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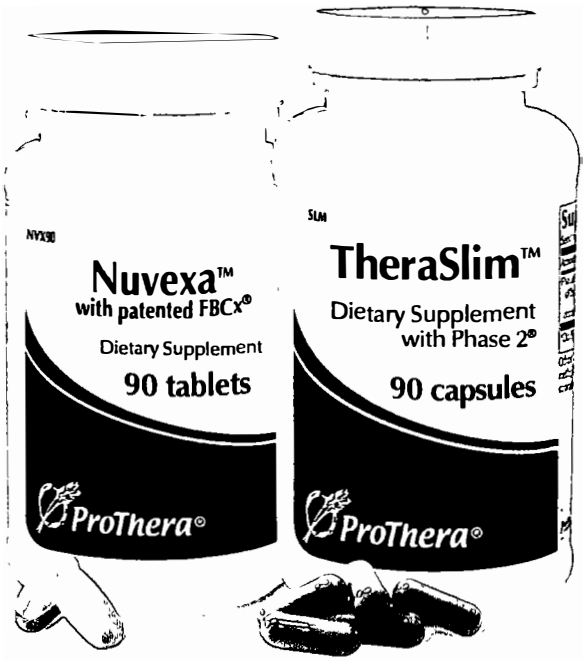

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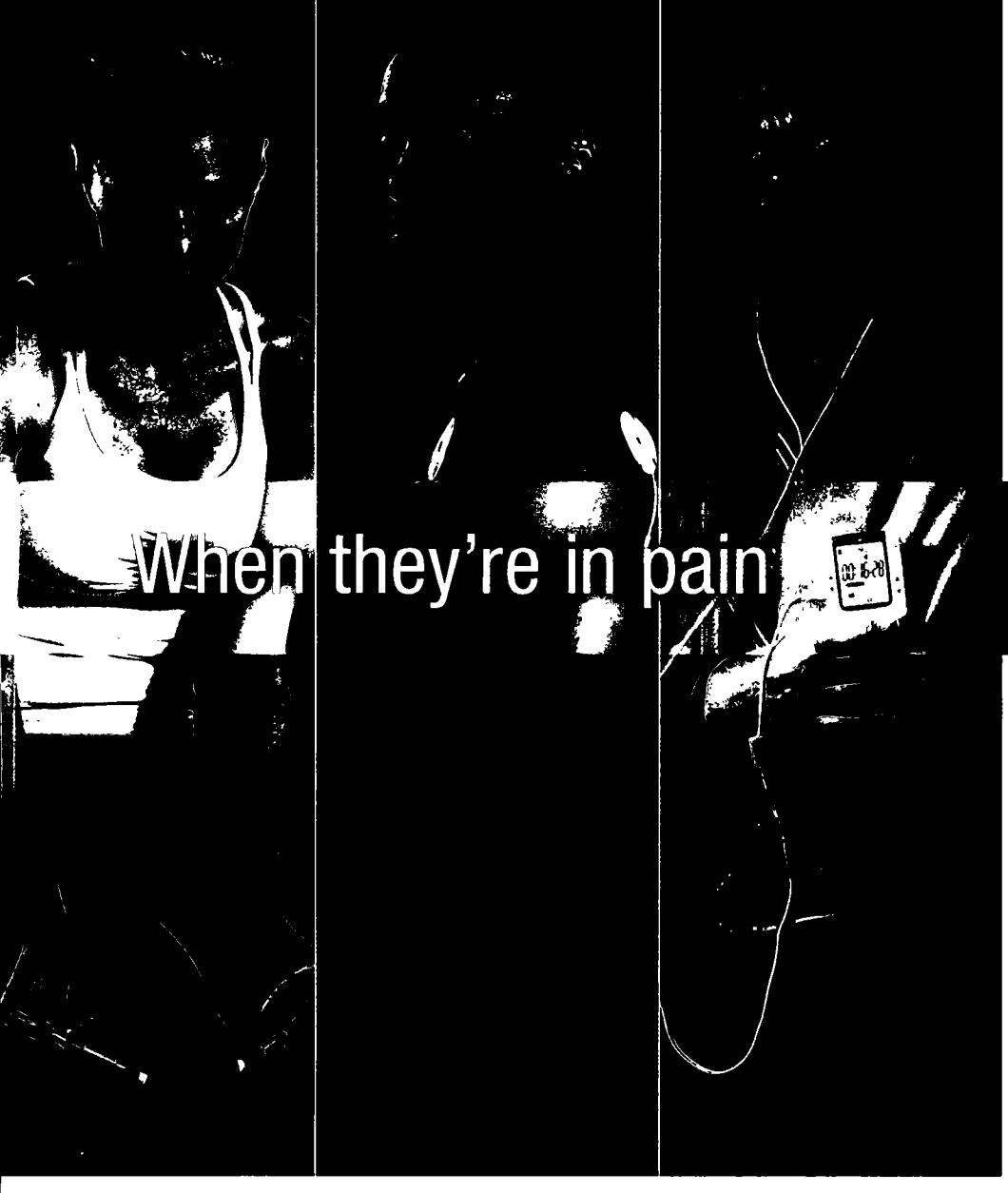

When they're in pain

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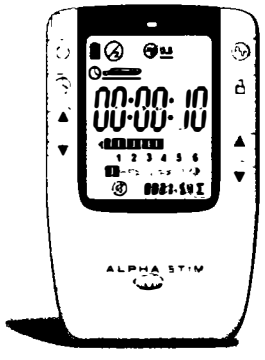

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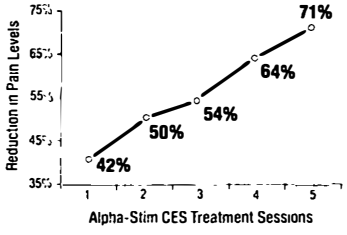

In a study of severe pain patients, Alpha-Stim reduced pain by an average of 71% after only 5 treatment sessions[1]

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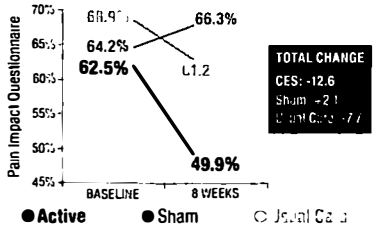

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REFERENCES

1 Holubec JT. Cumulative response from Cranial Electrotherapy Stimulation (CES) for chronic pain. *Practical Pain Management* 2009, 9(9) 80-83

2 Taylor AG, Anderson JG, Riedel SL, et al Cranial Electrotherapy Stimulation improves symptoms and functional status in individuals with fibromyalgia. *Pain Management Nursing* 2013 Dec, 14(4) 327-335

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[1] Pennisi, E. (2011). Body's Hardworking Microbes Get Some Overdue Respect. *Science, 330* (December 2010), 1619.

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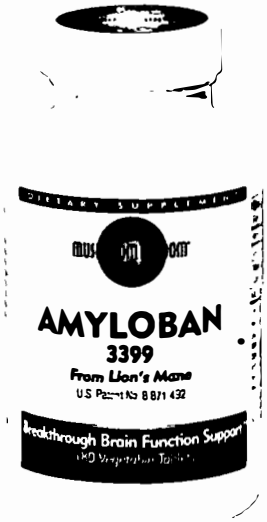

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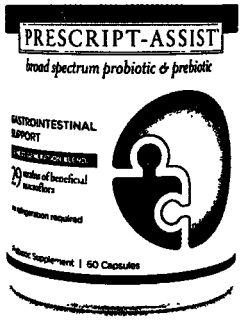

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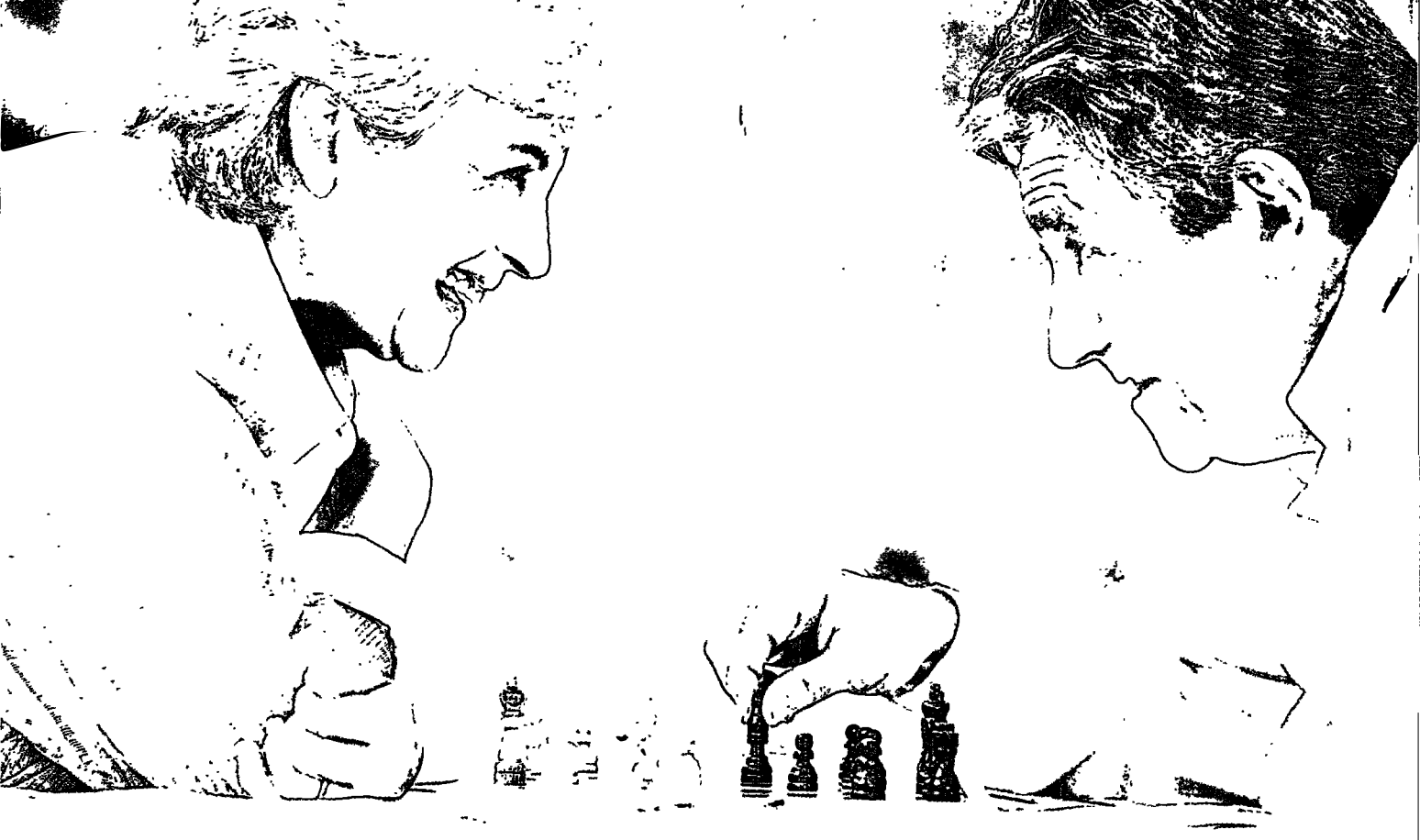

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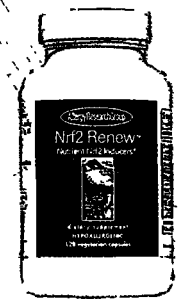

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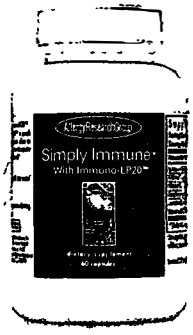

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From the Publisher

My Farewell Thoughts for Dr. Oliver Sacks

It is nearly two months since Dr. Oliver Sacks died at age 82 from cancer, and the media have trumpeted his outstanding work as a neurologist and writer. I have little to add to the many tributes that he has received – but I could not let this opportunity pass without offering my own goodbye.

I regret that I never had the chance to listen to Sacks in the classroom. His lectures at medical school were just as intriguing and entertaining as his book writing. He was very well received at Albert Einstein School of Medicine in New York City; after 42 years there, in his 70s, he moved from the Bronx, where he frequently swam in the East River, across town to Columbia Medical School, and then moved downtown in Manhattan to NYU School of Medicine. In February of this year, he wrote an op-ed in the *New York Times* titled "My Own Life," when he revealed that the eye melanoma that had been treated 10 years earlier had metastasized to his liver. Sacks never stopped examining his patients; in "My Own Life," he was the patient, and he was sanguine and content with his life and enjoying the moment. He knew that he was dying and he compared his experience to that of philosopher David Hume, who wrote about dying two centuries earlier in an essay titled "My Own Life."

Sacks grew up in war-stricken London in an orthodox Jewish household, the youngest child of two physicians. He spent his grade-school days in an academy far from home where he was routinely beaten by the headmaster and bullied by older classmates. When he returned home, he fled to the basement, where his uncle introduced him to chemistry; Sacks refers to him as Uncle Tungsten in his book (2001) of the same name. Sacks's love of chemical reactions and the periodic table led him to undergraduate work in chemistry, but then he studied medicine. In the 1960s he did his neurology residency at UCLA, but also participated in the hippie revolution, experimenting with

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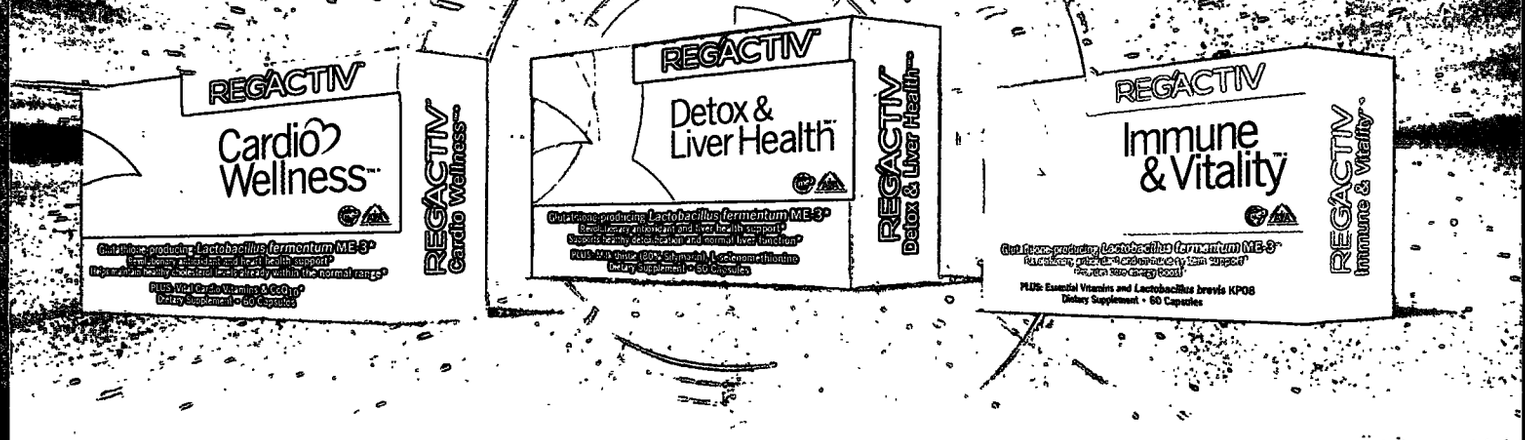

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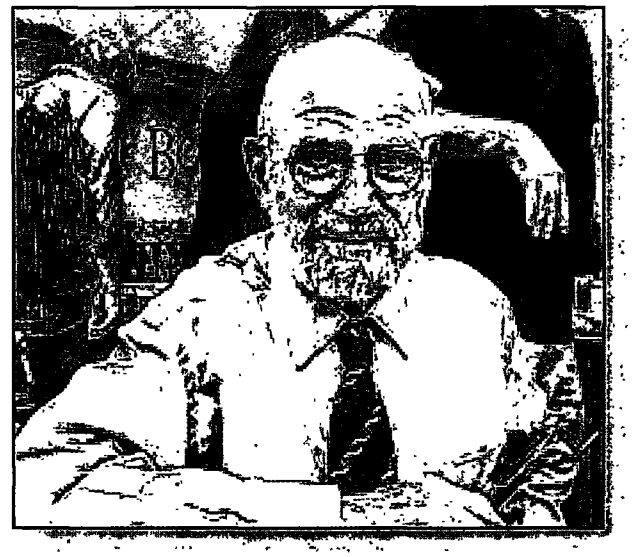
Letter from the Publisher

➤ continued from page 6

drugs and riding his motorcycle with the Hells Angels. Sacks thought that California was a wonderful life but he thought he would be given a better chance to see life's rough edges in New York City; as a neurologist he was seeing Tourette's syndrome everywhere while walking the streets.

In the 1970s, medicine did not offer many drugs for treating neurological conditions, but Sacks thought that the Parkinson's drug L-dopa might be of benefit to a group of catatonic patients in the Bronx hospital ward where he was working. His work experience became the basis for his 1973 book as well as the 1990 Hollywood movie of the same name, *Awakenings*. The book that brought me under Dr. Sacks's spell was *The Man Who Mistook His Wife for a Hat* (1986). In that book of clinical vignettes, Sacks describes a musician who had lost the ability to see objects and people for what they were, even though his visual acuity was normal. Sacks discusses the case in a manner understandable to the physician and the nonprofessional, the pathophysiology that led to this individual's inability to distinguish his wife's head from a hat. Sacks's knowledge of medicine and science, as well as his attention to portraying clinical details, in the language of storytelling rather than case presentation, reads like he is a doctor and a poet. I have noticed in my local hospital that at least one neurologist



Oliver Sacks 2009

has come to grand rounds, detailing a case much like Dr. Sacks did, and the physician audience has appreciated the presentation greatly. While Sacks had his critics, one wonders if sometimes the naysayers criticize just for the sake of needling those who have become accomplished.

