: self-censorship. Fear of persecution understandably prevents practitioners from publicly disputing government/corporate medical care. But as Scott Jensen says in his September 6, 2020 video, "This is not the time to stay silent."

And there is strength in numbers. If you are concerned about censorship, particularly censorship in medicine, find and support the groups that are trying to shine light on the information that corporate media wants to hide, groups like Physicians for Informed Consent (https://physiciansforinformedconsent.org/). And share information with others.

As Scott Jensen, MD, said in his September 6 video, "…COVID-19 has opened a door into a tremendously vicious non-discussion." It is an opportunity that we need to seize.

Jule Klotter

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# Ask Dr. J

**by Jim Cross, ND, LAc**
**thias1020@yahoo.com**

## Urban Myth Or Scientific Fact

My senior English teacher in high school, Father Becker, taught me two valuable lessons:

- To really ascertain the truth, you need to lift the rug up and look underneath it for what is really taking place.
- Always follow the money.

So, I am going to follow Father Becker's two golden rules and attempt to verify that SARS-CoV-2 is really a genetically engineered virus and not the result of a spontaneous mutation in the wild that created this infectious monstrosity.

To this point, researchers understand that the possibility of a lab escape of a pathogen such as COVID-19 was a plausible, if hypothetical, possibility. Just a conspiracy theory it most definitely may not be.

Bats are proven to be natural reservoirs for many zoonotic viruses that are now materializing in humans.[1] Zoonotic viruses are microbial diseases spread between animals and people. Intermediate hosts are usually needed to amplify a zoonotic virus so that it can then be transferred to humans, but direct bat-to-human transmission was shown in a Nipah virus in Bangladesh.[2] Research has documented the ability of different coronaviruses (CoVs) to infect the same bat species and the propensity for genetic recombination among these dissimilar CoV's.[3,4] Thus, it is not a gigantic leap to see that bats are a prime candidate for CoVs to mix and create novel CoVs. It is also entirely possible that it's only a matter of time before one of these recombined viruses would make the cross species jump to humans.

So, various CoVs could have been percolating in bats, natural genetic recombination could have occurred, and presto SARS-CoV-2 could have emerged from this witch's brew of viruses and jumped to humans. By coincidence, there happens to be not one but two virology institutes in Wuhan: The Wuhan Center for Disease Control and Prevention/WHCDC and The Wuhan Institute of Virology/WIV. WHCDC is a biosafety level 2 (BSL-2) lab, and WIV is a BSL-4.[5] Basically, a biosafety lab researching non-lethal agents would be considered a BSL-1. One working with microbial agents that can cause severe injury and death to humans would jump to a BSL-4 with BSL-2 and BSL-3 being somewhere in the middle. Preventing inadvertent introduction of microbes being experimented on from a BSL-4 lab into the natural environment would be of extreme importance. Workers in BSL-4 labs are required to shower and change clothes before and after each shift and wear ventilated protective suits with booties and face masks. Incoming and outgoing air is filtered, and water and waste are treated before exiting the facility.[6]

In addition, both WHCDC and WIV have conducted extensive research on novel bat viruses and maintain large research collections of novel bat viruses. WIV also houses bat virus RaTG13, which is the most closely related virus to SARS-CoV-2. RaTG13 was isolated in 2013 and its genome published on 23 January 2020. Also, at WIV, laboratory animals are infected with bat viruses.[5]

According to accepted theory, there was an intermediate host between the contaminated bats in the wild and people at the Wuhan fish market. A study in *The Lancet* notes that an intermediary host for SARS-CoV-2 hasn't been identified; and prior to the closing and sanitization of the Wuhan fish market, none of the possible intermediary animals were sampled. The same study also showed that 14 of the original 41 SARS-CoV-2 infected people had not visited the Wuhan fish market, which included the very first recorded case on 1 December 2019.[5,7]

Next, let's look at the remarkable stability of the virus, whose genome had barely changed from the earliest human cases, despite trillions of replications. If the virus had leapt from animals to humans in the market, it should have immediately started evolving to life inside its new human hosts. But it hadn't. Literature on the 2003 SARS virus, which had jumped from civets to people, mentioned its rapid evolution in its first months of existence. Observations from the cited article suggest that, by the time SARS-CoV-2 was detected in late 2019, it was already pre-adapted to human transmission to an extent similar to the late SARS-CoV. Next, these researchers pulled up the genomes for the coronaviruses that had been found on surfaces in the Wuhan seafood market. Were they at all different from the earliest documented cases in humans? No, they were 100 percent the same. The new virus looked a lot more like late-stage SARS. This definitely suggests the possibility that the virus originated from a lab where it had

been trained on human cells.[8] I love puzzle endorphins and fitting their pieces together!

So, what exactly are scientists trying to accomplish in these BSL-4 labs? They are attempting to utilize gain-of-function (GOF) studies in their research to improve the ability of a pathogen to cause disease, which can redefine the fundamental nature of that specific human/pathogen interaction and which could create the possibility of an epidemic with accidental release into an urban area. In GOF research, scientists are repeatedly passaging a bat virus through animal and/or human cells attempting to engineer specific genetic sequences into the virus.[9] These GOF studies then are possibly entailing biosafety and biosecurity risks and need to be better evaluated as to their safety.

By repeatedly passaging the bat virus through animal/human cells, the bat viruses can be forced to adapt and more easily infect human cells. This is accomplished by forcing the bat virus to increase the strength of binding of the coronavirus's spike protein to human ACE2 receptors, which also reduces its strength of binding to a bat ACE2 receptor.[10]

As these viruses are spending a large amount of time in a culture, they can also acquire other random mutations that don't affect their virulence. Now you have created a virus that more readily binds to ACE2 receptors but not one that resembles the original bat virus. The acquired random mutations can hide the signature of a human gene jockey's work in manipulating the virus to nefarious ends.[10]

Is there substantiated evidence of GOF research? After the 2002-03 SARS coronavirus outbreak, the National Institutes of Health funded a multiple center research effort, involving Chinese scientists, US military virologists from the bioweapons lab at Fort Detrick, and the National Institutes of Allergies and Infectious Diseases/NIAID (which just happens to be under the direction of our esteemed Dr. Anthony Fauci), to prevent future coronavirus outbreaks by studying the evolution of virulent strains from bats to human tissues. GOF research was included in this effort, which entailed creating COVID viruses more lethal and transmissible than wild COVID ones.[11]

Sometimes our government mysteriously works in positive ways. In 2014, the US instituted a temporary pause on funding GOF experiments after a series of lab accidents induced 300 global scientists to sign a petition banning these types of experiments. Unfortunately, there were exemptions to this pause as it only prohibited GOF research in US labs. From 2014-16 the Fauci-led NIAID continued funding GOF research at the Wuhan lab, and the ban was eventually lifted in 2017.[12-14]

Unfortunately, humans can be less than stellar in their precautionary behavior. Thus, the possibility exists of a lab accident where there was direct transmission of a virulent bat virus to a lab animal and then to a human or improper disposal of lab animals and/or lab waste and inadvertent human contamination.

The real question is why people would wish to engage in research with the possibility of creating super microbes that could lead to widespread illness and death. To ascertain that answer, maybe we should all listen to a really old Bill Cosby riff, "Why is there air?" Rational explanations exist for the explanation of why there is air and why people feel money is more important than human and planetary health. Unfortunately, humans just seem to prefer engaging in irrational behavior instead of protecting the health of this incredibly beautiful planet and of its eclectically, diverse inhabitants.

So, urban myth or scientific fact? Will the future give us an answer? Hopefully, but don't count on it. If there was a second or third JFK shooter, no one has ever squealed. Any extra JFK shooter(s) would probably have been in a shallow grave somewhere in the desert in a few hours afterwards anyway, but the shooters' shooter(s) hasn't/haven't talked either. So, unfortunately any scenario can and is possible. With regards to SARS-COVID-2, hopefully, someone in the know will eventually squeal!

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# Pediatric Pearls

**by Michelle Perro, MD**

## From Pineapples to Pomegranates: The Tale of Two Fruits and Infertility in Men

Pineapples have become the symbol of trying to conceive and get pregnant. They appear on IVF instagrams, chats, blogs, and have been likened to "womb warriors." Whether it is the bromelain enzyme in the pineapple that can help promote embryo implantation from an anti-coagulation perspective, or possible anti-inflammatory effects, or perhaps it's the crown-like prominence representing the need to stand tall walking in the fields of infertility, I wasn't quite clear about the symbolism but liked the fruity metaphor.

But why talk about pineapples?

One of the joys of being a pediatrician is you get to witness your patients grow up and return to see you with their own kids. I was alerted to a social media post by Maria, (having moved from California back to her home town in Illinois), a previous patient from 30 years ago, adorned with pineapples and sadness. Maria and Ron were trying to get pregnant for the last three years and were diagnosed with infertility. Ron was found to have a slightly low sperm count by a reproductive specialist, but no other findings. Maria is emblematic of an integrative practitioner's dream by maintaining a pristine diet, being well-versed in self-care and deemed fertile. Ron was more of a challenge, and he made it quite clear that he didn't buy into my treatments which he felt weren't "scientific." At that juncture, I couldn't decide what would be my biggest challenge: infertility or dogmatism? However, they agreed to proceed with an integrative approach as a couple to conceive at Maria's behest.