Sacks provides me the example of a doctor who would not treat a patient simply as a case, described merely by the

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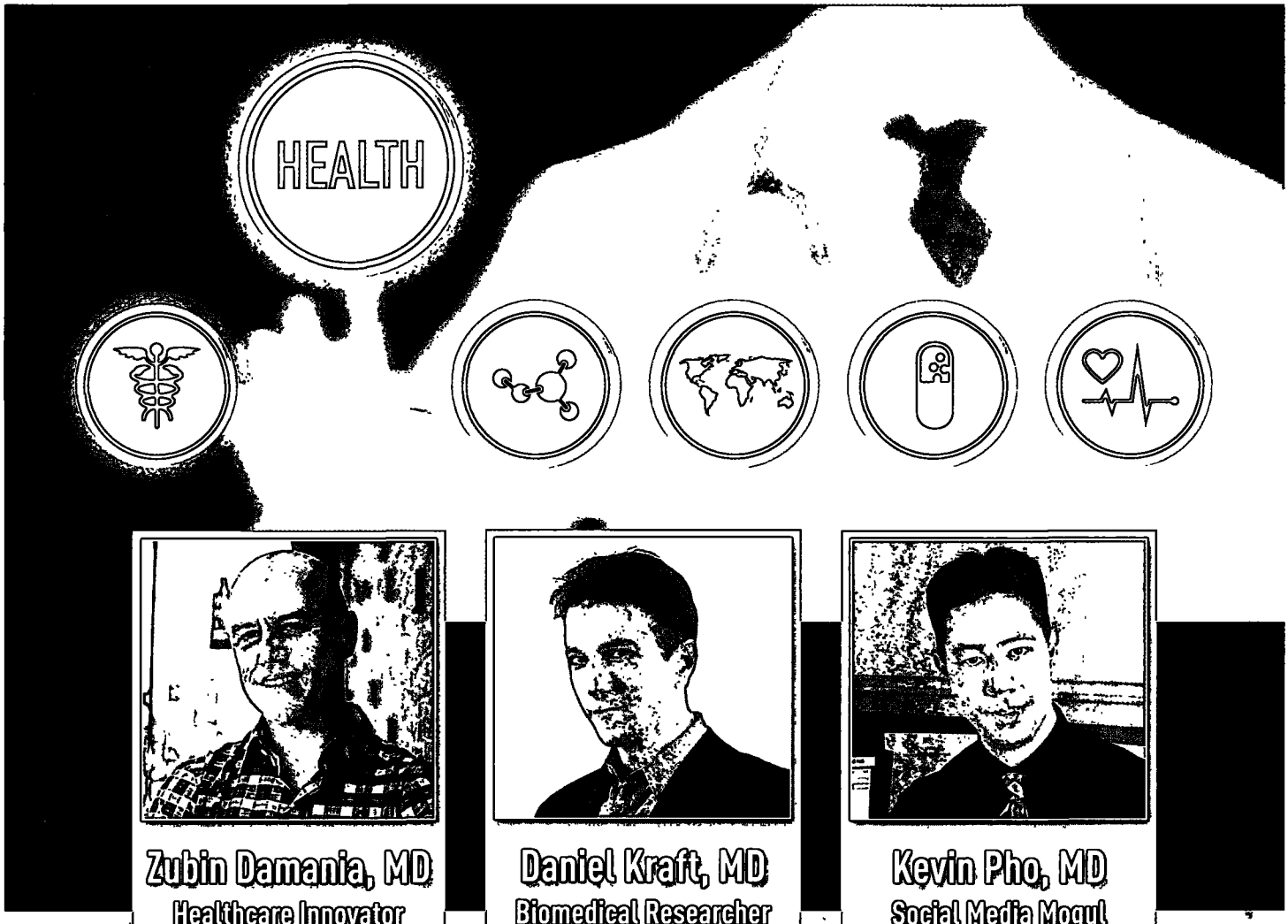

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Letter from the Publisher

➤ continued from page 8

name of a disease. Sacks wanted to explore and investigate, not just by scans and lab numbers, but by understanding the patient's overall complexity, the fullness of the disease. He was wary of the first impression – he wanted to delve into all the aspects until he had a full and complete diagnostic understanding. And if that meant working through many wrong diagnoses, he was compelled, even obsessive, to find the underlying story.

Up until the time that he became sickened, Sacks continued to see patients and lecture. I thank Dr. Sacks for being such a wonderful role model – a path worth following!

Physician Burnout, Physician Heal Yourself

It has been nearly 40 years since I completed my training in medicine, but in some ways it seems almost like yesterday. Examining patients, collaborating on medical rounds, reading medical journals, spending hours on paperwork, attending medical lectures, responding to insurance carriers and quality control committees, seem little different now than when I started. Of course, medical knowledge, diagnosis, treatment, procedures, and surgery have greatly changed, mostly for the better. But in many ways we approach medicine now much the same way that we did in the 1970s; in fact, doctors work much the same as they did in 1910. Not only is training in internship and residency long and rigorous, it is exhausting, tedious, and fraught with sleepless nights and bullying by older attending physicians. Medical faculty concede that the lack of sleep and the lengthy on-call duties are necessary not only to harden the physician, but to secure competency. No one disputes that the endless on-call duties are a hazing, and as with most hazing, individuals suffer physically and mentally. The physician who completes his/her residency is accomplished and a specialist. Too bad that more than a quarter of them become depressed and anxious, and not a few are suicidal.

In a special feature in August, *Time* magazine followed a surgical resident at Stanford Hospital for 72 hours. Her morning starts at 3 a.m. awakening to get ready for her work. By 5 a.m. she has made her own rounds on the surgical floor, so that by 6 o'clock, she can do rounds with the attending physician, her other

continued on page 15 ➤

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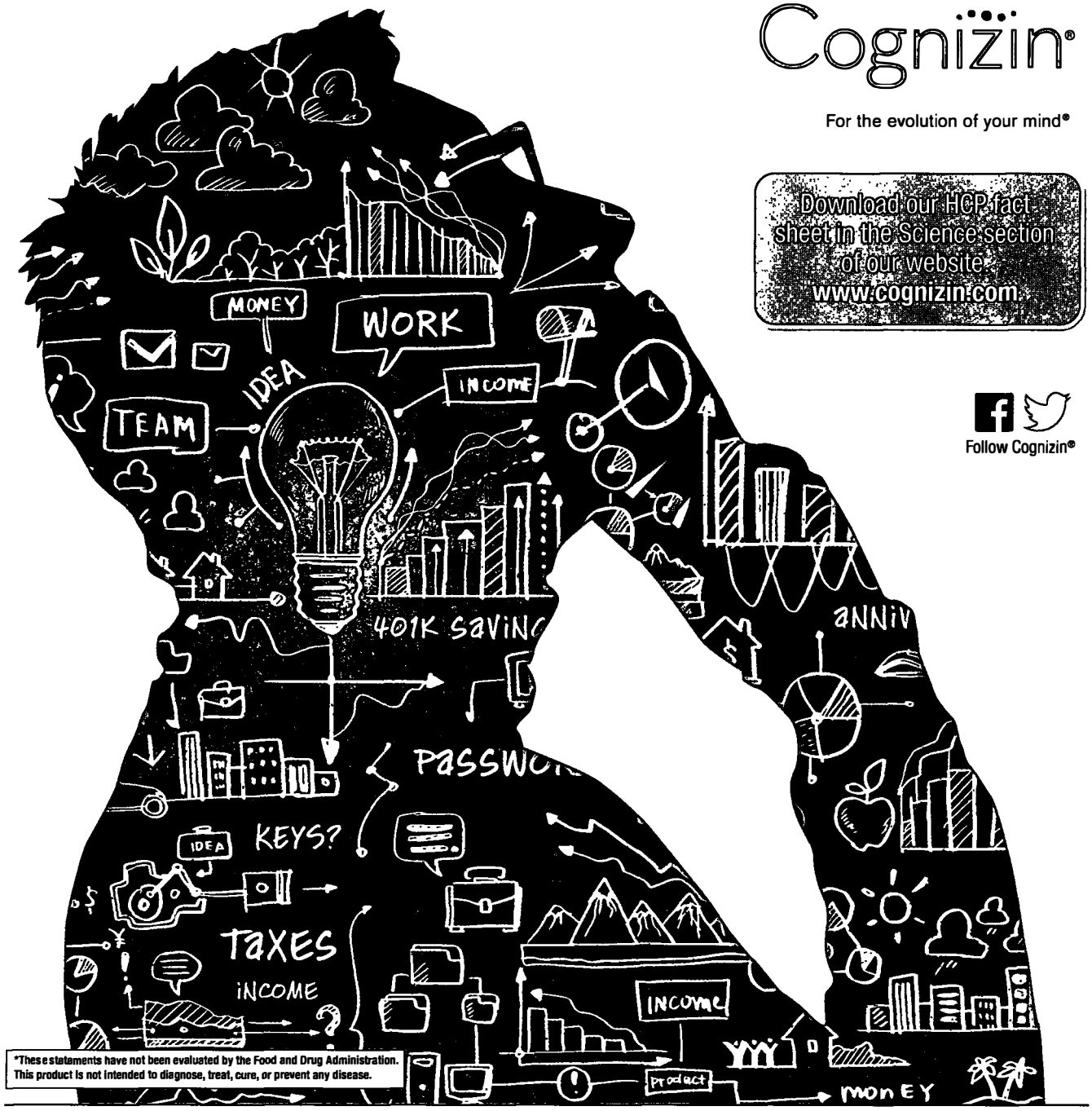

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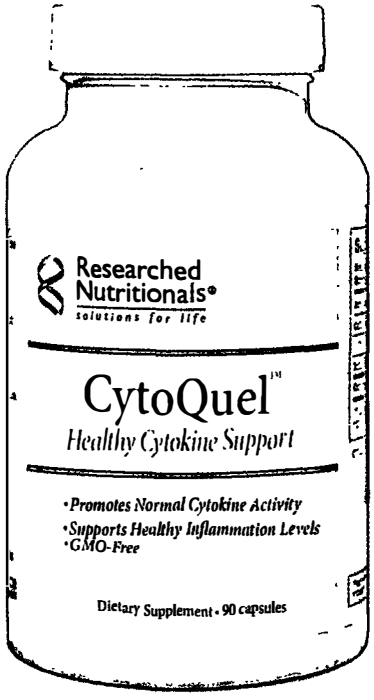

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The editors of the *Townsend Letter* recommend that all patients (and physicians) review further reports provided in the article's references and investigate the practitioner's techniques before undertaking an alternative diagnosis, examination, or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

Letter from the Publisher

➤ continued from page 10

residents, and interns. By 8 she has scrubbed into surgery – there are a few surgeries that morning. But the schedule is thrown off by some emergencies; her last surgery takes her into the evening hours. She grabs some lunch and dinner on the run; hospital food is not necessarily organic or the most nutritious. There are late surgery rounds, and then she is on call with another resident. During the night there are neither emergencies nor surgical complications, and she is able to grab a few hours' sleep. She meets the surgical team in the morning and once again, after rounds, she scrubs into surgery. Then after another lunch on the run, there are afternoon surgery clinics. Finally, evening arrives, late surgery rounds, and then she signs off to the resident on call. She heads home at 10 p.m.

No wonder young doctors, laden down with debt from their medical schooling, beholden to a medical system that demands long, brutal hours on call, eating poorly, unable to do much fitness, with nary a moment for relaxation, begin to become angry, frustrated, physically and mentally tired, and then anxious and depressed. Some doctors resign when it becomes too overwhelming. But others internalize, pushing their feelings deep into themselves. And a few have more than suicidal thoughts; a chief resident of surgery at Stanford, whom his attending thought of as a "bright star," committed suicide several years after his stellar Stanford work. That surgical professor learned surgery himself four decades earlier with the same rigorous on-call training required today. However, he recognizes that doctors need a better system, or at least a system that accommodates the physical and mental needs of the residents. Stanford has begun to provide these doctors with more time for meal breaks and higher-quality food. The doctors are required to meet as teams with a psychologist to discuss what is going on with them emotionally. There is talk about breaks for workouts, meditation, and walking.

Of course, following residency and postgraduate training, physicians are not subject to grueling on-call schedules. Still, many approach their practices, in or out of the hospital, with the same work ethic. Doctors work hours doing surgery and procedures, seeing patients in clinic, answering patient questions after hours, and then there is the endless paperwork. Electronic records have made the paperwork more efficient; on the other hand, physicians now spend more time looking at the computer than the patient in the 15-minute appointment. Now insurance companies require preauthorization for not only surgery and procedures but also many of the new wonder drugs (and some not so wonderful ones). The doctor's time is eaten up daily and much of the weekend. And when the overhead of the practice, the burden of school education debt, and the occasional malpractice case bite the doctor, many become fed up and burned out.

What to do?

Doctors break away from their practices to attend medical conventions for CME credit. Not a few of these breakaways are beginning to focus on refreshing the physician. At least one group, the American Holistic Medical Association, has always focused not only on healing the patient but also on healing the doctor. Doctors are beginning to include their sports or physical fitness as part of their daily schedule. Many are learning meditation and incorporate a period of meditation time daily. Not a few are beginning to incorporate regular massages, acupuncture, yoga, tai chi, and similar de-stressing activities. Despite the sarcasm of their colleagues, doctors are engaging in special diets, supplementation use, and seeing the naturopathic physician, the integrative doctor, the chiropractor, and even the alternative medicine physician. Perhaps the most important activity for the burned-out doctor is to take part in a physician counseling group, a group of docs who share their knowledge and activities, but also their emotional difficulties.

Burnout is part of the physician experience, but doctors can take steps to de-stress and heal!

Thiamine: 'New' Wonder Drug for Fibromyalgia?

Antonio Constantini, MD, a professor of neurology at the Viterbo, Italy, campus of Cattolica University of Rome, reports in the May 20, 2013, issue of the *British Medical Journal* that high-dose thiamine improves the symptoms of fibromyalgia (FM).[1] Kirk Hamilton, author of *Clinical Pearls*, interviewed Constantini last year about the remarkable benefits seen in fibromyalgia. Constantini had been studying inflammatory bowel disease and hypothesized

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that the fatigue seen in IBD may be an intracellular thiamine deficiency due to an enzyme impairment such as a deficiency of a thiamine receptor transporter. He thought that such a mechanism might be involved in a broad range of autoimmune disease. He conjectured that the fatigue of fibromyalgia might also be affected by a similar cause. Constantini's literature review found a 1998 study by Monroe suggesting a relationship between thiamine deficiency and FM.

Constantini distinguishes the "milder" symptoms of FM, such as fatigue, insomnia, depression, and anxiety that are due to a moderate thiamine "deficiency" from the severe pain of FM (chronic widespread pain [CWP]) that is due to a severe thiamine deficiency. The pain of CWP is manifested by diffuse thiamine deficiency in the spinal cord and brain that control sensory input. He conjectures that patients experience CWP because the thiamine enzyme impairment is much greater in the neurologic circuitry.

Unfortunately, biochemical testing is not very helpful. One can measure thiamine and thiamine pyrophosphate (TPP), the active form of thiamine, before initiating therapy. Generally these blood measurements are normal, even in patients requiring treatment. Lab testing of patients being treated with high-dose thiamine will show, as expected, high doses of thiamine and TPP, not a reason for discontinuation of treatment.

Constantini has found that thiamine hydrochloride is more effective than bioactive forms of thiamine, such as benfotiamine. High doses are required for FM starting at 600 mg/day orally, and gradually increasing the dose by 300 mg/day, each week. For CWP much higher doses of thiamine may be required, such as 1500 to 4000 mg daily. Side effects are generally not encountered. It is possible that these high doses may reduce the level of other B vitamins, particularly folic acid, and it is recommended to include B complex, particularly vitamin B12 and folic acid.

Injection therapy, as is usually the case, is more effective. Generally 100 mg/day, given twice weekly, of IM thiamine is comparable to 1800 to 2400 mg of oral thiamine. Thiamine dosing is determined both by effect on symptomatology as well as the patient's weight – heavier patients need higher doses.

Constantini's *BMJ* case report revealed greater than 50% improvement in fatigue and pain using thiamine. Kirk's interview of Constantini is not available here but a summary is online. (Search: "Fatigue Helped with High Dose Vitamin B1," a YouTube video.)

Axelrod and Teitelbaum Discuss Fibromyalgia

In this issue, Leslie Axelrod, ND, LAc, professor at Southwest College of Naturopathic Medicine, reviews the primary aspects of fibromyalgia. Axelrod reminds us that the new diagnostic criteria of FM have led to an increase in its diagnosis in the population. Most fibromyalgia patients face difficulties with insomnia. Axelrod offers her recommendations for the best botanicals and supplements supporting sleep disorders. She prescribes the Myers cocktail, a short intravenous injection of vitamin C, magnesium, B vitamins, and other nutrients as a general support for the fatigue and pain. Axelrod emphasizes that mind/body approaches are very important for the fibromyalgia patient. Interestingly, she suggests that wearing long woolen underwear is helpful in managing chronic pain.

The *Townsend Letter* is pleased to include Dr. Jacob Teitelbaum's thoughts on treating CFS and FM. Teitelbaum tantalizes us here with "35 Treatments for Tough Cases." Teitelbaum starts with assessing the patient's hormone status. He reminds us that we cannot depend strictly on hormone levels and must diagnose hormone dysfunction based on symptomatology as well. He likes to employ botanicals and nutrient therapy to support insomnia, fatigue, and pain, but if needed he will use drugs. Restless leg syndrome and nocturnal nasal congestion must be treated to support insomnia. Bioidentical hormone treatment is critical for helping fatigue. In addition to considering treatment for infection, including candida and Lyme disease, HHV-6 and CMV virus should be evaluated and treated. Teitelbaum emphasizes that fungus, particularly mycotoxin, is frequently present, perhaps needing home remediation as well as patient detoxification. Energetic therapies, available in a variety of modalities, are helpful in pain reduction.

Jonathan Collin, MD

Notes

1. Constantini A. High-dose thiamine improves the symptoms of fibromyalgia. *BMJ Case Rep.* May 20, 2013;50480.

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National College of Natural Medicine Nabs Prestigious Awards at AANP Conference

David J. Schleich, PhD

National College of Natural Medicine (NCNM) President David J. Schleich, PhD, and the college's Global Health Program Co-Chair Tabatha Parker, ND, were both honored in August by the American Association of Naturopathic Physicians (AANP), the national professional organization of licensed naturopathic physicians, at its 30th annual conference held in Oakland, California.

Schleich was named "AANP 2015 Champion of Naturopathic Medicine." Parker received AANP's top honor for a naturopathic physician, "2015 Physician of the Year."

Schleich, who is married to a naturopathic physician, was recognized for "changing the landscape of health care through his championship of naturopathic medicine." Schleich is known throughout the profession as a leader and catalyst for helping the profession of naturopathic medicine grow.

Since taking the reins of NCNM in 2007, he has ambitiously expanded the campus, built enrollment by nearly 78%, and increased the programmatic offerings of the nearly 60-year-old educational institution from three to nine, including two undergraduate degrees, which were announced in 2015.

During Schleich's tenure as CEO and president of Canadian College of Naturopathic Medicine, student enrollment increased from 86 students to 549 in seven years, and the college was relocated into a 4.43-acre campus. Today, Schleich often provides expert testimony before state legislatures across the US in support of naturopathic licensure with the goal of having licensed naturopathic physicians in all 50 states and US territories. He has developed articulation agreements with a variety of colleges nationally and internationally, and is presently assisting the Maryland University of Integrative Health as it develops its first naturopathic program.

In presenting the award, Laura Farr, executive director of the Oregon Association of Naturopathic Physicians and an AANP board director, noted, "His passion and commitment to naturopathic medicine is unparalleled. Most people simply identify [Schleich] with NCNM, the school he represents. In his tenure, among his many achievements, he's also raised the bar for NCNM's community clinics to a level of professionalism that is now attracting government funding to allow NDs in NCNM's community clinics to operate at their full capacity as primary care physicians."

Parker, cofounder of Natural Doctors International, the first and oldest naturopathic global health organization, and cochair of NCNM's Master of Science in Global Health program, the first global health program offered at a naturopathic medical school, was recognized for her leadership and individual achievement with a distinguished record of service to the profession and patients in the course of her career.

Lise Alschuler, ND, FABNO, president of the Oncology Association of Naturopathic Physicians, said that Parker is a visionary who has devoted her life to the advancement of social justice through her contributions to naturopathic medicine and education across the globe.

Calling Parker a change agent, Alschuler noted that Parker facilitated the development of the first permanent naturopathic clinic in Nicaragua, has developed international naturopathic internships, and petitioned the World Health Organization for acceptance of naturopathic doctors; in 2014, the World Health Organization opened the doors to naturopathic medicine for the first time.

Parker is also director of education at the Academy of Integrative Health & Medicine, an interdisciplinary organization of health-care professionals. In addition, she has been a leader in the formation of the newly developed World Naturopathic Federation, which aims to advance the naturopathic profession globally.

For more information about NCNM's Master of Science in Global Health, visit www.ncnm.edu/mscgh.

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Tabatha Parker

Hot Times in Geneva:

Or, How to Force More Drug Ill Effects on Billions of People and Make Tons of Money

by Scott C. Tips

Most people would not think of Geneva, Switzerland, as an uncomfortably hot city. But each and every time I've been here, it has been. The city was so hot this most recent trip that I actually saw two trees fighting over a dog.

Still, the reason for braving the heat here was a good and necessary one: The 38th session of the Codex Alimentarius Commission was being held this week of July 6–11, 2015, and one of the most important items to be debated on its agenda was the adoption of a maximum residue limit (MRL) for recombinant bovine growth hormone (rBGH) or recombinant bovine somatotropin (rBST).

It might sound inconsequential, but it isn't. As I have mentioned before, obtaining an MRL at Codex for rBGH is the marketing equivalent of a drug company's being handed the "keys to the city." It is a license to sell the vet drug throughout the Codex member-state world, with World Trade Organization (WTO) sanction power behind it. Many Codex members and member states – such as the European Union, Norway, Switzerland, India, Russia, and China – have banned this genetically modified veterinary drug's use on animals under a very sensible health policy that prohibits drug use on animals for anything other than therapeutic purposes. The vet drug rBGH, injected into cows, is not therapeutic; it is used to increase milk production. Yet, if an MRL is approved at Codex, then the Europeans and many others would be faced with a dilemma: acquiesce to its introduction into their food supply or else pay heavy trade sanctions imposed upon them by the WTO.

Industry Science Supposedly Says that rBGH is Safe

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) has conducted three safety reviews of rBGH, and its representative keeps insisting to the Codex delegates that these safety reviews have shown the veterinary drug to be safe, with no noticed increase in mastitis (udder infections) or antimicrobial residues from rBGH use. The JECFA representative at this meeting took the same position that she had expressed at the Codex Committee on Residues of Veterinary Drugs in Foods held in Costa Rica last April, that JECFA's "systematic review of the literature published since the 50th JECFA [1998] did not find any significant difference in the incidence of mastitis ... [nor] specific studies correlating the use of rbST with the development of antimicrobial resistance."

Pro-rBGH delegates at the current meeting were not shy about repeatedly pointing out that this was JECFA's *third* review of rBGH for safety. How could anyone, they hypnotically demanded time and again, possibly have an issue with *three* JECFA reviews that found no safety concerns for rBGH? And besides, they added, since this Codex standard has been on hold for 15 years, we would be harming Codex's credibility were we to turn our backs on JECFA science and refuse to adopt the MRLs for rBGH that JECFA assures us are safe.

Every Western Hemispheric country but Canada (which had to sit silently on its hands since Health Canada had declared rBGH unsafe) was in favor of adopting this MRL. Most African countries and many Asian countries declared the same, along with every two-bit Pacific or Caribbean island that the US could fly in so as to add weight to the clamor for adoption.

So, What's the Problem?

Only that the Codex delegates representing *more than half* of the world's population do not believe that the JECFA risk assessment was either sound or scientific. Indeed, many thought the risk assessment was very political and industry-influenced. The NHF had also strongly argued at the previous meeting that JECFA had overlooked negative study results from the industry itself, and even the product warning labeling for Monsanto's rBGH product (Posilac), which cautions users about a possible increase in mastitis in cows injected with Posilac.

Curiously enough, during its own first two reviews, JECFA had specifically excluded any consideration of mastitis issues, claiming that these safety problems were outside the scope of the JECFA review. So, contrary to pro-rBGH claims, there had not really been three JECFA reviews of all the issues.

My fellow NHF delegate, Robert Cohen – an expert on rBGH and its many dangers – argued that the goalposts for antibiotic use to treat mastitis had been moved so dramatically as to render them almost useless as a measure of antibiotic harm. It turns out, Cohen says, that FDA employee Dr. Margaret Miller (formerly with Monsanto) arbitrarily raised the FDA's allowable antimicrobial level 100 times from 1 part per hundred-million to one part per million. This has allowed more antibiotics to be passed along to humans in cow's milk, with a resulting increase in antimicrobial resistance (i.e., pathogens resistant to antibiotic use by humans to kill those bad bugs).

In addition, Cohen pointed out that a herd of Holstein cows injected with the genetically engineered bovine growth hormone presented extremely shocking results upon autopsy, which the FDA and Monsanto did not make public. It was only upon publication in a dairy magazine that consumers learned that rBGH-injected cows lost an average of 100 pounds after 6 months, while their hearts and spleens and other stressed organs had grown abnormally large.

Dr. Michael Hansen of Consumers International (CI) was at this meeting and argued, among other things, that studies have shown that: (1) rBGH use significantly increases mastitis rates; and (2) the average length of treatment for a case of mastitis is almost 6 times longer in the rBGH-treated cows compared with untreated cows.

Because some dairy farmers deliberately use off-label and other antibiotics not tested for by the government and use them for longer periods of time, antibiotic use in cows is far greater than reported by the government or industry. Given that rBGH-injected cows need more antibiotics to cope with their greater health problems, such hidden use is not surprising. If the milk coming from these dairy farms exceeds even the lax antibiotic levels permitted by the FDA, then the dairy farmers face huge economic losses as their milk is rejected for sale. Unfortunately, though, the bottom line is that rBGH-injected cows have more health issues, which in turn results in more antibiotic use, which in turn results in humans' developing antimicrobial resistance (AMR, as Codex puts it) to harmful pathogens.

Yet, despite this and an enormous amount of other evidence out there, JECFA and its worshippers at Codex continue to insist that rBGH is safe. With AMR, JECFA has even twisted *the lack of data* on AMR into a conclusion that AMR is not an issue with rBGH use! As every true scientist knows, an absence of data means that scientists wait to draw conclusions until they have the data.

Too, we suspect that JECFA's expert body on AMR may not be as disinterested as it should be in making its risk assessments of rBGH. An NHF investigator found that one of the Codex Antimicrobial experts, Y. Tamara, was working in 2004 for Mead Johnson's GMO division, where he obtained a US patent for a GMO grain.

The truth is that alarm bells are ringing everywhere, and have been for decades, about the dangers of this nonmedical drug use on animals; and yet our supposed scientific authorities sit there and act as if nothing is wrong. Others, conditioned to blindly accept "scientific" pronouncements no matter how badly based, shore up these rickety pronouncements with their unthinking support. If JECFA were truly doing its job, then it would be ruthless about tracking down each and every hint of evidence that rBGH poses a human and animal health problem. But, sadly enough, JECFA's reviews were third rate.

The Codex Dog-and-Pony Show

It happens every time. It happened with ractopamine, GMO labeling, melamine, and now rBGH. The countries and trade groups that want to make money off of some drug or food product will present their "science" showing how incredibly safe it is and how we would all be idiots if we didn't accept the product immediately. It is then up to us to show that they are wrong and that the science indeed shows health risks. If they are able to snag JECFA on their side, then they will also argue that Codex must not insult Codex and appear stupid for not following its own body's scientific risk assessment. The arguments go back and forth until one side wins.

The problem, though, is that Codex-system inertia and bias is on the side of any proposed standard. "We need this standard," the Burkina Faso delegate said about rBGH. "We will lose our credibility [look stupid] if we do not pass a standard," Brazil chimed in. Many others agreed. Typically, the countries and industries pushing the standard only think in one direction: Push the standard forward to completion. As I argued at the meeting, they are like drivers who have taken a wrong turn and are now claiming that the only way out is forward, not by retracing the route, otherwise the driver will "look stupid." No, as we all know, the driver will look stupid if he or she continues forward on the wrong path, just as with this rBGH standard.

Codex Steps Back From the Brink

With the rBGH standard having been held at Codex's final Step 8 for 15 years, the US and its minions had pulled out all of the stops at this year's meeting to give this standard a final push over the edge and get it adopted. In anticipation of forcing a rare vote on the standard, they had flown in every small and large country they could, with who-knows-what promises – a free vacation in Geneva, free mastitis for life, or maybe a simple promise not to wiretap its leaders' communications. We don't really know, but we do know that, otherwise absent from Codex meetings, these "now-you-see-them, now-you-don't" delegations mysteriously seem to appear on cue for any meetings where a vote might be taken. And they always support the US position.

If adopted at the final Step 8 at this commission meeting, then the rBGH standard would be a done deal, ready for use as a weapon by the US, Mexico, Brazil, and others who chose to export rBGH-doped milk into other Codex countries that actually care about their citizens' health. It was the European Union, India, Russia, China, Norway, Switzerland, Turkey, Uganda, Botswana, Georgia, Consumers International, and the NHF against the Western Hemispheric countries, plus most African countries, New Zealand, and the ICGMA (International Council of Grocery Manufacturers Associations). Cuba, Costa Rica, and Brazil were the most outspoken in favor of adopting the rBGH standard, while the European nations, India, NHF, and CI were the most adamant against its adoption.

India, which has a reputation for making the timeliest interventions, opposed adoption, stating that its own recent study showed problems with rBGH use in cows. It also argued that with 36 standards' already having been adopted by the Codex Alimentarius Commission at this session, Codex was hardly at risk of having its credibility questioned if it refused to adopt this one.

NHF's first intervention against adoption was from Robert Cohen, who proceeded to lambast the FDA for its position on rBGH. It was so strong that, after the day's session and while waiting for me to complete a radio interview, three FDA personnel confronted him

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with anger and hostility. And the next day, when I "flagged up" again for NHF to speak, the chairwoman, Awilo Pernet, was extremely hesitant to call upon me to speak, only doing so after I had spoken privately with their legal counsel and as the very last delegation to speak.

With the debate spread over two days and seemingly inexhaustible, the Australian delegate (who expressed support for rBGH) wisely suggested that in light of an unmentionable previous experience (the adoption of a standard for ractopamine) wherein a standard had been forced down the throats of a majority of the world's population by a mere one-country vote majority (remember, Tonga's vote carries the same weight as China's), the rBGH standard should be "parked" at Step 8 until such time as consensus could be reached. What Australia was telling everyone without saying it is that Australia did not support taking this up for a vote, which would be devastating for Codex and its member states politically. Weighing the cost, Australia very astutely found it wanting. Perhaps Australia had already felt the domestic heat from its ractopamine position, or perhaps Australia was simply being politically savvy. Regardless, the Australian position set the tone and any fervor by the pro-rBGH camp to vote on this standard evaporated, except for a few diehards such as Tonga.

The chairwoman proposed a face-saving compromise that the MRLs for rBGH continue to be held at Step 8 and revisited at each annual meeting until consensus could be reached. Because it was a slap in the face to JECFA for this commission not to adopt a standard that JECFA had found safe, the chairwoman couched her compromise with a soothing opening sentence, "The Commission recognized the validity of JECFA's risk assessments as the sound scientific basis for its deliberations on rbSTs." This statement was not true, though, as many delegations had challenged JECFA's risk assessment as incomplete; and when finally given the chance to speak on this compromise, I was the only one to state this fact.

In the end, however, the chairwoman had her way; and the rBGH standard was "parked" at Step 8, to be battled over in a future meeting. The world had won a reprieve.

Sanitized Codex Reports

Codex brags about its transparency. But its commission and committee reports say otherwise. Try to find out which delegation took a particular position on an issue. Good luck, because 95% of the time you won't. The names have been omitted. NHF has protested this nontransparent practice across time and in many meetings, as the world should know what positions delegations have taken. Unfortunately, our protests have fallen on deaf ears.

The final reports are deficient in other ways as well: they are scrubbed clean, sanitized. One egregious example occurred on July 11, during the reading and correction of the report of this meeting, when I asked for the floor so that NHF's last comment about not agreeing with the validity of JECFA's risk assessment could be inserted into the report. I pushed the microphone button so that the Pernet would see NHF on her screen, along with those other delegations asking for the floor. I propped our name sign up so it was also visible. The chairwoman called and kept calling on everyone but NHF. At strategic moments, I cancelled my computer-system request for the floor and pushed the request button again so that it would flash on her screen, again. I was still ignored. I even grabbed our NHF name placard off its stand and waved it at arm's length wildly above my head. Nothing. Thirty minutes in all had passed and the chairwoman had still refused to recognize me at all.

She clearly feared that I would want to insert something negative about JECFA into the report, but her refusal to recognize me to speak was absolutely inexcusable conduct on her part. And it is being protested and publicized far and wide as an example of misconduct. Even others came up to me afterwards and expressed their surprise at how we had been handled.

The bottom line on Codex reports is that they cannot always be trusted as a complete record of what transpired at the meetings. Future historians, as yet unborn, will have to mine articles such as this one to determine the substance of what really happened at these food-standard meetings.

RBGH Science is the Tartan Bag

In a hugely funny skit done by the British comedians Bill Bailey and Simon Pegg, the scene opens with Bailey sitting on a stool at his baggage-claim counter at some indeterminate airport. The phone rings and rings. Bailey lazily picks up the phone and answers in his most disinterested tone, "Lost luggage." "Have you seen my tartan bag with green tags?" the voice at the other end desperately asks. Without moving off his stool, Bailey slowly looks to his right and down and then turns and does the same to his left. "No," he eventually answers, "we haven't found it." And he hangs up.

The scene changes to Pegg, the fresh blood, now sitting on the same stool at the same counter, with his hand eagerly hovering over the phone, just waiting for it to ring. It barely rings before Pegg scoops it up and gets the same query as before, "Have you seen my tartan bag with green tags?" "Green tartan bag!" he barks back, "I'm there!" He leaps off his stool and is already running by the time his feet are barely on the ground. Pegg runs through the airport, hounding passengers, commandeering the public announcement, riding the baggage carousel and throwing off bags, until eventually hours later he finds the tartan bag. He triumphantly takes it back and plunks it down on the counter in front of Bailey, who, now sitting at the lost-luggage counter, then phones the owner and claims credit for having found it.

In this modern-day parable, we have JECFA as Bill Bailey and NHF, India, the European Union, and CI as Simon Pegg. We run around and find all of the evidence for the considerable health risks of rBGH while JECFA barely glances around, finding nothing. Yet, mark my words, when JECFA does eventually come around and sees the light, everyone will be acclaiming and applauding *JECFA* for its thorough search. And the funny thing is that we will be among those applauding, because, after all, one more health risk will have been removed from our food, and the committee can get the credit just so long as we get the health. ◆

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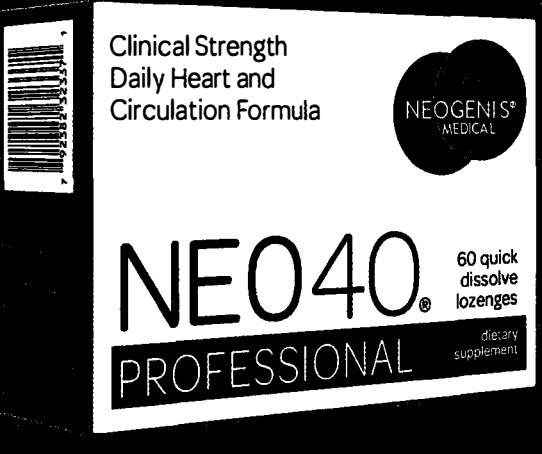

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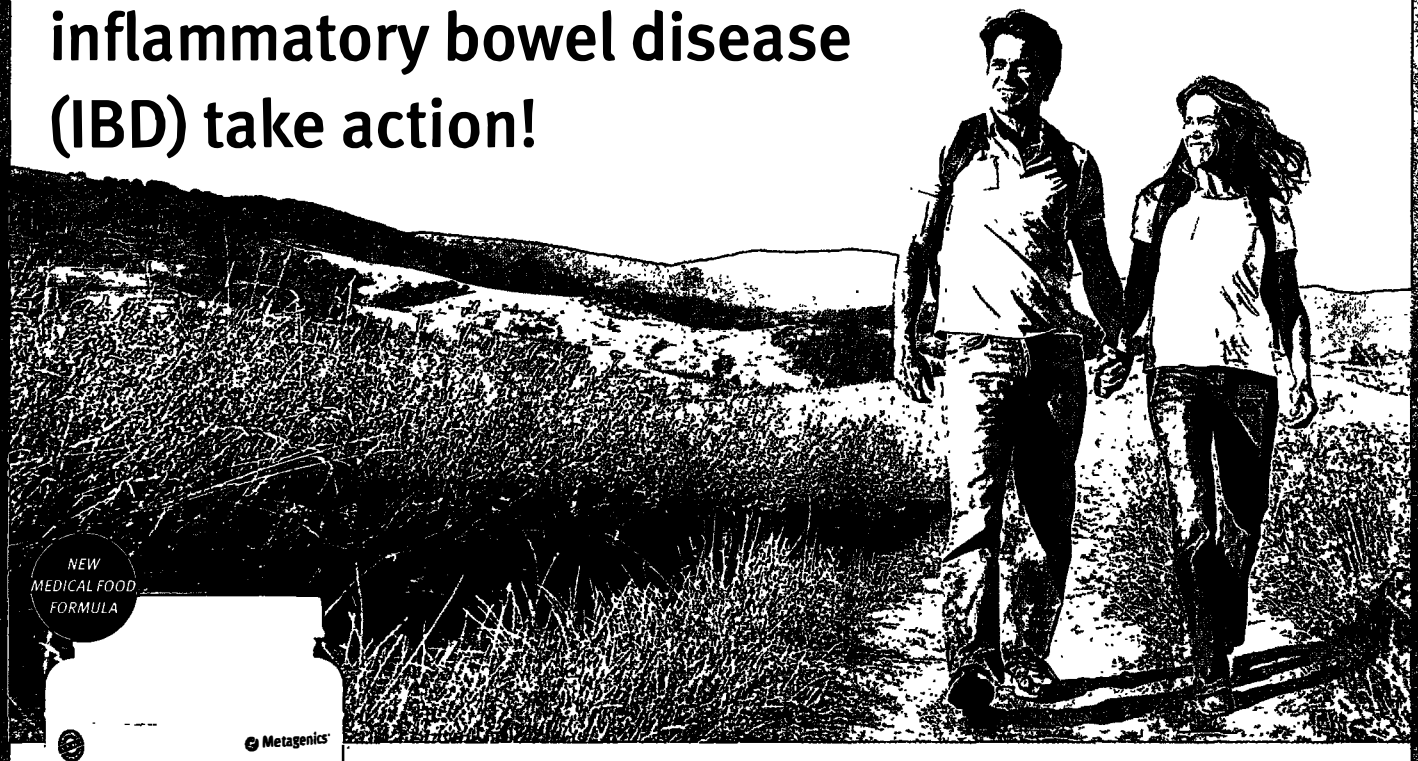

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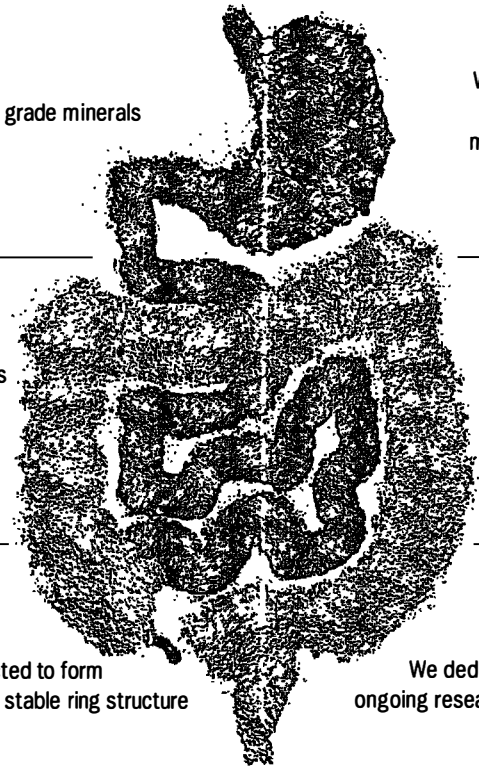

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briefed by Jule Klotter
jule@townsendletter.com

Amalgams, CFS, and FM

Toxic metal exposure from dental amalgam fillings may contribute to chronic fatigue syndrome and fibromyalgia in some people, according to a 2014 review led by Janet K. Kern, PhD. The safety of amalgams has been debated for decades. The American Dental Association and FDA assert that amalgam mercury, which makes up about 50% of a filling by weight, is inert and poses little or no hazard. Multiple studies, including this review by Kern et al., indicate that mercury in amalgam fillings is not inert and has numerous detrimental biological effects that can produce a wide variety of symptoms.