While infertility may not quite be in the realm of pediatrics, over the years I've cared for many adults with the same holistic principles of integrative medicine as I do for little ones. What has been the guiding light to understanding the root causes of dis-ease often lies in the history as I was taught in medical school eons ago. Usually embedded somewhere in the patient's story/journey, the key to unraveling the mystery awaits. In the tradition of full disclosure and my New York-no-nonsense background, I did relay my trepidation to the couple about venturing into an area that was not my usual domain or terrain, but we jointly decided to proceed.

A quick look at the rates of infertility will help us understand the scope of the problem. Infertility is on the rise. According to the US Department of Health and Human Services (HHS.gov), 12-13 couples out of 100 have trouble conceiving, with both men and women each accounting for one-third of the causes of infertility. The remaining one-third are due to "undetermined causes."[1] Global rates of infertility are also scaling up affecting 15% of couples. However, this number is an amalgam and may not accurately reflect specific countries or regions.[2]

Ron had consulted many specialists, which made my job a lot easier. Sperm disorders such as shape and movement, oligospermia (low sperm numbers) and azoospermia (absence of sperm in the ejaculate) were evaluated. The usual list of other potential causes was assessed and eliminated such as genetic disorders, smoking/alcohol consumption, obesity, certain medications, varicoceles, autoimmune issues (making antibodies against his own sperm) and retrograde ejaculation. In general, there are four main causes of infertility in males, including gonadal disorders (30-40%), sperm transport disorders (10-20%), hypothalamic or pituitary disorders (1-2%) and unknown causes (40-50%). Ron was found to have no discernible cause. Thus, for the majority of men like Ron, the causes of infertility are unknown. Is that true?

Despite initial reluctance by Ron, he made it clear that he really wasn't too excited by the assisted reproductive techniques offered by the consulting urologist. A little research on my part revealed an invasive list of procedures and treatments are now being offered for male infertility, such as In Vitro Fertilization (IVF), Intracytoplasmic Sperm Injection (ICSI), Sperm Retrieval (via Testicular Fine Needle Aspiration (TFNA)), Percutaneous Epididymal Sperm Aspiration (PESA), and Microsurgical Epididymal Sperm Aspiration (MESA).[3] It was difficult to hide the look of horror on my face despite being behind the screen-cloak of our virtual appointment regarding some of the therapies out there.

Even with the fear of becoming a millennial meme of 'glyphosate gal', I took an in-depth dietary history and stepped

back on the soap box of the role of dietary pesticides and GMOs and health. Several glaring potential factors of Ron's reproductive issue became apparent, including a diet debacle of sneaky take-out and junk food, emblematic of GMO/glyphosate-enriched, nutrient-deficient diets. Additionally, an Environmental Health Questionnaire (with a nod to NAEM)[4] revealed a golf addiction of three times a week with toxic fairways, adding another layer to be uncovered and addressed of possible exposures to reproductive toxicants.

Ron was also a techie/data guy and wanted to see proof that fertility can be linked to toxic exposures whether from his diet and/or the environment. I ordered a glyphosate urine test, which showed his level to be 2500 ppb: extremely elevated! I provided him with research papers showing that ultralow doses at 0.1 ppb of glyphosate caused nonalcoholic fatty liver and kidney disease in rats.[5] We also discussed how glyphosate at high doses exerts toxic effects on sperm motility and DNA fragmentation, which could be affecting his fertility as well.[6] Although there are some "organic" golf courses now emerging, most golf courses apply a cocktail of pesticides. A classic paper from *Long Island Golf Courses* revealed the usage of 20 fungicides, 21 herbicides and 8 insecticides.[7] What is particularly concerning is that combined effects of pesticides have anti-androgenic effects likely through the androgen receptor binding affinity of pesticides.

Ron was willing to try a treatment plan for three months. We did the usual dietary/environmental cleanup advice and connected him to a website that deals with vetting self and home-care products from an environmental/health perspective as well as personal clean-up, with a focus on pre-pregnancy.[8] I included fermented foods in his diet, particularly apple cider vinegar and sauerkraut, both containing acetobacter (one of the few microbes that can metabolize glyphosate). (Note: A recent ecological study recently published showed that countries that had higher consumption of fermented vegetables demonstrated lower mortality rates from COVID-19.)[9]

The first baby steps are to reduce the toxic allostatic load. We then focused on a homeopathic detoxification plan, which included the homeopathic detox kit for organs/joints/CNS, and Metab (https://desbio.com). Ron was willing to cut back on golf and shower immediately upon returning home. I also had him take homeopathic Addiclenz (https://desbio.com) two times a day to offset the toxic load exposure.