Unlike high exposure to mercury, chronic low-level exposure initially produces subtle, nonspecific health effects that progress over years. Kern et al. found that symptoms associated with amalgam toxicity match those that characterize chronic fatigue syndrome (CFS) and fibromyalgia (FM) including abnormal fatigue after physical exertion, muscular discomfort and pain, impaired memory and concentration, impaired sleep, depression, and GI problems. People with CFS and FM, unlike healthy controls, tend to test positive for allergies to nickel, mercury, and other metals found in amalgams. Moreover, careful amalgam removal has been associated with symptom improvement in people with CFS and FM in several studies.

Amalgams emit mercury vapor that is inhaled and also absorbed by structures in the mouth. Animal studies have confirmed that mercury from amalgams accumulates in body tissues. Human studies show a direct dose-dependent correlation between the number of amalgams and the amount of mercury in the kidneys. The kidneys along with the brain are the first organs to show pathological changes after mercury exposure. Once it is absorbed into the bloodstream, mercury can pass through the blood–brain barrier and the placenta. An autopsy study involving 35 infants (age 11–50 weeks) found a correlation between the amount of mercury in their cerebral cortex tissue samples and the number of amalgam fillings in their mothers' mouths. Studies have also found significant correlation between the number of maternal amalgam fillings and mercury levels in amniotic fluid. Kern et al. point out that urine or blood mercury levels may reflect acute exposure in some people, but the measurements cannot show mercury levels stored in organs and tissue. Moreover, some bodies have more difficulty eliminating mercury, resulting in higher body burden and low urine, blood, or hair test results.

Mercury binds with several important biomolecules, thereby inhibiting their function, including thiol (sulfur-containing) and selenol functional groups found in enzymes, cofactors, receptors, cytokines, ion channels, transport proteins, and transcription factors. Mercury also disrupts the balance between copper and zinc. Zinc is necessary for the function of over 200 enzymes. Mercury has several negative effects on the central nervous system, including the increased production of extracellular glutamate (an excitatory neurotransmitter) and neuroinflammation. In addition, mercury increases oxidative stress and changes gut flora.

Some countries, such as Norway and Sweden, have responded to the growing body of scientific research on mercury amalgam toxicity by banning amalgam use. Although they have not totally banned mercury amalgams, Germany and Canada forbid their use in pregnant women and children – a path that US Food and Drug Administration (FDA) was prepared to follow in January 2012. However, the Department of Health and Human Services (HHS) refused to approve the new guidelines, according to a Medscape article. The stalled guidelines are among plaintiff evidence, submitted on behalf of the International Academy of Oral Medicine and Toxicology (IAOMT) and coplaintiffs, in a lawsuit against FDA and HHS.

Kern JK, Geier DA, Bjørklund G, et al. Evidence supporting a link between dental amalgams and chronic illness, fatigue, depression, anxiety, and suicide. *Neuroendocrinol Lett.* 2014;35(7):537–552. Available at http://www.nel.edu/archive_issues/o/35_7/NEL35_7_Kern_537-552.pdf. Accessed August 24, 2015.

Lowes R. Did HHS cancel proposed FDA limits on mercury fillings? [online article] Medscape July 29, 2015. http://www.medscape.com/viewarticle/848835. Accessed August 26, 2015.

Shorts

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Whole Body Cryotherapy and Fibromyalgia

Whole body cryotherapy (WBC), a treatment used to reduce pain and inflammation in rheumatic patients, was tested on people with fibromyalgia (FM) in a 2013 Italian study led by Lorenzo Bettoni. WBC, first investigated in the 1980s, exposes the entire body to very cold, dehumidified air (−110 to −160 °C) in a cryochamber for just 2 or 3 minutes. The treatment tends to regulate cytokine expression, increasing anti-inflammatory cytokines such as IL-10 and decreasing pro-inflammatory cytokines such as IL-2 and IL-8. People with fibromyalgia have high levels of IL-8 and other pro-inflammatory cytokines in their skin and peripheral blood. IL-8 activates the sympathetic nervous system and increases sensitivity to painful stimuli. FM patients have a lower pain threshold than healthy controls.

The Italian study involved 100 people with fibromyalgia, who were divided into two groups. The first group (46 females and 4 males, aged 17–67 years) was prescribed WBC by their doctors. The second group (46 females and 4 males, ages 19–70 years) acted as the control. People in the WBC group received 15 sessions of WBC over a 3-week period, consisting of a 30-second preconditioning at −60 °C and a 3-minute-long exposure at −140 °C. To avoid frostbite, patients wore bathing suits, socks, clogs or shoes, surgical masks, and hats or headbands to protect the ears. They also kept their fingers moving as they walked in the chamber. Each session was followed by 30 minutes of aerobic exercise (stationary bike or treadmill). It is unclear whether control patients also engaged in 30 minutes of aerobic exercise. All participants were assessed at the beginning and end of the study using the Italian version of the Short Form (SF-16) to measure physical and mental health, the Visual Analogue Scale (VAS) to measure chronic pain intensity, Fatigue Severity Scale (FSS), and Global Health Status (GHS) self-assessment.

Patients in both groups improved according to all four measures, but the WBC group improvement was significantly greater. Patient perception of pain (VAS score) decreased by 58% in the WBC group compared with 22% in the control. Fatigue severity (FSS) and health status (GHS) improved by the same magnitude, according to the authors. The WBC group also showed greater improvement in physical functioning, vitality, social functioning, and mental health, according to SF-36 scores. Is WBC's pain reduction effect in people with fibromyalgia due to its effect on cytokine levels? Can it "reset" the inflammatory imbalance in FM patients, or is the effect short-term?

Bettoni L, Bonomi FG, Zani V et al. Effects of 15 consecutive cryotherapy sessions on the clinical output of fibromyalgic patients. *Clin Rheumatol.* 2013,32:1337–1345 Available at http://www.clinicafisioterapiamalaga es/wp-content/uploads/2013/12/Bettoni-L-Bonomi-F.C_-Effects-of-15-consecutive-cryotherapy-sessions-on-the-clinical-output-of-fibromyalgic-patients.pdf. Accessed September 4, 2015.

New IOM Definition for Chronic Fatigue Syndrome

Systemic exertion intolerance disease (SEID) is the latest name proposed for the condition called *chronic fatigue syndrome* in the US and *myalgic encephalomyelitis* in the UK. A 2015 US Institute of Medicine report recommends the name change because CFS/ME patients typically exhibit debility and exhaustion after exerting themselves. The authors hope that emphasizing this symptom will encourage doctors to see this "serious, complex, multisystem disease" as "real," according to Medscape. *Fatigue*, even chronic fatigue, is less specific and can be experienced for many physical and emotional reasons. Although *myalgic encephalomyelitis* ("brain and spinal cord inflammation with muscle pain") points to a more physiological condition, not all patients experience muscle pain.

The 235-page report, *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness*, defines SEID as "a substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest," according to Medscape. Postexertional malaise, unrefreshing sleep, and cognitive impairment and/or orthostatic intolerance are the other defining characteristics of SEID. Some patients may also experience sore throat, sensitivity to external stimuli,

gastrointestinal and genitourinary problems, and tender axillary/cervical lymph nodes. In addition to new diagnostic criteria, the IOM report recommends that SEID be given a new diagnostic code in the *International Classification of Diseases,* 10th revision.

The belief that patients' complaint of fatigue after exertion is simply the result of poor physical conditioning, remedied with exercise, is inaccurate, according to the report authors. Dr. Ellen Wright Clayton, chair of the IOM panel, says that patients with SEID exhibit reproducible signs of decreased exercise capacity with 2-day cardiopulmonary testing, orthostatic intolerance, and slowed processing on neuropsychiatric tests. "This is not a figment of their imagination,'" she told David Tuller at the *New York Times.* Dr. Lucinda Bateman, another member of the IOM panel, told Tuller, "We are hoping [the criteria] provide a very clear path for clinicians to make a diagnosis. ... We want to make sure that symptoms that maybe have been overlooked by clinicians have been put front and center."

The full report is available at http://iom.nationalacademies.org/Reports/2015/ME-CFS.aspx.

Tucker ME. IOM gives chronic fatigue syndrome a new name and definition [online article] *Medscape.* February 10, 2015. Available at http://www.medscape.com/viewarticle/839532. Accessed September 2, 2015.

Tuller D. Chronic fatigue syndrome gets a new name. *New York Times.* February 11, 2015. Available at http://well.blogs.nytimes.com/2015/02/10/chronic-fatigue-syndrome-gets-a-new-name. Accessed September 2, 2015.

Mitochondrial Dysfunction and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

In a 2012 study, Norman E. Booth and colleagues used an ATP Profile Test to identify mitochondrial dysfunction in 138 patients diagnosed with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). Test results corresponded with illness severity. The British researchers also noticed that patients exhibited two different ATP compensatory pathways for mitochondrial dysfunction. One group showed increased glycolysis, which produced lactic acid burn, acidosis, and cellular damage. The other group did not exhibit excess lactate. Instead of muscle soreness, their main symptom was delayed fatigue. Booth and colleagues suggest that the delayed fatigue may be due to loss of adenine nucleotides needed to make ATP that occurs during the adenylate kinase reaction.

What produces mitochondrial dysfunction in the first place? Booth and colleagues say that one cause is the partial blocking of translocator protein sites – sites where ADP is moved into mitochondria for recycling and ATP is moved out of the mitochondria to the cytosol. The other cause is lack of substrate or essential cofactors – that is, nutrients. Magnesium, for example, is required for ATPase (the enzyme that releases energy from ATP) to function. Most patients with CFS/ME have low intracellular magnesium levels.

Garth L. Nicolson, PhD, discusses several nutrients to treat mitochondrial dysfunction in a 2014 review. In addition to providing magnesium, phosphate, thiamine, and other factors necessary for energy production, he recommends the use of phospholipids to repair mitochondrial membranes damaged by oxidative stress. "The dietary replacement of mitochondrial membrane phospholipids (lipid replacement therapy [LRT]) using food-derived molecules to remove damaged, mainly oxidized, membrane lipids in mitochondria and other cellular organelles has proved very effective at increasing mitochondrial function and reducing fatigue," he writes. Phospholipids and vitamins reduced severe chronic fatigue in elderly patients by 40.5% in 8 weeks in a 2003 pilot study led by R. R. Ellithorpe. Other nutrients that support mitochondrial dysfunction and relieve fatigue, according to Nicolson, are CoQ10, microencapsulated NADH, L-carnitine, and alpha-lipoic acid.

Booth NE, Myhill S, McLaren-Howard J. Mitochondrial dysfunction and the pathophysiology of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). *Int J Clin Exp Med.* 2012:5(3):208–220. Available at www.ncbi.nlm.nih.gov/pmc/articles/PMC3403556. Accessed August 25, 2015.

Nicolson GL. Mitochondrial dysfunction and chronic disease: treatment with natural supplements. *Altern Ther.* Winter 2014;20(Suppl. 1) 18–25. Available at http://todayspractitioner.com/wp-content/uploads/2014/09/athm_s1_nicolson.pdf. Accessed September 5, 2015.

Metal Oxide Nanoparticles and Gut Microbiota

Metal oxide nanoparticles (NPs) commonly used in foods, cosmetics, drugs, and medical diagnostics significantly affect gut microbiota, according to a 2015 study. The study, led by Alicia A. Taylor, used a custom-built device that simulates the colon to investigate the effects of titanium dioxide (TiO2), zinc oxide (ZnO), and cerium dioxide (CeO2) nanoparticles on microbiota from a healthy 26-year-old female. TiO2 NPs are added to toothpastes, sunscreens, and cosmetics. ZnO and CeO2 NPs are used in coatings, paints, pigments, and cosmetics. These two NPs have species-specific antibacterial effects. They also cause membrane damage in eukaryotic cells (nonbacterial cells with nuclei). "It is estimated that 15,600 metric tons year^{-1} of TiO2 nanomaterials, 3700 metric tons year^{-1} of ZnO nanomaterials, and 300 metric tons year^{-1} of CeO2 nanomaterials enter water systems with the majority of these NPs discharged from wastewater treatment plants," say the authors. As a result, these NPs are in drinking water.

Before adding NPs to colon media, the environmental engineering science team ran the simulation device for two 5-day-long experimental trials to determine the bacterial community's baseline composition. They then ran at least two consecutive 5-day trials for each NP. The researchers used NP concentrations that reflected typical human exposure from drinking water and food. During the 5-day trials, waste samples were taken 3 times a day, at which time the colon was "fed" with sterile media.

Findings indicate that gut bacteria are stressed by NPs and react defensively. All three metal NPs produced significant decreases in bacterial cell size compared with baseline control. Decreased cell size is a survival adaptation that occurs in other stressful situations such as starvation. All three NPs increased cell hydrophobicity compared with

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the control. With increased hydrophobicity, cells tend to clump together, reducing their surface exposure. Biofilms (aggregates of microorganisms) occur during increased hydrophobicity. All three NPs affected electrophoretic mobility (EPM), an indicator of the relative surface charge associated with microorganism attachment and stability. The EPM indicated more instability during midweek, increasing the possibility of aggregate formation.

The researchers also looked at microbial production of the short-chain fatty acids (SCFAs) butyric acid and acetic acid. (They were unable to measure a third important SCFA, propionic acid, accurately.) For the most part, SCFA levels changed little compared with controls. The one exception was butyric acid production, which decreased during the CeO2 trials. Butyric acid inhibits gut inflammation and supports gut lining integrity. "This indicates that NPs could have a two-fold impact on the intestine by first affecting SCFA production, then leading to systemic circulation of the NPs via an inhibited intestinal barrier," say the authors.

The authors acknowledge that their study, using microbiota from one woman, cannot give a definitive picture of NPs' effect on gut microbes in vivo long term. Chemical composition and surface charge of digested food, diet variability, and individual differences in microbiota composition may contribute to the health effects of NP exposure. Still, this study looks at a little-discussed environmental exposure with potential health effects. "To date, this is the first paper analyzing the effects of environmentally relevant concentrations of NPs and their effects on the physical-chemical components of the gut community," the authors write.

Taylor AA, Marcus IM, Guysi RL, Walker SL. Metal oxide nanoparticles induce minimal phenotypic changes in a model colon gut microbiota. *Environ Eng Sci*. Epub April 24, 2015. Available at www.silae.it/files/ees_2014_0518.pdf. Accessed August 24, 2015.

Pain, Anger, and Compassion Meditation

Many patients who suffer chronic pain are angry – angry at the pain, angry at their physical limitations, angry with practitioners for not healing them. While this anger is understandable, the stress-induced biochemicals triggered by the emotion contribute to the pain. Anger and frustration correlate with reduced treatment response. Unresolved negative emotions also damage relationships with spouses, adding more stress. Recognizing the need to address anger in people with chronic pain, Heather L. Chapin and colleagues at Stanford University (Palo Alto, CA) recently conducted a pilot study to test compassion meditation. "Compassion meditation," they explain, "is prescribed as treatment for persistent anger in Eastern cultures." During the practice, the meditator focuses on the distress of oneself or another person and cultivates the desire to alleviate that distress (compassion). This form of meditation has increased psychological well-being, improved interpersonal relationships, and enhanced immune and stress responses in research studies.

This pilot study used patients' perceptions and the observations of a spouse, relative, or close friend to evaluate compassion meditation's effect on pain, anger, and quality of life. Although 28 patients were enrolled initially, only 12 completed the study; the other 14 withdrew or were withdrawn for a variety of reasons. All participants had experienced chronic pain for at least 6 months and an average pain intensity of ≥ 4 on a scale of 0 (no pain) to 10 during the month before enrollment. After an initial interview, all patients took part in a 5-week wait period before receiving group instruction in compassion cultivation training. At the end of the waiting period, patients completed online surveys that measured anger, pain severity, and pain-related functional interference (baseline).

The Compassion Cultivation Training course, used in the study, is a 9-week curriculum develop by Stanford's Center for Compassion and Altruism Research and Education. Weekly 2-hour classes provide instruction in compassion meditation practices, small and large group discussions, and in-class meditation practice sessions. Patients in the study also received a CD with guided meditations for individual practice and were asked to keep a record of the amount of time that they meditated each day. To avoid influencing the third-party observations, patients were instructed to avoid discussing this training with their significant other who had volunteered to take part in the study.

After the 9-week course, patients completed online questionnaires again as well as a survey with quantitative and open-ended questions. Then, their significant others were asked to complete online surveys that asked them to rate their partner's pain, quality of life, and possible changes in their relationship. If significant others reported seeing any improvement, they were asked to provide more details and give examples.

Compassion training produced a moderate but "clinically important" reduction in pain severity, according to patient responses. Anger also decreased about 25%. In addition, significant others observed reduced anger and improved life quality. Even though none of the questions in the posttreatment survey mentioned anger, significant others reported a lessened tendency for the patient to "go off the handle" and faster recovery from anger. The authors state: "Our results indicated that greater change in anger for the chronic pain patients' correlated with significant others' ratings for post-treatment improved quality of life in their chronic pain partners ($r=.68$, $n=12$, $p=.016$)."

Larger studies with an active control group (engaged in a group class without a meditation component) are needed to assess the benefits of compassion training for patients with chronic pain. Nonetheless, compassion meditation has a long traditional history and may well benefit people with chronic pain.

Chapin HL, Darnall BD, Seppala EM, Dotay JR, Hah JM, Mackey SC. Pilot study of a compassion meditation intervention in chronic pain. *J Compassionate Health Care*. 2014;1(4). Available at www.biomedcentral.com/content/pdf/s40639-014-0004-x.pdf. Accessed August 24, 2015.

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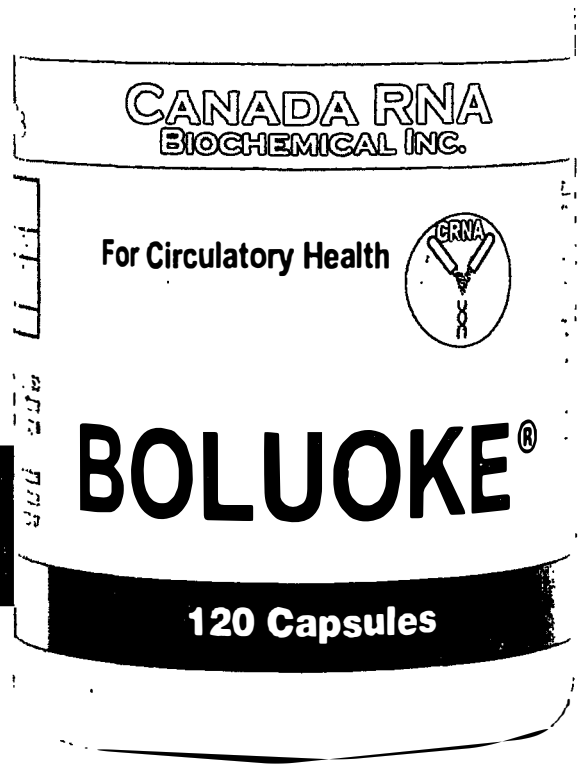
- ✔ No significant effect on INR or PTT



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by Ingrid Kohlstadt MD, MPH
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2015 Healthy Aging Summit: What's Coming and What's Not

The 2015 Healthy Aging Summit was held July 27–28 in Washington, DC. Congress was in recess, street parking was ample, and the Potomac River was shrouded in mist until late morning. But inside the conference halls there was a strong sense of mission. Attendees were passionate about health and vitality in older age and had diverse professional vantage points. This conference would herald the next wave of health-care resources and how to tap into them. In this column, I elaborate on how practitioners of integrative medicine might be able to catch the wave.

Erase That from the Smart Board

Many of the ills that people chalk up to old age don't belong there. They are diseases rather than a natural part of healthy aging. Most of the diseases either have treatments or they clue us in to other important ways to help our patients. In fact, fatigue, pain, fibromyalgia and the other aches addressed in this month's issue of *Townsend Letter* are among the conditions getting a careful look-over at the National Institutes of Health.