Ron's overall health quickly improved and within the three-months' time he allotted, he lost 16 pounds, started sleeping better, and had renewed energy. I cautioned that there should be no unprotected nookie-nookie during detox and preferred to wait at least six months before even thinking about baby making. A year later, however, still no baby and Ron and Maria were discouraged. At that time, I was researching the role of the placenta and whether there was a placental microbiota. Hmmm? Could there be bacteria harbored in the male reproductive system that could result in DOHaD (developmental origins of adult disease and health)? There is some speculation as to whether *Propionibacterium acnes* (the causative agent of chronic prostatitis) may be a factor and I decided to pursue that route.[10]

There is a time where practitioners act on their cumulative experience, embracing gut-brain sensors, literature searches and emailing with friends.[11] I decided to treat both Ron and Maria with herbal antibiotics for three weeks Biocidin® capsules (https://biocidin.com/products/biocidin-capsules), probiotics (https://microbiomelabs.com/home/products/megasporebiotic/), and included an overall overhaul of their oral care, including irrigation with hydrogen peroxide and tongue brushing. Again, no unprotected nookie-nookie.

Occasionally, serendipity and a little skill intervene on your behalf and Ron and Maria were pregnant four months later. They delivered a sparkling little boy at home with a midwife and I was honored to examine this healthy baby after a relatively uneventful birth. Whether there was a low-grade infection not discovered or an imbalanced seminal fluid dysbiosis (if this really exists) is not known, but the herbal antibiotic (along with its potential for dissolving biofilms) seemed to move the needle.

For thousands of years, pomegranates have been a source of not only food, but herbal medicine with its many seeds symbolizing fertility, since one fruit could produce many more. Ron and Maria's story takes us through *The Tale of Two Fruits*, hopefully leading to this couples' own cornucopia.

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# Curmudgeon's Corner

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

## Basket Weaving 101

A few years back, during a period of extended convalescence, I began building a canoe. Hesitant to invest money into a project I wasn't sure to finish, I initially scrounged construction materials from neighborhood alleys, a self-imposed requirement that slowed construction. Our COVID-induced home quarantine provided idle time to finish the boat. I recently caned the seat bottoms, a skill outside my prior experience.

Caning is closely akin to basket weaving, an activity long associated with those in need of mental rehabilitation, at least before the advent of psychoactive medications. The term basket-case is still used to describe someone in a less than ideal state of mental stability. I found my caning activity mentally soothing and slightly addictive and have started watching for an old caned chair in the alley that I might repair. It is easy to conceive that engaging in a simple repetitive act like caning or basket making could provide desirable benefits to mental function, especially in trying times.

The focused mental rhythm of weaving, the mental cross-crawl of moving the active strand over and under the standing strands seems like it could well be associated with improved cognitive function and emotional stability.

I recall that the late Terry Willard, PhD, who ran the Wild Rose Herbal School in Calgary, suggested knitting as a therapy for chronic fatigue patients. He rationalized that humans had made all of the materials needed for daily life with their own hands through most of human evolution and that deprivation of the nearly constant mind-hand-coordinated-activity that filled the lives of our ancestors through evolutionary prehistory might cause some deficiency in mental function. He likened the output handwork created as a balance to the mental input provided by stressful stimuli. I've always found this thinking appealing and still have no reason to argue against it.

Something unique happens to my mind when engaged in caning and I will assume basket weaving (my basket weaving supplies, recently ordered, have yet to arrive). My mind is actively engaged and attentive to outer activity yet at the same time my awareness is relatively undirected and goes to interesting places.

At this point in most articles, I typically pivot to review the scientific literature on whatever topic I am exploring, but much to my surprise there is almost nothing published in recent years on the therapeutic action of any craft activities. No one actually talks about baskets anymore; but there are various euphemisms that describe arts and crafts in our modern era. Shimada et al (2018) reported that 'individualized occupational therapy' was a useful adjunct in treating patients with schizophrenia. In their study individualized occupational therapy (IOT), consisted of a combination "… of effective psychosocial treatment programs that are very relevant to OT practice: motivational interviewing, self-monitoring, individualized visits, handicraft activities, individualized psychoeducation, and discharge planning."[1] But basket weaving? No, just " ... constructive handicraft activities with clear procedures and good feasibility, such as Japanese paper collages, plastic models, Japanese paper crafts, and jigsaw puzzles, were used in the handicraft activities program. Handicraft activities were implemented 3-5 times per week. Implementation time was about 30 minutes per session at the start of OT and was gradually extended to about 60 minutes."[1]

Using the search term "cognitive leisure activities" leads to a 2019 systematic review examining various activities and whether they impact cognitive decline in the elderly. The study's authors conclude, "Activities related to learning new skills, that cause strong intellectual stimulation and that include communication elements were considered particularly effective tools."[2]

It wasn't until I stumbled upon J. Laws' 2011 article, "Crackpots and basket-cases: a history of therapeutic work and occupation"[3] that I realized the search needed to extend further back in time and that we were not going to find evidence based support for

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this therapy. The practice of art and craft therapies dates back to an era when the opinions of respected practitioners took precedence; our current requirement of proven evidence-based efficacy had yet to emerge.

We need to turn back the clock more than a century to a time when art and medicine intersected or we might say, collided with one another. All the way back to the mid-1800s when John Ruskin and William Morris initiated the birth of the Arts and Crafts Movement in Great Britain. It is from them, if from anyone, that our still retained appreciation of basket making originated. Ruskin was of the belief that machines and factory work limited human happiness and urged a return to a more authentic and simpler way of life, a romanticized version of the Middle Ages where people made their livings engaged in cottage crafts. He judged the manufactured, factory-produced goods that were then becoming commonplace in the 1800s to be "… both aesthetically and morally unsatisfying because the worker was treated like an extension of the machine, completing only a part of the finished product." Little did he realize how far down that path we would go.

William Morris took up Ruskin's philosophy and ran with it, creating a decorative arts empire of textile, furniture and wallpaper designs (plus multiple books of poetry). He put the art into artisanal. Ruskin and Morris' philosophy and ideas about home furnishing styles crossed the Atlantic and became popular among America's well-to-do.

> Proponents were eager reformers celebrating nature, authentic experience, and honest design. Like their British contemporaries, they displayed a patrician contempt for the system of mass production, which was keyed to lower class tastes. They advocated the use of natural materials and processes and the purchase and use of handmade items that were straightforward and simple in design. Indeed, for some advocates, the Arts-and-Crafts movement meant quality of design as much as quality of life.[4]

This is no doubt the same cultural divide that we find today if we were to compare the worldviews of Whole Foods' shoppers with those found at Walmart. (I've mentioned William Morris before in connection with his wallpapers. The colorful dyes he used to manufacture the rich colors in his designs contained toxic amounts of arsenic, enough to create symptoms in inhabitants of homes papered with products of his manufacture.[5])

The Arts and Crafts Movement reached its high point at near the same time as the epidemic of neurasthenia swept across America. Although the term neurasthenia was first used in 1829, it wasn't until 1869 that George Miller Beard and E. H. Van Deusen of the Kalamazoo asylum, popularized the term as a medical diagnosis, even if they didn't quite agree on a definition.[6,7] Van Deusen thought the condition was caused by social isolation and a lack of engaging activity in rural women while Beard saw the condition as something busy society women and overworked businessmen were susceptible to.

Neurasthenia was often called a weakness of the nerves. At that time, medical thinking viewed the body as akin to an electrical machine with the nervous system distributing energy. The fast paced, rapidly shifting, modern world back then, with people living in big busy cities with so much stimulation led people to expend too much of their 'nervous energy' and they were left depleted. The resultant state of collapse was neurasthenia.

Possible symptoms of neurasthenia included headaches, muscle pain, weight loss, irritability, anxiety, impotence, depression, "a lack of ambition," and both insomnia and lethargy. Julie Breck writing in a 2016 issue of *The Atlantic*, describes neurasthenia, as, "… a disease of culture as much as of the mind and body. Beard thought that people in earlier societies could not have been neurasthenic because they weren't exposed to the modern things that depleted nervous energy, particularly 'steam power, the periodical press, the telegraph, the sciences, and the mental activity of women.'"[8]

Silas Weir Mitchell (1829–1914) developed an early treatment for neurasthenia in the mid-1800s. Mitchell, who began his medical career studying rattlesnake venom but ended up specializing in nervous diseases in Civil War veterans for most of his career, developed the Rest Cure to treat neurasthenia and hysteria in women. The Rest Cure involved six to eight weeks of isolation, bed rest, a high calorie diet, massage, and electrotherapy. For men, he suggested a very different approach. In his 1871 book, *Wear and Tear: Or Hints for the Overworked,* he suggested that neurasthenic men should strengthen their nervous systems by engaging in "a sturdy contest with Nature." This idea became known as the West Cure: neurasthenic men were sent out West to engage in vigorous physical activity, prolonged periods of cattle roping, hunting, roughriding and male bonding … and to write about the experience.[9] Teddy Roosevelt and Walt Whitman were both among the many neurasthenics who underwent this treatment.