Research scientists at NIH who are studying the biology of aging are a small group compared with their colleagues studying the biology of diseases. But they turned this seeming disadvantage into an opportunity to collaborate and name their new field of study *geroscience*. Geroscientists separate aging from disease. As the diseases posing as natural aging are erased from the healthy aging smart board one by one, we can make diagnoses earlier, when existing therapies are most effective.

Scientists are also hot on the trail for demonstrating age-reducing activity in small molecules and new drugs, creating an entirely new therapeutic class of drugs called senolytics. The current list includes aspirin and metformin and may soon expand to 20 more molecules. These molecules do more than treat the diseases; they seem to interrupt some other aspect of the normal aging process. Metformin is given with diabetes as an indication, the time until onset of a comorbidity was less than the healthy aging group in one study. Rapamycin has a fascinating history. It was identified from bacteria found on Easter Island, where its antifungal properties were noted. Causing too many immune-system side effects, it was seldom used as an antifungal when it was discovered to have a chemotherapeutic action against cancer. As it turns out, the drug has now been shown to extend the life of mice, raising great interest as a promoter of longevity. It remains in the research phase.

Aging Mice and Why It Matters

While the research in senolytics holds great promise for extending longevity, it's also shedding new and inconvenient light on some recesses of pharmaceutical research. Mice and people respond similarly – as we age we are less able to manage toxins, be they stress, junk food, or medications. Pharmaceutical animal research is usually conducted in young mice regardless of the likely age of the intended patient recipients. Now that geroscientists are studying old mice, they are finding more side effects to medications.

Fall Prevention

It currently takes 17 years for research findings to reach patients, according to David Reuben, MD, of the University of California, a geriatrician and member of the Institute of Medicine. Everyone agrees that this is much too long. The federal government has put $30 million toward shortening this time frame for fall prevention. Since falls are a leading cause of disability, the investment should pay off. But the voices on what to prioritize around fall prevention were reflected in the diversity of the conference.

Johanna Dwyer, DSc, RD, has long advocated for making nutrition a vital sign. She emphasizes that sarcopenia, which puts patients at risk for falls, should

be recorded routinely in nurses' notes. But little progress has been made in communicating the importance of this physical exam finding, let alone nutrient deficiencies such as vitamin D and vitamin B12, which tend to manifest with more subtle physical exam findings.

Interagency communication remains a challenge. For example, HUD has prepared a simple and thorough checklist for how to reduce the risk of falls in the home. Attention to lighting, handrails, and carpets can be lifesaving, but presumably since the checklist was developed outside usual health channels, it is not on the NLM's resource list for care providers.

The Riptide of Aging and Disability

The number of older people with disabilities is greatly increasing. What's less understood is that it's increasing in two ways: (1) people who age *into* disabilities and (2) people who age *with* disabilities.

Here's why health professionals will want to distinguish between these two groups even though they receive similar health-care services. Aging into disabilities is viewed as a failure of the health-care system. Disabilities in this group tend to be from preventable falls or blindness. Health professionals will want to emphasize all preventive services in this group.

In contrast, those who are aging into disabilities such as cerebral palsy, multiple sclerosis, and spinal cord injuries are a success of the health-care system, since these conditions used to preclude longevity. Unfortunately, most of the research on disabilities and aging has been conducted without this group, largely because they didn't meet the inclusion criteria. So access to services for those aging with disabilities may require some advocacy and clear communication of the preexisting disability in the patient's chart.

Innovations That Improve Quality of Life Around Dementia

At the summit, I was heartened by the innovations to improve the quality of life for older people with cognitive decline. For example, the Netherlands has assisted-living facilities that look like farms and villages where patients can feed the animals, tend the garden, take a walk, and sip coffee at an outdoor café. It all leads to keeping people active. Another example is an interactive robot made to look like a harp seal pup and to provide the physiologic and social components of animal therapy. Approved as a therapeutic device by the FDA in 2009, this item continues to demonstrate how fewer medications are needed and that Alzheimer's disease doesn't have to stop a smile.

No Ahh-Perations, a Missed Ahh-Portunity

A look inside the mouth can reveal a lot about a patient's aging process. Simply asking the person to say "ahh" can guide the workup. Yet the summit contained no mention of dental health, and I saw no dentist on the speakers list. The closing plenary by WHO aging expert Dr. Somnath Chatterji presented a telling slide. In 1990, edentulism (toothlessness) was the 12th leading condition among the elderly worldwide. Twenty years later, it was no longer on the charts. Hopefully, the leaders in aging will have an "aha moment" that dental health is more than missing teeth.

Summary

Clinicians have important roles in the healthy aging of their patients. Integrative medicine practitioners are already diagnosing and treating diseases that have up to this point masqueraded as "normal" aging. Medications offer both benefits and downsides which become more pronounced in older age. The need for prevention is also more apparent with new resources, but advocating for those resources is still essential for now.

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(CRC Press; 2013)

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Environmental Medicine Update

by Marianne Marchese, ND
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Can the Environment Cause Cancer? Myth versus Fact

Cadmium Accelerates Aging

A recent study published in the *American Journal of Epidemiology* by Ami Zota and colleagues showed that low-dose exposure to cadmium can cause shortened telomeres.[1] It looked at the relation between both cadmium and lead and leukocyte telomere length. Shortened telomeres are associated with premature aging and increased risk of diseases related to aging. Utilizing data from the National Health and Nutrition Examination Survey (1999–2002), blood lead and cadmium levels from over 6000 adults in the US (n = 6796) and urine cadmium from over 2000 adults (n = 2093) were examined for changes in telomere length. They divided the participants into four groups based on the concentrations of cadmium found in their bloodstream, finding that people in the group with the highest amount of cadmium had telomeres about 6% shorter than those in the lowest group. There was no association between lead levels and telomere length. This study suggests that cadmium exposure can cause premature aging of cells by shortening telomeres.

Comment: Cadmium is a heavy metal that is ubiquitous in the environment. People are exposed daily at low levels from food sources including leafy vegetables such as lettuce and spinach, potatoes and grains, peanuts, soybeans, and sunflower seeds. Some are exposed to higher levels through cigarette smoking, secondhand smoke, and air pollution from nearby industrial areas. The World Health Organization calls environmental exposure to cadmium a "major public health concern" and notes that this heavy metal has been associated with cardiovascular disease, respiratory problems, cancer, and other serious diseases. Exposure to cadmium can weaken bones and cause osteoporosis, and damage the kidneys. It is a known human carcinogen in high doses.[2]

Cadmium causes inflammation, oxidative stress, and the inhibiting of DNA repair, all of which could promote telomere shortening. Telomeres are the caps on the tips of chromosomes that help protect the genetic code. Telomeres naturally shorten as people get older, but other factors, including cadmium, may speed up that process. When the telomeres get too short, the cell can no longer divide and chronic diseases can be the result. Telomere testing is available to patients through their doctors. This study does not prove that exposure to cadmium actually causes telomeres to get shorter but finds a correlation. The link was strong and independent but must be proved with additional research.

Drinking Canned Beverages Raises Blood Pressure

Most canned food and beverages are lined with bisphenol A (BPA). BPA has been associated with numerous health issues. A recent study looked at whether increased BPA exposure from consumption of canned beverages actually affects blood pressure and heart rate variability.[3] A randomized, crossover trial was conducted with noninstitutionalized adults over age 60 who were recruited from a local community center. A total of 60 participants visited the study site 3 times, and they were provided the same beverage in 2 glass bottles, 2 cans, or 1 can and 1 glass bottle at a time. Urinary BPA concentration was measured, as well as blood pressure and heart rate variability, 2 hours after the consumption of each beverage. The urinary BPA concentration increased after consumption of canned beverages by >1600% compared with that after consumption of glass-bottled beverages. Systolic blood pressure adjusted for daily variance increased by ≈4.5 mmHg after consumption of 2 canned beverages compared with 2 glass-bottled beverages, and the difference was statistically significant. There was no difference in heart rate variability. The study concludes that consuming canned beverages increases BPA exposure, thus increasing blood pressure.

Comment: BPA is used in epoxy resins lining food and beverage containers and in polycarbonate plastics in many consumer products. Widespread and continuous exposure to BPA, primarily through food, drinking water, dental sealants, dermal exposure to paper receipts, and inhalation of household dusts, is evident from the presence of detectable levels of BPA in more than 90% of the US population.[4] The

health effects of BPA have focused on its estrogenic activity, but there are other mechanisms of action, including liver damage, disrupted pancreatic beta cell function, thyroid hormone disruption, and obesity-promoting effects.[5] Other studies have linked BPA to diabetes and cardiovascular disease, showing an association with only 1 standard deviation (SD) increase in BPA concentration in the body.[6]

This study linking BPA in canned beverages to high blood pressure is interesting on many fronts. The researchers used canned soy milk in the study due to the fact that it has no known ingredient that raises blood pressure. The study sample was very small, only 60 participants, and was an older population which could have variable blood pressure throughout the day due to aging. Also, given the age of the study population, we don't know if they were chronically exposed to BPA earlier in life. We also don't know the state of kidney function, which also could affect blood pressure. That said, BPA exposure from canned foods and beverages is widespread. Given the known adverse health effects of BPA, people may want to consider eating fresh foods and using glass beverage bottles instead of cans. More research is needed in this area on a younger and larger population.

Vaginal Hygiene Products Are a Source of Phthalate Exposure

Phthalates are a group of chemicals used to soften and increase the flexibility of plastic and vinyl. Diethyl phthalate (DEP) and di-n-butyl phthalate (DBP) are two phthalates found in consumer products that may increase risk of adverse health effects. A recent study looked at whether vaginal douching and other feminine-hygiene products increase exposure to phthalates among reproductive-aged women in the US. Researchers conducted a cross-sectional study on 739 women (aged 20–49) from the National Health and Nutrition Examination Survey (NHANES) 2001–2004 to examine the association between use of feminine hygiene products (tampons, sanitary napkins, vaginal douches, feminine spray, feminine powder, and feminine wipes/towelettes) with urinary concentrations of monoethyl phthalate (MEP) and mono-n-butyl phthalate (MnBP), metabolites of DEP and DBP, respectively.[7] More than half of the women in the study were overweight or obese, and many of the women said they hadn't douched at all in the past 6 months.

Results of the study revealed that a greater proportion of black women reported using vaginal hygiene products than white and Mexican American women. Roughly 1/3 of black women said that they douched at least once a month, as did 11% of white and Mexican American women.

Twenty percent of black women reported douching at least twice a month, compared with just 7% of white participants and 3% of Mexican Americans in the study. Douching in the past month was associated with higher concentrations of MEP but not MnBP. No other feminine-hygiene product was significantly associated with either MEP or MnBP. A dose–response relationship between douching frequency and MEP concentrations was observed. Women who douched at least twice a month had 152.2 % higher MEP concentrations than nonusers. Black women had 48.4 % higher MEP levels than white women. Women who douched at least once in the past month had 52% higher levels of MEP in the urine. Adjustment for douching attenuated this difference to 26.4%. The study concludes that vaginal douching may increase exposure to DEP and contribute to racial/ethnic disparities in DEP exposure.

Comment: Phthalates are used in cosmetics and personal care products, including perfume, hair spray, soap, shampoo, nail polish, and skin moisturizers. They are used in flexible plastic and vinyl toys, shower curtains, wallpaper, vinyl miniblinds, food packaging, and plastic wrap. Most people are exposed to phthalates whether they know it or not. Diethyl phthalates are often used to bind cosmetics and fragrances and are in plasticizers, detergent bases, and aerosol sprays.[8] They are used in fragranced personal-care products such as cologne/perfume, hair products, deodorant, lotion, body wash, and nail polish to retain scents. Because of the frequent dermal exposure of humans to DEP, the question of toxicity is crucial. Several studies suggest that DEP can damage the nervous system as well as reproductive organs in males and females.[9]

Feminine-care products that are used vaginally, such as douches, may be an unrecognized exposure source of phthalates. Researchers found no link between DEP and other feminine-hygiene products such as tampons, sanitary napkins, powders, sprays, or towelettes. Most commercial douches contain fragrance, and synthetic fragrances are a mixture of compounds that often contain phthalates. While the study can't rule out other sources of phthalate exposure or prove that chemicals in douches cause specific health problems, the findings suggest that this vaginal cleansing habit may be unsafe. Health practitioners should consider advising patients against douching to eliminate a source of exposure to phthalates. This study that highlights the presence of environmental chemicals in vaginal douches warrants further examination.

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Literature Review & Commentary

by Alan R. Gaby, MD
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Probiotic for Hepatic Encephalopathy

One hundred twenty patients with cirrhosis of the liver and minimal hepatic encephalopathy were randomly assigned to receive standard treatment (lactulose, 30–60 ml per day) or a probiotic preparation (VSL#3, 450 billion colony-forming units per day) for 2 months. Among the 77 patients (40 lactulose, 33 probiotic) who completed the trial, 62.5% of those receiving lactulose and 69.7% of those receiving VSL#3 showed an improvement in neuropsychometric tests. Statistical analysis revealed that VSL#3 was noninferior to lactulose.

Comment: VSL#3 is a proprietary probiotic preparation that contains 8 different strains of bacteria. In previous studies it has been found to be an effective treatment for ulcerative colitis, irritable bowel syndrome, and nonalcoholic fatty liver disease in children. The results of the present study suggest that VSL#3 is at least as effective as standard treatment for patients with cirrhosis and minimal hepatic encephalopathy. The mechanism of action of probiotics in the treatment of advanced liver disease is not known, although they may work by modifying the intestinal flora.

Pratap Mouli V et al Effect of probiotic VSL#3 in the treatment of minimal hepatic encephalopathy: A non-inferiority randomized controlled trial. *Hepatol Res* Epub 2014 Sep 29.

Vitamin D and Sunlight Are Not the Same

In a cross-sectional study of 264 patients with multiple sclerosis (mean age, 47 years; mean disease duration, 14.6 years) and 69 healthy controls, increased summer sun exposure during the preceding 2 years was associated with increased brain gray matter volume ($p < 0.02$) and increased whole brain volume ($p = 0.004$), after adjusting for disability and serum 25-hydroxyvitamin D levels.

Comment: In this observational study, increasing sun exposure was associated with less neurodegeneration in patients with multiple sclerosis, independently of serum 25-hydroxyvitamin D levels. Although observational studies cannot prove causality, the findings of this study are consistent with the possibility that immunomodulation resulting directly from sun exposure may influence outcomes in patients with multiple sclerosis. For example, corticotropin-releasing hormone, which is produced by sun-exposed skin, plays a role in regulating immune function (Slominski A et al. Corticotropin releasing hormone and the skin. *Front Biosci*. 2006;11:2230–2248.). Other potentially beneficial effects of sunlight might result from stimulation of the hypothalamic-pituitary axis through the retina.

It has been known for many years that the incidence of multiple sclerosis is lower in regions around the equator than at higher latitudes. Researchers have assumed that this difference is due to differences in vitamin D levels, but clinical trials of vitamin D supplementation as a treatment for multiple sclerosis have produced conflicting results. Moreover, high-dose vitamin D has been shown to produce worse outcomes than low-dose vitamin D (Stein MS et al. A randomized trial of high-dose vitamin D2 in relapsing-remitting multiple sclerosis. *Neurology*. 2011;77:1611–1618.). A clinical trial of moderate sunlight exposure as a treatment for multiple sclerosis would seem worthwhile.

Zivadinov R et al. Interdependence and contributions of sun exposure and vitamin D to MRI measures in multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2013;84:1075–1081.

Lifestyle Changes May Improve Urinary Incontinence

One thousand nine hundred and ten obese or overweight men (mean age, 60 years; mean body mass index, 35.2 kg/m^2) with type 2 diabetes were randomly assigned to an intensive lifestyle program of caloric restriction and exercise, or to a control group that received diabetes support and education for 1 year. After 1 year, the intervention group lost a significantly greater percentage

of their body weight than did the control group (mean, 9.4% vs. 0.7%; $p < 0.001$). The proportion of individuals who experienced urinary incontinence at least once a week decreased in the intervention group from 11.3% at baseline to 9.0% at 1 year, and increased in the control group from 9.7% at baseline to 11.6% at 1 year ($p = 0.07$ for the difference in prevalence at 1 year). Among men with urinary incontinence at baseline, the probability that the incontinence had resolved at 1 year was significantly higher in the intervention group than in the control group (56% vs.41%; $p = 0.03$).

Comment: The results of this study suggest that an intensive lifestyle program designed to promote weight loss may be useful for the prevention and treatment of urinary incontinence in overweight and obese men with type 2 diabetes. Although the effect on urinary incontinence was only modest, such a lifestyle program would also be expected to have other benefits, such as improvements in diabetes, cardiovascular risk, and bone health, and possibly improvements in mood and energy level.

Breyer BN et al. Intensive lifestyle intervention reduces urinary incontinence in overweight/obese men with type 2 diabetes: results from the Look AHEAD trial. *J Urol.* 2014;192.144–149.

Ginger for Heavy Menstrual Bleeding

Ninety-two Iranian high-school girls with heavy menstrual bleeding, regular menstrual periods, and no evidence of gynecological diseases were randomly assigned to receive, in double-blind fashion, 250 mg of powdered ginger or placebo 3 times per day, starting on the day before menstruation and continuing until the third day of the menstrual period, for 3 menstrual cycles. Compared with the 3 menstrual cycles before the study, the mean amount of blood loss during the study was significantly lower by 46.6% in the ginger group and nonsignificantly lower by 2.1% in the placebo group ($p < 0.001$ for the difference in the change between groups). The mean amount of blood loss per cycle decreased progressively in the ginger group; during the last cycle, the mean amount of blood loss was 53% lower, compared with baseline.

Comment: These results suggest that ginger is beneficial as a treatment for heavy menstrual bleeding in Iranian teenagers. The mechanism of action is not certain, but it may be due to inhibition of the synthesis of certain prostaglandins.

Kashefi F et al. Effect of ginger (Zingiber officinale) on heavy menstrual bleeding. a placebo-controlled, randomized clinical trial. *Phytother Res.* 2015;29.114–119.

Honey for Recovery Following Tonsillectomy

Eighty children (aged 5–15 years) undergoing tonsillectomy were randomly assigned to receive 5 ml of oral honey every 6 hours postoperatively while awake or no honey (control group) for 10 days. Those assigned to receive honey were also advised to consume honey again (dosage not specified) when pain developed, and to take acetaminophen if pain persisted for more than 15 minutes.

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The control group took acetaminophen for pain. Mean pain severity during the first 9 days ($p < 0.05$), mean time before pain resolved (5.53 vs. 7.65 days; 28% decrease; $p < 0.001$), and mean time before oral intake was resumed (3.8 vs. 4.5 days; 16% decrease; $p < 0.001$) were significantly less in the honey group than in the control group.

Comment: Postoperative hemorrhage and pain are common complications of tonsillectomy. Honey has been used to promote wound healing and to reduce inflammation. The results of the present study suggest that consumption of honey can reduce pain and accelerate recovery in children undergoing tonsillectomy

Mohebbi S et al. Efficacy of honey in reduction of post tonsillectomy pain, randomized clinical trial. *Int J Pediatr Otorhinolaryngol*. 2014;78:1886–1889.