These treatment ideas about neurasthenia reflected underlying beliefs in traditional gender roles that some of us today would find objectionable, what we might call historical medical misogyny. The thinking was that God created men to work outdoors, and if men spent too much time indoors, they were at risk for neurasthenia. Women were supposed to stay home tending their households; too active a social life and time spent outside of the home left women vulnerable.

As old fashioned as some of these ideas seem, we owe many popular conventions to the accepted views from that era on how to reduce risk of neurasthenia. Creation of our national park system is often credited to the belief that neurasthenics needed to retreat into nature to heal. Nature was a healing force, an idea that some of us still cling to.

Recess times in public schools were established out of fear that sitting too long in a classroom was bad for children's nervous systems. Activities such as bike riding, traveling for vacations, and sports leagues were popularized because of similar beliefs that they reduced risk of developing neurasthenia.[10]

In 1910 Herbert Hall, MD, opened a clinic in Marblehead, Massachusetts, promoting a 'workcure' for neurasthenia based on ideas borrowed from the Arts and Crafts Movement. A similar program was started in Worcester, Massachusetts, by Adolf Meyer. William Rush Dunton started one in Maryland. Patients spent a good part of their day engaging in art and craft activities. Apparently, this approach seemed to work well and spread widely. Residential workshops were created to both foster skill development and generate income through selling the items participants produced.

A textbook titled *Studies in Invalid Occupation: A Manual for Nurses and Attendants,* written by Susan Edith Tracy, was published in 1912. Tracy offered detailed descriptions of the arts and crafts training courses used at the Boston Nervine Hospital and her program was copied widely. The book became the

**Figure 1: Portrait of George Miller Beard, the 'father' of neurasthenia. (Wikimedia Public Domain).**

blueprint for training practitioners of what later became known as occupational therapy.

Curiously, or perhaps oddly, neurasthenia seems to have entirely disappeared in the United State by the 1930s. The diagnosis was dropped from the DSM in 1980. However, The *Tenth Revision of the World Health Organization's International Classification of Diseases* (ICD-10) continued to contain well-defined criteria for neurasthenia diagnosis.[11] Even if the disease disappeared in our country, it persisted and actually worsened for periods in other countries.

In Japan, neurasthenia is known as *shinkeisui-jaku*, meaning "nervousness or nervous disposition."[12] The condition is often treated in Japan with Morita therapy, which involves a period of mandatory rest and isolation followed by progressively harder work, leading to resumption of one's social role. This treatment, based on the work of a Japanese psychiatrist Shoma Morita, (1874–1938), has its basis in Zen Buddhism and is aimed at breaking the cycle of sensitivity and anxiety. The goal of Morita therapy is to 'have the patient accept life as it is.'[13] The Japanese practice of 'forest bathing', *shinrin-yoku*, has been part of their national health program since 1982.[14]

In China, neurasthenia remains a valid medical condition defined in terms of traditional Chinese medicine and the etiology, to no surprise, is described as a decrease in vital energy (Qi). There was a significant increase in neurasthenia cases in China during the Great Leap Forward during the 1950s to mid-1960s to the degree that it was considered a major national health issue.[15] Both exogenous and endogenous harmful factors reduce functioning of the five internal organ systems, (heart, spleen, liver, lungs and kidneys). In Chinese, neurasthenia is called *shenjingshuairou* (weakness of nerves).[16]

The dominant fatigue expected in our American version of neurasthenia is not required in China for a diagnosis. Three of the following five symptoms are required: "weakness," "emotional," "excitement," tension-induced pain, and sleep disturbance. The duration of illness must be at least three months, and one of the following must have occurred: disruption of work, study, daily life, or social functioning; significant distress caused by the illness; or pursuit of treatment.

Chinese immigrants to the United States appear to retain their tendency to develop neurasthenia and exhibit a symptom picture distinct from a US diagnosis of depression or other categories

**Figure 2: Portrait of Silas Weir Mitchell, the man behind the rest cure. (Wikimedia Public Domain).**

that have been suggested as equivalents. In a 1997 study, Zheng et al showed that Chinese immigrants to Los Angeles continue to display symptoms of pure neurasthenia.[17]

Modern medicine describes neurasthenia as having 'no organic basis', and the current assumption is that the condition was psychosomatic. That idea doesn't sit entirely well with me.