Preventing Peanut Allergy

Six hundred and forty infants (aged 4–10 months) with severe eczema, egg allergy, or both were randomly assigned to consume or to avoid peanuts. Infants assigned to consume peanuts underwent a baseline food challenge, in which those who had a negative skin-prick test were given 2 g of peanut protein in a single dose, and those who had a positive skin-prick test were given incremental doses up to a total of 3.9 g of peanut protein. Infants who reacted to the baseline food challenge were instructed to avoid peanuts, but were included in the intent-to-treat analysis. Infants assigned to consume peanuts and who did not have a reaction to the baseline challenge were fed at least 6 g of peanut protein per week, divided into 3 or more meals per week, until they reached age 60 months. Among the 530 infants in the intent-to-treat population who initially had negative results on the skin-prick test, the prevalence of peanut allergy at 5 years of age was 13.7% in the avoidance group and 1.9% in the consumption group ($p < 0.001$). Among the 98 participants in the intent-to-treat population who initially had positive test skin-prick results, the prevalence of peanut allergy was 35.3% in the avoidance group and 10.6% in the consumption group ($p = 0.004$). Similar results were seen in the per-protocol analysis. Increases in levels of peanut-specific IgG4 antibody occurred predominantly in the consumption group; a greater percentage of participants in the avoidance group had elevated titers of peanut-specific IgE antibody.

Comment: The prevalence of peanut allergy has been increasing in recent years among children in Western countries. The results of the present study indicate that early introduction of peanuts significantly decreased the incidence of peanut allergy and modulated immune responses to peanuts in children at high risk for peanut allergy. IgG4 antibodies consist of both symptom-evoking and symptom-blocking antibodies. It is possible that early exposure to peanuts prevented the development of peanut allergy by increasing the concentration of peanut-specific IgG4 blocking antibodies.

Du Toit G et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med*. 2015,372:803–813.

Editor's note: Sanders and Schor review peanut allergy on page 38.

Existence of Non-Celiac Gluten Sensitivity Confirmed

Sixty-one adults who did not have celiac disease or wheat allergy (negative wheat-specific IgE) but who believed that ingestion of gluten-containing food was the cause of their intestinal and extraintestinal symptoms were randomly assigned to receive, in double-blind fashion, 4.4 g per day of gluten or placebo (rice starch) in capsules for 1 week. After a 1-week washout period on a gluten-free diet, each person was crossed over to the other treatment for an additional week. Among the 59 patients who completed the trial, compared with placebo, gluten ingestion significantly increased overall symptoms ($p < 0.04$). Abdominal bloating ($p = 0.04$) and pain ($p < 0.05$), among the intestinal symptoms, and foggy mind ($p < 0.02$), depression ($p = 0.02$), and aphthous stomatitis ($p < 0.03$), among the 13 extraintestinal symptoms assessed, were significantly more severe with gluten than with placebo.

Comment: Many patients without celiac disease believe that they experience adverse reactions from gluten, and the number of people reporting such adverse reactions has been increasing in recent years. Despite these anecdotal reports, not everyone in the medical community is convinced of the existence of non-celiac gluten sensitivity. The results of the present study confirm that gluten challenge can trigger both intestinal and extraintestinal symptoms in patients with self-reported nonceliac gluten sensitivity.

Di Sabatino A et al. Small amounts of gluten in subjects with suspected nonceliac gluten sensitivity: a randomized, double-blind, placebo-controlled, cross-over trial. *Clin Gastroenterol Hepatol*. Epub 2015 Feb 19.

Olive Oil Promotes Healing of Burns

One hundred patients (mean age, 33 years) hospitalized with third-degree and deep second-degree burns on 10% to 20% of body surface area were given a very low-fat diet and randomly assigned to receive additional olive oil or sunflower oil, to bring total fat content to 20% of total energy intake. Mean time required for wound healing was significantly lower by 17% ($p = 0.04$), and mean length of hospital stay was significantly lower by 17% (7.4 vs. 8.9 days; $p = 0.05$) in the olive oil group than in the control group.

Comment: The results of this study suggest that consumption of a low-fat diet, in which olive oil was a major source of dietary fat, accelerated wound healing and decreased the duration of hospitalization in burn patients. The mechanism of action of olive oil is not clear, although olive oil contains polyphenols that have anti-inflammatory activity.

Najmi M et al. Effect of oral olive oil on healing of 10-20% total body surface area burn wounds in hospitalized patients. *Burns* 2015,41.493–496.

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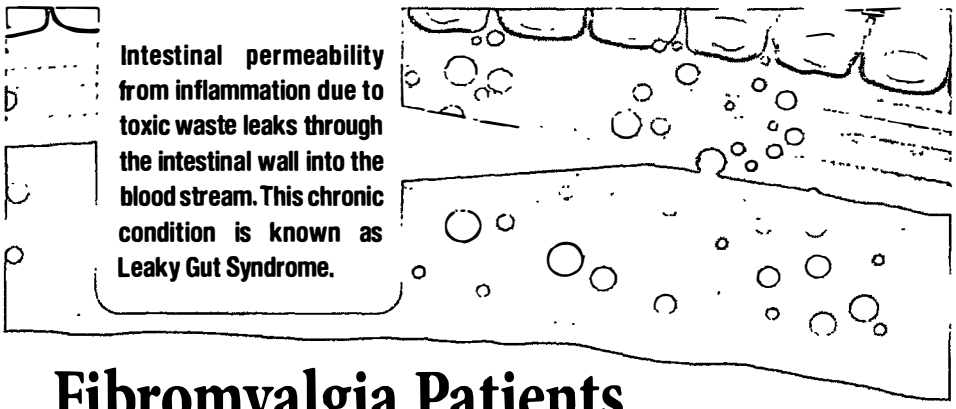


Intestinal permeability from inflammation due to toxic waste leaks through the intestinal wall into the blood stream. This chronic condition is known as Leaky Gut Syndrome.

Fibromyalgia Patients Feel Relief with Colostrum-LD®

The Leaky Gut Connection

A majority of people with fibromyalgia and/or chronic fatigue syndrome also have leaky gut syndrome (LGS), which is the primary cause of autoimmune diseases. LGS allows undigested food particles and toxins to cross into the bloodstream whereby the immune system attacks them as foreign substances which leads to inflammation, swelling, and pain. This ongoing, hyperimmune reaction affects the fibromyalgia pressure points and causes intense pain and stiffness for fibromyalgia sufferers.

Colostrum-LD® to the Rescue

Colostrum's healing benefits are multi-faceted and its unique blend of growth and immune factors can produce relatively quick relief, typically within a month. Colostrum-LD® is the only colostrum laboratory-certified to contain the growth factors clinically proven to heal and prevent LGS. Once a patient's leaky gut is healed, the toxin crossover is halted and nutrient absorption is improved. Magnesium absorption is particularly important in fibromyalgia patients who typically have low tissue levels even with supplementation. When LGS is attenuated, mineral absorption is balanced.

Another mechanism of action is colostrum's effect on growth hormone (GH) and insulin-like growth factor-1 (IGF-1) deficits in fibromyalgia patients. IGF-1 is a good indicator of GH, which is otherwise difficult to measure. Approximately one-third of fibromyalgia patients have low IGF-1 levels. The liver converts growth hormone (GH) to IGF-1; low growth hormone levels are associated with decreased muscle strength, fatigue, impaired brain and memory function, immune dysfunctions, and stymied healing, cell regrowth, and tissue repair. Research has shown that daily injections of synthetic growth hormone can bring relief, but we also know that synthetic human growth hormone is unsafe.

Manufactured GH by nature of its recombinant DNA origins is only seventy percent bio-identical to natural growth hormone. As a result, GH injections may lead to cancer, joint pain, carpal tunnel syndrome, arm and leg swelling, glucose intolerance, increased risk of diabetes, and gynecomastia.

Conversely, GH and IGF-1 in bovine colostrum are nearly bio-identical to growth hormones in the human body, many of which actually help prevent cancer, improve glucose tolerance, and reduce inflammation and pain. IGF-1 is also thought to correct low levels of serotonin and its precursor, tryptophan, which are associated with the sleep disturbances in patients with either fibromyalgia or chronic fatigue syndrome. Colostrum-LD® is the only medicinal food source of all the growth hormones required by the human body.

Additionally, colostrum contains several anti-inflammatory compounds that bring about pain relief. The proline-rich polypeptides (PRPs) have been shown to modulate the thymus gland which produces leukocytes, or activated T-cells, by which the inappropriate hyperimmune reaction is toned down. The anti-inflammatory action from cytokines and lactoferrin is beneficial in reducing symptoms and providing more mobility and comfort. Powdered colostrum contains some PRPs, but is most effective when combined with IRM® oral spray, a concentrated formula of PRPs.

For maximum results, daily use of Colostrum-LD® and IRM® is recommended by physicians and healthcare providers. Both Colostrum-LD® and IRM® are sourced from the highest quality bovine colostrum collected year-round from pasture-fed, antibiotic-free and hormone-free cows living in the Southwest United States. *For more information and clinical research, visit ColostrumTherapy.com (for professionals) or CenterforNutritionalResearch.org (for consumers).*

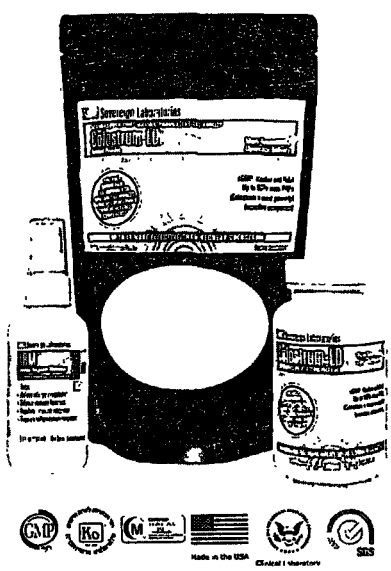
8 of 10 Colostrum-LD® users get Significant Pain Relief

If you treat any of the estimated three to six million Americans suffering with either fibromyalgia or chronic fatigue syndrome, Colostrum-LD® and IRM® should be part of the healing plan.

FIRST STEP: Stop, Heal, and Prevent Leaky Gut Syndrome with Colostrum-LD®.

SECOND STEP: Restore Balance to the Immune System with IRM Immune Response Modulator®. Alleviate inflammation and pain and halt the body from destroying its own tissue and organs.

Recommended by Health Care Professionals for over 20 Years



To receive professional pricing, protocols and clinical studies, register today on www.ColostrumTherapy.com or call Sovereign Laboratories at 928.202.4031. Consumers may purchase online at www.SovereignLaboratories.com

Sovereign Laboratories

Junk Food May Reduce Heart Attack Deaths

by Kimberly M. Sanders, ND, and Jacob Schor, ND, FABNO

Let's Start This Train of Thought in Israel

The all-time most popular, most highly processed snack food eaten in Israel is a product named Bamba. It has been sold since 1964 and accounts for 25% of the nation's snack food market sales. These snacks are made of peanut-flavored puffed corn meal. Think of the American snack Cheetos, leave out the cheese entirely, and instead coat the puffs lightly with peanut butter.

And follow it to England

In 2008 George Du Toit et al., writing in the *Journal of Allergy and Clinical Immunology,* reported that peanut allergy was

> 10 times as high among Jewish children in the United Kingdom as it was in Israeli children of similar ancestry. This observation correlated with a striking difference in the time at which peanuts are introduced in the diet in these countries: in the United Kingdom infants typically do not consume peanut-based foods in the first year of life, whereas in Israel, peanut-based foods are usually introduced in the diet when infants are approximately 7 months of age, and their median monthly consumption of peanut protein is 7.1 g.

This led Du Toit to "... hypothesize that the early introduction of peanuts to the diet may offer protection from the development of peanut allergy."[1]

Israeli kids do not eat peanuts, but they do eat an awful lot of Bamba.

This hypothesis led these researchers to conduct a large-scale clinical trial in which they introduced peanuts at an early age to infants some of who already tested positive for peanut allergy. The results from this trial were published in February 2015 in the *New England Journal of Medicine*.[2]

Peanut Allergy Study

Du Toit's new study is a randomized, open-label, controlled trial. Infants were first divided into two groups based on wheal formation secondary to skin-prick testing for peanut allergy. Each group was then further divided into two groups, where one group consumed 6 grams of a peanut snack per week and the other group was advised to avoid peanuts. Peanut intake was maximized at 3.9 grams in those who had a positive skin-prick test. The peanut snack was distributed in three or more meals a week until the children reached 60 months of age.

In total, 640 infants between 4 and 11 months old with severe eczema, egg allergy, or both were enrolled in the study. The primary outcome was the proportion of patients with a peanut allergy at 60 months of age as determined secondary to an oral food challenge.

Of the 640 infants, 542 had negative skin-prick tests at baseline and made up group 1. In this group, at 60 months, 13.7% of the avoidance group and 1.9% of the peanut consumption group were allergic to peanuts. This statistically significant difference represents an 86.1% reduction in peanut allergy prevalence.

At baseline, 98 children had positive skin-prick tests and these more sensitive infants made up group 2. At 60 months, 35.3% of the avoidance group and 10.6% of the consumption group were allergic to peanuts. This statistically significant difference represents a 70.0% reduction in peanut allergy prevalence.

A significant increase in wheal size was found only in the peanut avoidance group. Patients who were allergic to peanuts at 60 months also had higher peanut IgE levels at this time. Peanut IgE levels increased over time in both the peanut avoidance and consumption groups, but there were few patients in the consumption group that had very high peanut IgE levels.

This Is a Big Deal

"Food allergies are a growing concern, not just in the United States but around the world," said National Institute of Allergy and Infectious Diseases (NIAID) Director Anthony Fauci in a statement. "For a study to show a benefit of this magnitude in the prevention of peanut allergy is without precedent. The results have the potential to transform how we approach food allergy prevention."[3]

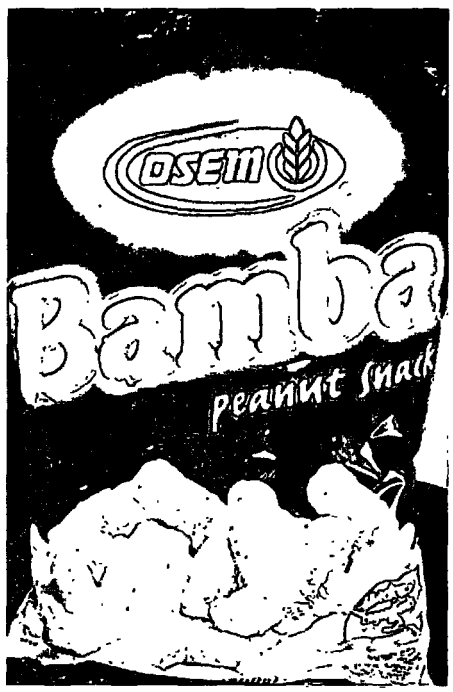
Opposite of What We Thought

These results turn the dietary guidelines about peanuts upside down. In the UK since 1998 and the US since 2000, practice guidelines have advised exclusion of allergenic foods, in particular peanuts, from the diets of infants and of their mothers during pregnancy and lactation.[4,5] Some of you may recall when United Airlines served peanuts as a snack during flights.

This isn't the first study that cast doubts on the validity of food allergen avoidance during infancy. A 2008 study using data from the 2073 children in the LISA cohort evaluated the relationship between timing of solid food introduction and the presence of atopy at 6 years old. The authors found that delaying introduction of solid foods past 4 or 6 months did not reduce the incidence of developing atopic conditions, and those who delayed solid food introduction had more frequent food allergies.[6] A 2007 prospective study assessed the association between solid food exposure and eczema. Among 4753 infants, there was an increased risk of eczema for those who avoided egg in their first year of life. The authors of that study rejected the notion of delayed solid food introduction and stated that allergenic foods should not be delayed past 6 months of age in order to prevent atopy. A 2008 paper in *Pediatrics* milked data from the KOALA cohort in the Netherlands. After analyzing data from 2558 infants in this ongoing cohort, the conclusion was, "More delay in introduction of cow milk products was associated with a higher risk for eczema. In addition, a delayed introduction of other food products was associated with an increased risk for atopy development at the age of 2 years."[7]

A 2013 study concluded that the trend towards lower egg allergy prevalence in infants fed eggs early in life, when studied against a control group, alleviates concerns that early introduction of allergenic foods would pose an increased risk for allergy.[8] If nothing else, this study revealed that early introduction of egg does not increase the egg allergy.

But in the recent Du Toit study, it tells us that introducing peanuts at an early age appears to be safe and well tolerated, even in those who have a positive skin-prick test reaction to peanuts, appears to cause no adverse reactions, and most importantly is associated with lower risk of developing an allergy to peanuts later in life.



The past practice of keeping children in an allergen-free bubble during infancy was the wrong approach. Doing so may turn common foods into dangerous allergens. Our national fear of peanuts may have broader implications on general health.

Peanuts Are Not Nuts

Technically speaking, peanuts are not nuts at all. Rather they are peas. Their Latin name is *Arachis hypogaea*. *Arachis* is the genus of flowering pea plants. *Hypogaea* means below (*hypo*) the earth (*Gaea*). Peanuts are annual plants. After the plants produce their typical-looking pea-flowers, the flower stalks do something unusual: they elongate, bend over, and push the flower ovaries into the ground where the legume pods mature. Nuts grow on trees. Peanuts are just peculiar peas that ripen underground. It is curious, perhaps a marketing/branding thing, that they are grouped in our minds with nuts. For some reason, though, this works, as both nuts and peanuts have similar health benefits.

Nuts Are Good for Your Heart

Over the years multiple studies have associated nut consumption with health benefits, especially in regard to cardiovascular disease morbidity, and overall mortality. A 2014 meta-analysis by Lou et al. of 11 studies found that nut consumption was inversely associated with total mortality, though it did not provide information on cause-specific mortality.[9] Bao et al., in a 2013 report that analyzed data from the Nurses' Health Study and the Health Professionals Follow-up Study, found that nut consumption was inversely associated with all-cause, cancer-specific, and heart disease mortality.[10] Data from the PREDIMED trial cohort reported that baseline nut consumption was associated with reduced mortality.[11] Perhaps the most recent paper on this topic is a meta-analysis by Grosso et al. These researchers combined data to include 354,933 participants, 44,636 cumulative incident deaths, and 3,746,534 cumulative person-years. One serving of nuts per week resulted in a 4% decreased risk for all-cause mortality. One serving per day was associated with a 27% decreased risk of cardiovascular disease mortality.[12] Nuts are clearly good, but it wasn't clear whether peanuts should receive the same acclaim.

Peanuts Are Also Good

Eating peanuts appears to provide similar benefits as does eating tree nuts. A March 2015 study by Luu et al. found that peanut consumption was associated with the same reduction in mortality rates, and in particular ischemic heart disease, as nut consumption. Actually this new study told us two things: first, peanuts are as beneficial as tree nuts; second,

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Junk Food May Reduce Heart Attack Deaths

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the benefits are seen across racial and socioeconomic lines.

This Luu study examined the association of nut consumption with total and cause-specific mortality in Americans of African and European descent, who were predominantly of low socioeconomic status (SES), and also in Asian individuals living in Shanghai, China.

Data were extracted from three separate and large cohorts: 71,764 participants were US residents of African or European descent, primarily of low SES. These participants were part of the Southern Community Cohort Study (SCCS) conducted in the southeastern US between March 2002 and September 2009. Another 134,265 participants were drawn from two cohorts in Shanghai, China, the Shanghai Women's Health Study (SWHS) and the Shanghai Men's Health Study (SMHS).

Food frequency questionnaires completed by participants allowed assessment of overall nut and peanut consumption. In the Shanghai cohorts, tree nut consumption was rare and the majority of nuts consumed were peanuts. In the US cohort, about half the nuts consumed were peanuts.

Nut intake was inversely associated with risk of total mortality for all 3 groups. Individuals in the upper 20% of nut consumption compared with those in the lower 20%, had a 17% to 21% lower risk of dying during the study follow-up period.

Higher nut consumption was associated with a 30% to 40% lower risk of ischemic heart disease. The nut–mortality association was similar for men and women and for blacks, whites, and Asians and was not modified by the presence of other health conditions. The benefit of eating nuts crossed all racial and economic lines. No difference was seen between eating peanuts or tree nuts.[13]

We Are Talking About Peanuts Here

It would appear that the common health-care belief and practice of delaying introduction of potential food allergens, in this case peanuts, has now been thoroughly disproved. Our national practice of avoiding peanuts has probably increased allergy incidence rather than lowering it. In the long run it may also have deprived many people of an inexpensive food that might provide significant health benefits. While we may not want to be seen as advocates for junk food, the benefits of eating Israeli Bamba, because of the protective effect against developing peanut allergies, might far outweigh our classic concerns about eating empty calories; we might consider an exception to our rules – at least for Bamba.

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Pinky and the Brain

by Jim Cross

One of my son's favorite cartoons, when he was young (mine also), was *Pinky and the Brain*. Of course Steven Spielberg was the executive producer, so it shouldn't be any great surprise that this cartoon was complex and contained a large amount of humor geared toward the adults watching with their children. Pinky and Brain are genetically enhanced laboratory mice who live in the Acme Labs research facility. Brain is self-centered and always attempting to take over the world, whereas Pinky is good-natured but feeble-minded. In each episode, Brain devises a new plan to take over the world that ultimately ends in failure.

In terms of mental illness, many of our patients are similar to either Pinky or Brain or sometimes both. What I will attempt to elaborate on in this article is the steps we can follow to truly individualize our treatment plan for the patients who walk into our offices. It doesn't matter if they are depressed/schizophrenic/anxious. We need to evaluate some basic parameters in their bodies which, upon correction, tend to have some powerful biochemical effects on their brains at the level of the synaptic cleft, which is where true change has to occur if they don't just want to take some type of drug for the rest of their lives.

I would like to focus on these areas that I have found to be the most clinically relevant and able to effect the most vibrant change in my patients: food intolerances, leaky gut > leaky brain, stress/Earthing, increased/decreased reuptake of neurotransmitters at the synaptic cleft, toxic metal overload, and hypothyroidism. To avoid an overly long article, which I also never like, I will focus just on the first three here and hopefully the other three in a later article.

This is not going to be so much a research article as it will be a guide geared to ascertaining which of the above variables you need to look at first to maximize your clinical outcomes. It's as if you and your patients are in a giant game show and you need to figure out behind which door is the prize or behind which of the above doors lies the clinical choice/key that will begin to unlock the blockages in their bodies to allow their mental illness to improve.

A great example of this individualization of treatment comes from my good naturopathic friend Wade Boyle, who used to give a speech every year at the annual naturopathic convention. He would title it: "What Works and What Doesn't." He would then proceed to hold court on what he had found to work and what didn't and why. They never scheduled anyone opposite him, because everyone would come to his talk. One great gem from Wade was how to distinguish the use of valerian from hops in the treatment of insomnia. He found in the old Eclectic literature that hops worked better if the carotid pulse was stronger than the radial pulse and vice versa for valerian. Great clinical anecdotes from my brother!

We must then approach this patient with a chronic mental illness from a new paradigm. Just focusing narrowly on one and maybe two variables is perfect for a person who has just fallen off their bike and fractured their distal radius or for a person with a 104° fever and acute bacterial pneumonia. The fall on the bike tends to affect us all in the same manner. Why a person has a complex mental illness will not be dealt with using the simple linear relationship above.

Chronic illness is complex because it is the interaction of our own uniquely biochemical bodies, the traumas they have been exposed to in this life, and the degree to which we are aware of all that has happened to our bodies. How sensitive some patients are over others determines whether they will develop an easily treatable illness or a complex, chronic condition that will stump most caregivers. This is our task as true caregivers of the 21st century: determine the one or two clinical factors that need immediate attention to begin the healing our mentally ill patients' minds to the point where they will no longer need drugs to allow them to function in our dysfunctional society. After we have unlocked these first couple of doors, then our detective work can hopefully continue and lead us to other areas of their lives that have physical/emotional/mental blocks.

Door #1: Food

So, without further adieu, let's examine my first three roadblocks to optimal mental health. Behind magic door #1 lies: food. How important is food, you may wish to know, and why would you list it atop your roadblocks? I taught various classes

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at American College of Traditional Chinese Medicine in lovely San Francisco for 6 years. One of them was Western nutrition. I would start the class asking my Chinese medicine students how many times a year they visited a medical doctor. Most laughed at the thought, as they were in acupuncture school. A few raised their hands because they had semiserious illnesses that required skilled Western medical intervention. Then I asked them how many times a year they received acupuncture. Surprisingly, as they were studying Chinese medicine, 1 to 2 times a month! Then I asked them, how many times a year did they eat? Most acupuncture students didn't take science and math courses like medical students did for their prerequisites. I helped them out: I went with what I would consider a typical American who would eat 3 main meals and 2 snacks, so 365 × 5 = 1825 ×/year. Now maybe you are beginning to see why I put food as #1. Just think of the damage that is happening in a body that consumes what is sold in supermarkets, fast food stores, and most restaurants 1825 times a year. That thought terrifies me!

Bruce Ames is a professor emeritus of biochemistry and molecular biology, University of California, Berkeley. He is also the originator of the triage theory. This theory states that our bodies, if they do not receive the daily needed amount of a nutrient, will triage what they receive of that nutrient to the areas that need it functioning in the present. The future is of no concern in that scenario.

For many years, I had marveled at the resiliency and strength of the bodies of my patients who eat a typical American diet. How could they not fall acutely sick and/or die? Dr. Ames appears to answer this question extremely proficiently. I might also add that Dr. Ames also seems to have discovered the source of chronic disease. As this triaging continues to happen in most Americans (none of the readers of this magazine of course!), the areas of the body not receiving the required nutrients will begin to function sub-optimally, which will eventually lead to actual disease in that area.

Back to that 1825 figure: I use this number because it is a powerful motivating tool. When my patients start to grasp the number of times that they eat per year, they begin to understand the powerful impact that food has on their bodies. Now comes my next metaphor. It requires a large effort to eat food that is optimal for you in our society. You must

Symptoms and Signs Associated With Food Allergy

GI System	canker sores, celiac disease, chronic diarrhea, ulcers, gastritis, irritable bowel syndrome, malabsorption, bloating, gas, ulcerative colitis, Crohn's disease, constipation
Genitourinary	bed-wetting, chronic bladder infections where the urine shows only white blood cells but no bacteria
Immune	chronic infections, frequent ear infections in kids, chronic nasal drip, chronic environmental allergies, frequent colds/flus
Mental/Emotional	brain fog, fatigue, anxiety, depression, hyperactivity, inability to concentrate, insomnia, irritability, mental confusion, personality change, seizures, headaches, migraines
Musculoskeletal	bursitis, joint pain, low back pain, tendonitis
Respiratory	asthma, chronic bronchitis, chronic sinusitis, itchy nose or throat
Skin	acne, eczema, hives, itching, any skin rash, psoriasis

Modified Elimination Diet

Food Group	Allowed	Avoid
Meat/Fish/Poultry	chicken, turkey, lamb (all free range), wild game	processed meats, beef, pork, fish, eggs
Legumes/Nuts	almonds, walnuts, pecans, lentils, peas	peanuts, cashews, sunflower seeds, beans, any containing sugar/salt
Dairy Products	unsweetened/live yogurt, rice milk	milk, ice cream, sour cream, cream cheese, butter, cottage cheese
Breads/Pastas/Cereals	rice/buckwheat pastas, breads, or cereals	wheat, barley, rye
Grains	brown rice, millet, tapioca, buckwheat	anything containing rye, wheat, or barley
Soups	clear, vegetable-based, home-made soups	canned soups
Vegetables	fresh veggies	anything canned, potatoes, tomatoes, peppers, eggplant
Fruits	fresh	juices, dried fruits, citrus fruits, strawberries
Beverages	water (filtered or spring), herbal teas	coffee, alcohol, sodas, all juices, black/green tea
Oils/Fats	extra-virgin olive oil, flax oil	margarine, all other oils, butter, dressings
Salt	sea salt	table salt

purchase the food, prepare the food, and not let anybody talk you out of eating this food. This is where I use a line from the song "Equal Rights" by Peter Tosh: "Everybody wants to go to heaven/But nobody wants to die." It takes substantial *Yuan qi*, intestinal fortitude, or just plain guts to withstand the barrage of edible foodlike substances that American corporations attempt to throw at you.

Now, how do you individualize each person's diet to make their metabolism run as quietly and efficiently as a 1965 Rambler? Everyone has a slightly different idea as to how they can accomplish this Herculean task (plus everyone thinks that their way is the only way!). There are various food allergy tests, radionics testing, and so on. The list is interminable. I personally use little vials whose water contains the electromagnetic signature of whatever food I am muscle testing. To me, it doesn't matter what test you use. I just want them to be able to pass my food test: immediately after you eat a meal, do you feel physically and especially mentally clear? Do you also feel mentally and physically clear 1 hour, 2 hours, 3 hours, and 4 hours after eating? If you can say yes to this statement, then I believe that you are eating in a way that is biochemically feeding the cells of your body so that they are humming like that old '65 Rambler I wish I had never sold!

Before I move on to Door #2, to the left is a handout that I give to patients that further reinforces the power that food has on their bodies and how noncompatible foods can wreak havoc everywhere in their bodies. Also, I will include my Modified Elimination Diet that I have people follow for 14 days so that they can see how wonderful they will feel when they remove possible offending foods from their daily consumption. After the 14 days are up, there are multiple ways that you can test to see which foods are contributing to the source of their problems. The crucial key is that most true food allergies are moderated through IgG antibodies via a type IV hypersensitivity reaction. These symptoms can show up anywhere from fairly quickly to 48 hours later. Due to this slight inconvenience, patients must reenter one type of food every 2 days, or they may confuse the issue as to which food they are actually reacting to.

Door #2: Leaky Gut/Leaky Brain

There are many causes of leaky gut, which I will list below. The most important one, in my estimation, is continued consumption of reactive foods, which leads to continual inflammation in your small intestine, which causes those tight junctions between the simple columnar epithelial cells to loosen up and let antigenic substances into your bloodstream. This then is the initiating factor leading to all the possible downstream side effects from this initial insult.

Causes of leaky gut:

- **Diet**: alcohol, gluten, casein, processed foods, excess sugar, food allergies
- **Meds**: corticosteroids, antibiotics, antacids, xenobiotics
- **Infections**: *H. pylori*, bacterial overgrowth, yeast overgrowth, intestinal virus, parasitic infection
- **Hormonal**: decreased thyroid hormone/testosterone/estrogen/progesterone
- **Stress**: increased cortisol and catecholamines and CRH
- **Neurologic**: brain trauma, stroke, neurodegeneration
- **Metabolic**: glycosylated end products, intestinal inflammation, autoimmune conditions

Now, with regard to our present brain conversation, what does leaky gut lead to? Drumroll, and our winner is: leaky brain. Do you mean the brain leaks something? Yes and no. It doesn't leak any CSF out, but inflammatory products from that leaky gut compromise the blood–brain barrier (BBB) and now enter a defenseless brain and begin to activate the immune system of the brain or the microglia. So, your fire in the gut is leading to a fire in the brain. Wasn't that a Steven Seagal movie?

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Next up, what do the microglia do? They destroy plaque, remove dead cells, and can overreact to these inflammatory products that don't normally enter the brain and begin to cause collateral damage and injury to brain neurons and brain degeneration. Does this sound like some of our politicians? How about many of our patients?

So, how do we begin to fix this leaky brain? What I learned in naturopathic school was, go back to the source. Fix the leaky gut! You all should know how to accomplish this task. There are many products for leaky gut, but I think you have to fix the source of the problem to achieve lasting results. This definitely includes removing any food sources that are initiating the process.

An extremely interesting article by Andrew Heyman, MD, appeared in the July 2012 *Townsend Letter*: "Testosterone, Cortisol, and Insulin." He makes a great point that, interestingly, the adaptogenic herbs used traditionally for the adrenal glands (ginseng, ashwagandha, and rhodiola) actually work primarily in the brain by decreasing neural inflammation and neural excitotoxicity and aid in the repair of neurons and dendrites. This was a eureka moment for me. Chronic overexcitation of the adrenal glands doesn't initially burn out the adrenal glands; it affects the BBB and thus the brain – wow! More on this next.

Cyrex Labs has a new test that allows you to assess the integrity of the BBB or the degree of leaky brain. Its Array 20 gives you a unique tool to investigate the breach of the BBB by stress, trauma, or environmental triggers, even in the absence of apparent concussion or traumatic brain injury.

Before we move on to Door #3, let's look a little deeper at gluten, as this substance is also a prime initiator of leaky gut and hence leaky brain. Also, Lou Gehrig was on the box of

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Wheaties and was probably a big consumer of wheat products. Did he possibly not die of ALS?

There are two main groups of proteins in gluten, called the gliadins and the glutenins. Upon digestion, the gluten proteins break down into smaller units, called peptides (also, polypeptides or peptide chains) that are made up of strings of amino acids – almost like beads on a string. One particular peptide has been shown to be harmful to celiac patients when instilled directly into the small intestine of several patients. Other peptides may be harmful, including some derived from the glutenin fraction.

When celiac patients talk about "gluten-free" or "gluten-free diets," they are actually talking about food or a diet free of the harmful peptides from wheat, rye, barley, and possibly oats. This means eliminating virtually all foods made from these grains, regardless of whether these foods contain gluten in the very strict sense.

In barley, gliadin is called hordein. In rye it's called secalin. These three proteins, gliadin, hordein, and secalin, are in a category of proteins called prolamins that are present in all the grains of the grass family. The family also includes oats, corn, rice, millet, and others. In oats the prolamin is called avenin. Avenin may cause problems in some people with gluten sensitivities because it contains some of the same problematic amino acids as the prolamins in wheat, rye, and barley, just in lower amounts.

In addition, there is also HLA-DQ, or human leukocyte antigen, which assesses the probability of developing celiac disease rather than actually diagnosing the disease itself because some people have the genes that makes them sensitive to gluten but have not developed detectable evidence of the immune reaction to gluten or have no observable symptoms yet. Here are four possibilities:

A. If positive, gluten exposure can cause phenotypic expressions of celiac disease.
B. Useful if diagnostic confusion like atypical intestinal biopsy.
C. HLA-DQ 1, 2, and 8 are predisposed to celiac, 3–7 are not.
D. HLA-DQ: positive markers 1/2/8 exist in 95% of all celiacs.

Next, many people do not have celiac disease but just non-celiac gluten sensitivity (NCGS), an ongoing immune reaction to gluten in the diet usually detected as an immune response or sensitivity against the gliadin fractions of wheat, barley, rye: gliadin, hordein, and secalin. It is an IgA, IgM, or IgG antibody response to these proteins. Thus, typical allergy skin testing will not elicit positive responses because they are testing for IgE antibodies. Gluten sensitivity also promotes an immune response that increases systemic inflammation and has been associated with a multitude of health conditions in peer-reviewed literature.

Also, there are many nonintestinal manifestations of gluten. Tissue transglutaminase (TG) is an enterocytic enzyme that digests gluten. Antibodies (tTG) can be formed against this enzyme which can destroy enterocytes and initiate leaky gut. There are subtypes of this enzyme that can be tested through Cyrex Labs Array 3. If tTG2 is positive, then it indicates that there is autoimmune damage to the intestinal mucosa. If tTG3 is positive, it indicates NCGS and some sort of skin involvement. If tTG6 is positive, it indicates NCGS and some sort of neurological involvement.

Numerous studies in respected journals have shown CNS involvement with minimal or no GI symptoms or signs. I will list a few here:

A. *Neurology*. Feb. 2001;56:385–388. Gluten sensitivity can be primarily and at times exclusively a neurological disease, affecting not only the brain and nervous system directly but also cognitive and psychiatric illness
B. *Neurology*. Feb. 2001;56:385–388. 10 participants who had headaches, gait abnormalities, and elevated antigliadin antibodies demonstrated complete resolution of symptoms in 7 patients on a gluten-free diet, and 6 out of 10 had no intestinal complaints.
C. *J Neurol Neurosurg Psychiatry*. 1997;62:770–775. Our findings imply that the immune response triggered by sensitivity to gluten may find expression in organs other than the gut and the central and peripheral immune system are particularly susceptible.
D. *Pediatrics*. 2001;108. Gluten sensitivity should be considered as a state of heightened immunologic responsiveness to ingested gluten proteins in genetically predisposed individuals. *The brain seems to be particularly vulnerable*.
E. *Pediatrics*. 2001. Kleslich et al. found that gluten exposure in a sensitive individual essentially shut down blood flow to the frontal and prefrontal cortex (a process called *cerebral frontal/prefrontal hypoperfusion*). This is the part of the brain that allows us to focus, to manage emotional states, to plan and organize, to consider the consequences of our actions, and to exercise our short-term memory. Over time, this can result in the generation of actual brain lesions, which in turn result in chronically impaired neurological functioning. This hypoperfusion is additionally powerfully associated with cognitive impairment and conditions such as depression, anxiety, and ADHD.
F. *BMJ*. 1999. Feighery: Gastrointestinal symptoms are absent in many patients and there may be neuropsychiatric symptoms.

Here also are unconventional sources of gluten that most people would not think of, for those people who can't sniff a molecule of gluten without triggering a reaction somewhere in their bodies:

Supplements
Artificial food colorings
Food emulsifiers
Food Stabilizers
Malt extract, flavor, or syrup
Soy sauce
Beer
Modified food starch
Dextrins
Cosmetics
Envelope glue
Pharmaceuticals

Finally, some people completely eliminate gluten and there is no change. One large possibility here is cross-reactivity with antigens from other foods that are similar enough to gliadin that they will still initiate sensitivity reactions. Cyrex Labs has an Array 4 that evaluates proteins from other foods that have the ability to cross-react with the gliadin antibodies. You run the risk of false negatives if you haven't eaten the food in 2 weeks. Here is Cyrex's list of cross-reactive foods: cow's milk, casein, whey, oats, sesame, corn, chocolate, yeast, coffee, buckwheat, sorghum, millet, hemp, amaranth, quinoa, tapioca, teff, soy, rice, potato, egg.

Door #3: Stress/Earthing

What is stress? Stress is really unmanaged emotions or emotional reactions to everyday aspects of our lives. *Stress* is one of the words that people use, but what they are really expressing is anger or fear or some other type of emotion. This is extremely important, because emotions are the primary drivers of our physiological processes. What then happens at a cellular level, whether in the liver or stomach or lymphatic system, is primarily a response to the emotions that we feel. Just getting a better handle on being able to self-regulate can lead a person back into internal bodily coherence.

Continued stress in our lives is also a very common cause of leaky gut, which, as we already know, is also a cause of leaky brain

Fortunately, our brains are plastic and we can retrain or rewire them to change the neural circuitry so we won't have unmanaged emotional reactions to daily events. Over time patients can learn what a coherent state feels like. They then also learn to feel when they're slipping into a dysfunctional state and can then take the appropriate steps to shift back into the coherent state.

So, what does chronic stress and the ensuing elevated cortisol lead to in the brain?

A. hippocampal cell destruction, which leads to memory issues and also release of cortisol at inappropriate times as the hippocampus determines the rhythm of cortisol release
B. increased peripheral inflammatory cytokines, which further break down the BBB and stimulate those pesky glial cells to produce inflammatory cytokines in the brain and consequently stimulate inflammation in the brain and all the side effects from this brain inflammation
C. inhibition of the peripheral conversion of T4 into T3 and type II hypothyroidism or an inhibition of the peripheral conversion of T4 to T3 and subclinical hypothyroidism, which will have many downstream effects on the brain

These are pretty scary consequences of chronic stress and the resulting cortisol elevation: decreased memory, increased brain inflammation, and inhibition of peripheral conversion of T4 to T3! So, to be truly preventive medicine practitioners, we must head off chronic stress at the pass, so to speak. Simply put: identify the causes of our patients' chronic stress and have them deal effectively with these root causes of chronic stress.