Historically, in many patients diagnosed with neurasthenia, their gastrointestinal symptoms predominated, and this subset of sufferers were typically diagnosed with "*neurasthenia gastrica.*" At the time, "… there was considerable debate as to how the gut interacted with the central nervous system in the development of these ailments. Some of these discussions may be seen as historical precedents for the current debates on the brain-gut-microbiota axis, particularly in relation to the so-called functional gastrointestinal disorders."[18] Other researchers argue that modern maladies such as fibromyalgia, chronic fatigue and depression are simply updated manifestations of the same disease.[19] There is little question that at least in today's popular wisdom that a spectrum of disease stretches between feeling stressed on one end to post traumatic stress disorder (PTSD) on the other extreme. Would neurasthenia fit somewhere on that spectrum?

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Assuming neurasthenia was something 'real' and not just in the sufferers' heads, there are questions that I am unable to answer. Is, or was, neurasthenia a matter of nature or nurture or something else altogether? Was it a disease of the times? Could there be a genetic component that predisposes some people to neurasthenia leaving them more vulnerable? Could it have been infectious, the aftermath of a bacterial or viral infection? We know today of some rather strange repercussions of parasitic infections that seem to take control of the host's behavior. Toxoplasma probably is the most famous of these.[20] Evidence is mounting that fibromyalgia has a genetic component[21] and that something distinct is chemically amiss in the blood of those with chronic fatigue.[22] A more primary question is whether neurasthenia is, or was, a real condition? If the many physical symptoms attributed to neurasthenia have no organic basis and were just psychosomatic, then we are left in an awkward place. Historically many fundamental beliefs of the naturopathic profession were developed parallel to the neurasthenic 'epidemic' in the US and many of the philosophic and treatment approaches we employ still reflect that history.

Our critics might say that naturopathic medicine evolved around treating an imaginary condition and has continued into the present day treating other imaginary conditions that have come along to replace neurasthenia. Think of the many conditions that we and our colleagues specialize in that have never been accepted as "real" by mainstream physicians. Many of these 'conditions' have come into and out of fashion over the years even in our own practices. We, of course, prefer to view our profession as on the cutting edge of scientific discovery and believe our colleagues are more accepting of new theories and treatments, long before mainstream medicine, but what if we are wrong?

Perhaps neurasthenia really was just some sort of psychosomatic illness that is triggered by stress? Symptom pictures of other psychological diseases do seem to evolve over time.

Basket weaving and the other arts and crafts seem to have been dropped from most modern occupational therapy training curricula. To this outsider, occupational therapy is now more about teaching patients how to perform activities of daily living after mishaps; accidents, strokes, functional degeneration and so on. I suspect the practice of arts and craft has become similar to the practice of spinal manipulation for osteopathic doctors, "something they used to do." No one is going to risk their academic career to study basket weaving unless one's goal is to win an Ignoble Award.

Some things may not need randomized controlled trials to prove their worth. (We don't need a control group to prove the worth of parachutes. Well, that has changed. In 2018 a RCT of parachutes was published and concluded that they don't make a difference in survival.[23]) While basket weaving isn't that popular, knitting is commonplace. Ask any habitual knitter if they would agree to willingly stop knitting for a few weeks so that you might assess changes in their mental well-being; their adamant refusal should convince you that they experience benefits they do not want to forego. Just the expression on their face should be adequate evidence.

While we don't have the sort of data on basket weaving that I had hoped to quote you, we can make some educated guesses. Consider other therapies once used to treat neurasthenia and what we know about the impact of those therapies on health. Spending time in nature was seen as curative. Today we know a lot about what nature exposure does to our physiology and mental health. If we make an educated guess that basketry does something similar, there's a good chance we will be correct.

Exercise was also considered therapeutic for neurasthenia—at least for men as part of the West Cure. To suggest that there might be a different response to the same treatment that might vary by the patient's gender is probably not worth our consideration these days.

Perhaps neurasthenia was an era appropriate response to stress. We now speak of "adrenal fatigue" in much the same way as doctors a century ago spoke about neurasthenia. In considering the older therapeutic interventions, the dramatic differences between Rest Cure and West Cure stand out and might have theoretical application. What would our modern equivalent be to a West Cure? What kind of impact would more time in nature, rigorous exercise, and fresh air have on adrenal dysregulation in contrast to enforced rest? Clearly, we will not segregate treatment prescriptions based solely on gender. Yet we might wonder if there is a dichotomy of possible treatments that we might segregate patients between. Is there a way to predict who might do better with rest and who would do better with a rigorous approach? One approach might lower cortisol demand and production while the other might increase it. Either approach might serve to rebalance hypothalamic function.

Whatever the case, I need to pause now and check our front porch to see if the UPS truck has dropped off my basket making materials that I am waiting for, somewhat anxiously.

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These examples may reflect the well-known bias in mainstream medicine against nutritional therapies. But they are more than that: they illustrate the fact that modern medicine too often delivers substandard care by failing to embrace safe, effective, low-cost treatment options. These two points are actually related, because being biased against nutritional therapies virtually guarantees that medical care will in many cases be substandard. That is because nutritional therapies are often safer, less expensive, and at least as effective as drug treatments.

As noted above, the practice of medicine continues to become more complicated and more specialized. Many doctors choose to become specialists so that they can be expert in at least one portion of the vast body of medical knowledge (and, of course, they also make more money). Ironically, however, achieving the best outcomes for patients often depends more on the doctor having broad knowledge of the basics than on being an expert in one narrow area. I am reminded of a patient I once saw, an adolescent male who had a five-year history of severe joint pain, as well as asthma, recurrent headaches, and severe abdominal pain. He was under the care of three different specialists for his various problems. None of these specialists had considered hidden food allergy as a cause of the patient's symptoms. I recommended an elimination diet followed by individual food challenges, which implicated corn as a major symptom-evoking food. On a diet free of all corn products his joint pains, asthma, and headaches resolved rapidly, and his abdominal pain improved by 90%.

Medical schools, residency programs, and specialty organizations should review their curricula to make sure that trainees achieve proficiency in basic aspects of medical care. It will likely remain an uphill battle to convince these programs to embrace elimination diets and certain other nutritional therapies. At the very least, however, trainees should be required to be knowledgeable about those nutritional therapies that have already made their way into official practice guidelines.

Alan R. Gaby, MD

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# Modern Medicine Neglects the Basics, Part 2

In an editorial in the January 2020 issue of the *Townsend Letter*, I reviewed research showing that as many as 50% of patients with heart failure have iron deficiency; and that iron deficiency, even in the absence of anemia, is a strong and independent predictor of mortality in these patients. I also cited evidence that correction of iron deficiency can improve functional capacity, symptoms, and quality of life, and decrease the number of hospitalizations for worsening heart failure. However, despite the strong evidence of its clinical importance, iron deficiency is not being adequately evaluated or treated in heart failure patients. In a retrospective study of 10,631 patients hospitalized in Philadelphia for heart failure, only 1.5% had adequate laboratory tests for iron status. Moreover, of the patients who were tested and found to be deficient, less than half were given an iron supplement.[1] The editorial concluded that the widespread incompetence regarding this basic aspect of healthcare represents a system failure in modern medicine. As medical care continues to become more complicated and more specialized, we must remember not to forget the basics.

Since the editorial was written, other examples of how modern medicine is overlooking the basics have appeared in the medical literature. One study examined the use of vitamin A in children hospitalized in the United States with measles. Several randomized controlled trials have shown that vitamin A can significantly decrease morbidity and mortality in children with acute measles infection. The American Academy of Pediatrics recommends using vitamin A in severe or hospitalized cases, and the World Health Organization recommends vitamin A for all acute cases. The recommended dosage is 50,000 to 200,000 IU per day (depending on age) for two days. The new study was a retrospective review of 142 children hospitalized for measles in 52 US children's hospitals that are considered "advanced" and that are said to adhere to "the most demanding standards of pediatric service." Only 47 of the 142 children (33%) received vitamin A. Of those given vitamin A, 62% received 10,000-IU doses and 13% received 50,000-IU doses. None of the children were given the dosage that is currently recommended for their age.[2]

Another study examined the use of intravenous magnesium in children aged 2-17 years who were treated for acute asthma in one of seven emergency departments in the United States from 2012 to 2017. Systemic reviews and meta-analyses suggest that intravenous magnesium improves pulmonary function in asthmatic patients and may decrease hospitalizations by as much as 30%. Based on this evidence, guidelines from the National Heart Lung and Blood Institute of the National Institutes of Health recommend intravenous administration of magnesium as adjunctive treatment for asthma in the emergency department. In the new study, intravenous magnesium was administered in only 10.5% of 61,854 emergency department visits for acute asthma. The median time from triage to magnesium treatment was 154 minutes (interquartile range, 84-244 minutes). Of 22,495 children who required hospitalization after emergency department treatment, only 25.7% received intravenous magnesium. Transient hypotension occurred in a small proportion of children receiving magnesium, but the treatment was otherwise well tolerated.[3]

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