Some Easy and Effective Methods to Reduce Your Patients' Stress

A. **Relaxation biofeedback products:** The emWave Program from HeartMath (www.heartmath.org) gives a rich graphical interface that displays on your computer and induces a state of synchronization between your heart, brain, and autonomic nervous system. The Stress Eraser is a handheld

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Handouts

Limbic Breathing

1. Sit comfortably in a chair with your spine straight and your feet flat on the floor.
2. Place both hands on your belly. Imagine filling your abdomen with air, rather than your lungs. Inhale deeply, then exhale. Your hands should rise and fall. *Only your belly* should be moving during inhalation and exhalation.
3. Draw your attention inward. Listen to the sounds around you or notice the sensation of air passing through your nostrils. Begin to slow your breathing down. You want to try to slow it down to 3–4 breaths/minute.
4. Try to achieve an inhalation that lasts 5 seconds ("one thousand one, one thousand two, one thousand three, one thousand four, and one thousand five").
5. After the inhalation, hold your breath for 2 seconds.
6. Exhale for double your inhalation, here for 10 seconds.
7. Continue for 10–20 minutes.

Breath of Life

1. Imagine two circles on the ground, Circle 1 and Circle 2.
2. Step into Circle 1 and imagine a situation where you would like to alter your reaction. See what you see, hear what you hear, and feel the sensations associated with this situation.
3. Step out of Circle 1 and shake off any sensations attached to that context (small hops or spinning around or shaking your arms will help here).
4. Step into Circle 2 and do the following breathing cycle for 10 cycles *while you visualize what you want your new situation to look like.*
   a. Breathe in for 5 seconds.
   b. Hold for 2 seconds.
   c. Breathe out for 10 seconds.
   d. Repeat the above cycle 10 times.
5. Without hesitation, step back into Circle 1 and into the original imagined situation, then take a moment to sense how the pictures, sounds and internal sensations have changed. You will have an effect of "bridging" or connecting your optimized physiology to future situations involving this feeling. This will allow new circuits to be wired in your brain so that your reaction to these situations will now be altered in a positive way.

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biofeedback unit that monitors heart-rate variability (www.StressEraser.com).

B. **Leg Elevation**: Lie supine with your legs elevated (on a chair or a bed) for 15 minutes in silence with your eyes closed. This technique shifts blood from the extremities to the abdomen which turns on parasympathetic nervous system and turns off the sympathetic nervous system.

C. **Limbic or Feather Breathing**: A handout for patients is given on p. 45. This is a type of breathing that very quickly engages the parasympathetic nervous system and can reverse stressful thinking and stressful situations in their lives.

D. **Neurolinguistic Programming (NLP)**: A simple NLP exercise can begin to build new neurological circuits in patients' brains so that they can learn to react in a positive rather than a negative way. The handout, "Breath of Life," is on p. 45.

E. Earthing is another powerful antistress tool. The theory is that when you walk barefoot on the earth, it allows for the transfer of free electrons from the earth into your body, via the soles of your feet. It mediates inflammation in your body by improving the zeta potential – the pulse capacity of your red blood cells.

Numerous studies have documented the significance of the earth's electrical rhythms for optimal biological function. Normal rhythms in the body establish a stable reference point for repair, recovery, and rejuvenation of our bodies. Clearly, internal biochemical chaos is the result of our disconnection with the earth. Our biological rhythms need to be continually calibrated by the pulse of the earth that governs the circadian rhythms of not only our bodies but also of all life on this planet.

Our feet have been referred to as a kind of radar-sonic base that provides little-known but vital functions to extract energy from the earth, similar to plant roots' extracting moisture from the ground for nourishment. Our ground-to-foot vibrations are an important energizing power helping to serve the body's life forces. We draw electrical energy through our feet in the form of free electrons fluctuating at many frequencies which continually reset our biological clock and provide the body with electrical energy.

Earth qi is absorbed, without our thinking about it, when we walk barefoot. This may explain why it's so relaxing to walk without shoes and why yoga and qi gong are often practiced without footwear. A central focus in Chinese practices involves "growing a root" and has to do with opening up communication between the bottoms of the feet and the earth. This process occurs thru the YongQuan point, or Kidney 1.

Remember, don't go a day without your "Vitamin E for Earth"!

In my next article, I will write further on these causes of mental illness: increased/decreased reuptake of neurotransmitters at the synaptic cleft, toxic metal overload, and hypothyroidism. This article is my interpretation and, as such, is open, hopefully, to hot debate because this is the only way that we do not fulfill the prophecy that "science progresses one funeral at a time." Hopefully, you all read this and go, "Yeah, baby that's great there, but that needs work there," and contact me through my e-mail or talk with colleagues and friends and modify and improve my ideas. It's all about dialogue – nothing more, nothing less – to keep extending the envelope to unheard-of heights!

Acknowledgments

I would like to thank the following people/companies for the information I obtained from them:

Thomas Alexander, MD, lecture given at Walter Crinnion's "Advanced Topics in Environmental Medicine" seminar in Tempe, Arizona, March 15–16, 2014.

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Greg McDonald, ND, for use of his Modified Elimination Diet.

Eric Gordon, MD, for letting me read his article on Lyme's disease that he will hopefully send to the *Townsend Letter* so other practitioners can really begin to understand what it means to truly individualistically to treat patients with complex chronic diseases.

My mother, for teaching me to take no prisoners in life!

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Jim Cross graduated with a degree in biology from the University of California at Davis in 1975 and with a secondary teaching credential in life science from California State University, Sacramento, in 1976. Wanting to initially see more of the world and expand his knowledge of different regions and their people, he traveled and worked in Germany, Switzerland, Holland, Taiwan, and Alaska. Having been helped by a naturopath, he became part of the first-year class at Pacific College of Naturopathic Medicine in little Monte Rio on the Russian River in Sonoma County, California. After PCNM folded, he finished his naturopathic studies at National College of Natural Medicine in Portland, Oregon, in 1984. He later earned his LAc at San Francisco College of Acupuncture in 1989. He has practiced acupuncture and naturopathy in the tiny Northern Sierra town of Quincy since 1990. He has also taught anatomy and physiology at tiny Feather River College in Quincy since moving there. He and his family are extremely lucky to live in a beautiful area where there are more trees than people and that also allows him to practice the hydrotherapy that he learned in naturopathic school from Wade Boyle, ND, by jumping in the local creek one or two times each week all winter. He also wishes that his mother had lived to see him become a doctor, because she was an RN and his first medical teacher. As a child, whenever he was sick, he was made to fast on ginger ale until his symptoms abated. She also taught him, being the good German that she was, to alternate hot and cold in injuries that he incurred playing basketball in high school and college. His true passion is to open an in-patient medical facility in the Sierra Nevada for people with chronic disease.

Navigating the Convoluted Road to and from Depression

by Nora T. Gedgaudas, CNS, CNT, BCHN

A Growing Epidemic

Major depression, the most common form of mental illness, is by some expected to be the second leading cause of disability by 2020 *worldwide* – second only to ischemic heart disease, according to the CDC.[1] The World Health Organization projected that depression may become the biggest health burden in the world within a mere 20 years (as of 2001).[2] Much more than having a simple "emotional disorder," persons with major depression (along with schizophrenia) commonly experience disproportionately higher rates of disability and mortality. There is literally a 40% to 60% greater chance among such persons of dying prematurely than in the general population.[3] Women seem to be at greatest risk.

In short, the prognosis for mental health of the population isn't a good one. In the US alone, the lifetime risk for major depression is already just over a quarter of the population (26%).[4] It is a debilitating condition characterized by prolonged feelings of sadness, loss of interest in activities, and decreased energy. Other symptoms include loss of confidence and self-esteem, inappropriate guilt, thoughts of death and suicide, diminished concentration, and disturbance of sleep and appetite. A variety of somatic symptoms may also be present. Though short-term forms of depression and anxiety may be natural adaptive responses to emotional stressors and setbacks in our lives, what is officially termed *depressive disorder* is typically diagnosed when the symptoms reach a certain threshold and last at least 2 weeks.

Perhaps the greatest myth among those who have not experienced significant depression is the idea that depression is somehow a "passive" condition, characterized by a "failure" of appropriate habits such as exercise and positive thinking. In fact, depression is truly a state of "chronic *efforting*" wherein its sufferers are continually spinning their wheels on the edge of an icy road, exhausting themselves without being able to go anywhere; trapped in a perpetual state of helplessness and hopelessness. In my experience, most depression appears to additionally lie on the flipside of a coin paired with anxiety, ultimately constituting a state of what could be termed "anxiety to exhaustion."

99.99% of our genes were formed before the development of agriculture.

– S. Boyd Eaton, Medical Anthropologist

A Premise

We all see the world through a lens that is our biochemistry: our hormones, our neurotransmitters, and (the degree to which we choose to depend on it) our blood sugar. These factors are inherent to our interpretation of the world around us. I would propose that all of these factors are additionally *interrelated*, and that from a foundational perspective, *we largely generate the focus our own internal lens by what we choose to eat.*

Every single physiological process and biochemical reaction in the human body is wholly dependent upon the nutrients in our diets and other (perhaps less than nutritive) compromising substances that we supply these processes with. Genes are almost wholly controlled by epigenetic factors (i.e., dietary and other environmental influences). Therefore, our underlying mental state is very powerfully influenced by what we feed it (on multiple levels) – or don't.[5,6]

The fact is that understanding the *foundational requirements* behind our unique human design and where things might be lacking is essential to virtually anyone's restoration of function.

So where do we start?

Going Back to Our Humble Evolutionary Beginnings

It makes practical sense to take our long evolutionary history into account when it comes to this equation. The premise is this: those foods that we would have habitually consumed as a species for the longest period of time would constitute our greatest genetic and dietary adaptations and

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would be most foundational to our underlying physiological makeup and nutritional requirements. To me this consideration is an *essential starting place*.

To the wild hominids that we once were, resources and food availability would have been variably limited; therefore quality *nutrient density* would have been of paramount importance and highly coveted. As understood by most paleoanthropologists today, it was likely our dependence on the meat and especially fat of the animals which we hunted that not only allowed us to survive but also consequently resulted in the very rapid enlargement of the human brain.[7]

Primal Fat-Heads

On average, humans are designed to and also tend to consume significantly higher levels of dietary fat than other primates.[8] We also evolved consuming much higher levels of particularly key long-chain polyunsaturated fatty acids (LC-PUFAs) that are critical to brain development, which we got directly from the wild (grass-fed) meat, organs, and tissues of the animals we hunted.[9,10] Human brain growth and function are in fact primarily dependent on dietary fats (particularly 20 and 22 carbon fatty acids, DHA, and AA) – in other words, *dietary animal source fats*.[11]

Curse of the 'Sugar-Burning Blues'

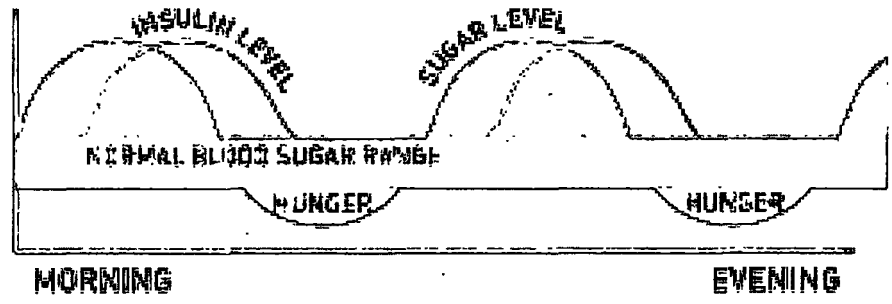
The mantra of mainstream medicine and conventional dieticians/ nutritionists commonly taught and blindly accepted as an "absolute truth" is that glucose is required by all tissues, including the brain, for everyday energy. This is misleading and only conditionally true; it is only true if we have metabolically adapted ourselves to the *unnatural dependence* on glucose as our primary source of fuel by the excessive and chronic consumption of sugar and starch (a hallmark of the Western diet and even of USDA dietary recommendations). Glucose as a primary source of metabolic fuel is a volatile, inefficient, and unreliable source of prolonged energy and requires frequent replenishment as well as constant management for its stability. But, luckily, Mother Nature was not so stupid as to force a dependence upon a single fuel – and certainly not one as fickle as blood sugar. The inflammatory tidal waves of insulin generated in the name of blood sugar management as a result of the modern standard American diet are something that would have been largely foreign to our ancient ancestral forebears. The emergency physiological need to "lower blood sugar" (via chronic insulin demand) is a strictly modern phenomenon to which we as human beings are ill suited. A significant percentage of physical, cognitive, and mental health-related problems can potentially be traced to this modern-day, perpetually abnormal metabolic state, which I discuss in much more depth and detail in my book, *Primal Body, Primal Mind: Beyond the Paleo Diet for Total Health and a Longer Life*.[12]

The human brain is fortuitously designed to make use of more than just one primary form of fuel, however. It is in fact ketones (i.e., the energy units of fat) and not blood sugar (glucose) that can most readily provide our metabolically expensive brain's absolute best and most efficient form of long burning, sustainable energy.

Sugar and Starch As Prime Fodder for Mood-related Issues and Neurological Instability

The presence of significantly elevated blood sugar has the effect of initially increasing L-tryptophan levels in the bloodstream (called the plasma-tryptophan ratio) that may then (assuming the availability of necessary cofactors) technically be diverted to serotonin production. In the short term, this undoubtedly feels good and may have a brief mood-enhancing effect. Long term, however, sugar- and starch-based foods lack sufficient raw materials necessary in their composition (i.e., amino acids and/or B-vitamins required to supply more L-tryptophan and/or manufacture serotonin). As such, the effect over time is ultimately more depleting than anything. Tryptophan is the least abundant amino acid in our food supply and is particularly lacking in grain-based diets. Sugar additionally lights up opiate centers in the brain, which triggers its own desire for more. The potential for addiction and a downward spiral in mood is ever present and in certain sensitive individuals may lead to other carbohydrate-related/blood-sugar dysregulation issues such as metabolic diseases and alcoholism. The short-term sugar high rarely leads to any form of long-term health or happiness.

One 2013 study of more than 23,000 mothers and their children suggested a link between a mother's consumption of sweets and processed foods during pregnancy and behavioral and mental health issues



Life in the "level zone" (depicted above) becomes more constant on a ketogenic diet and blood sugar influence upon mood and energy becomes effectively irrelevant.

Source: Nora T. Gedgaudas by permission

in her child at age 5. The results stated, "Higher intakes of unhealthy foods during pregnancy predicted externalizing problems among children, independently of other potential confounding factors and childhood diet. Children with a high level of unhealthful diet postnatally had higher levels of both internalizing and externalizing problems. Moreover, children with a low level of postnatal healthy diet also had higher levels of both internalizing and externalizing problems." The authors concluded, "Early nutritional exposures were independently related to the risk for behavioral and emotional problems in children."[13]

Hypoglycemia and reactive hypoglycemia are relatively common in the population today, and especially among those with mood lability, irritable tendencies, depression, and anxiety-related issues. As such, many individuals deal quite poorly with our government-sanctioned standard carbohydrate-based diet. In fact, there is nothing more destabilizing to the brain and nervous system than a diet fundamentally based on sugar and starch – especially refined carbohydrates.

The Better Alternative

Cultivating more of a natural, ancestrally aligned, fat-based, ketogenic metabolism (typically requiring an intake of no more than about 50 g/day of utilizable sugar/starch) may be the single most effective means of both optimally feeding and stabilizing any brain or nervous system. In this particular ketogenic approach (as there are many), grass-fed meat and accompanying fats, uncontaminated and wild-caught fish/seafood dairy, nuts, olive oil, and avocado – together with unlimited amounts of organic, nonstarchy fibrous vegetables and greens – are top of the list in terms of foods that comply.

A similar dietary approach has shown efficacy in at least one study related to bipolar II disorder. In the 2013 peer reviewed study the authors stated,

> Two women with type II bipolar disorder were able to maintain ketosis for prolonged periods of time (2 and 3 years, respectively). *Both experienced mood stabilization that exceeded that achieved with medication*; experienced a significant subjective improvement that was distinctly related to ketosis; and tolerated the diet well. There were no significant adverse effects in either case. These cases demonstrate that the ketogenic diet is a potentially sustainable option for mood stabilization in type II bipolar illness. They also support the hypothesis that acidic plasma may stabilize mood, perhaps by reducing intracellular sodium and calcium.[14] (emphasis mine)

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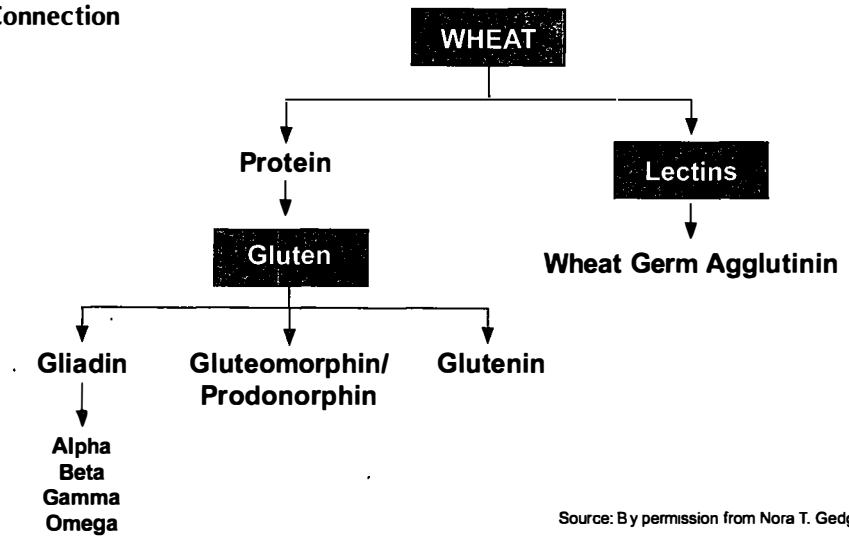
Not only this, according to an article published in the *American Journal of Physiology* in 1996, *"A ketogenic state results in a substantial (39%) increase in cerebral blood flow, and appears to reduce cognitive dysfunction associated with systemic hypoglycemia in normal humans."*[15] (emphasis mine). Seeing as cerebral hypoperfusion to the frontal cortex is one typical hallmark associated with depressive symptoms, improving brain circulation by a whopping 39% is potentially *highly* significant!

Researchers observing the comparative impact to a glucose vs. ketone-based metabolism in a study published in the *Neurobiology of Aging* had the following observation:

> As compared with glucose metabolism, central ketone metabolism generates lower levels of oxidative stress (Prins, 2008) and has been shown to produce greater cellular energy output and antioxidant capacity, the latter by increasing glutathione peroxidase in hippocampal cells (Veech et al., 2001; Ziegler et al.. 2003). In addition, the presence of cerebral ketones is associated with decreased apoptosis and inflammation (Gasior et al., 2006; Malouf et al., 2009), which along with oxidative stress, have been identified as fundamental factors contributing to neurodegeneration (Cotman, 2000).[16]

The anti-inflammatory effects of a state of ketosis here (along with the pro-inflammatory effects of increased blood sugar) are especially pertinent to this discussion, as the neurotransmitter deficiency model and theory of depression is currently being replaced by independent researchers by something now referred to as "the cytokine model of depression."[17] In other words, today depression is being increasingly understood by researchers as an inflammatory disorder rather than any sort of foundational "neurotransmitter deficiency." Naturally, the old, largely ineffective pharmacologic SSRI model, still profitable enough, persists in spite of this.

The Gluten–Mental Health Connection



Source: By permission from Nora T. Gedgaudas

One more highly inconvenient truth: Sugar is far from the only culprit when it comes to the impact of postagricultural foods on the dysregulation and deleterious impacts on the human brain. Welcome to the post-woolly mammoth agricultural age. ...

A review paper published in the *New England Journal of Medicine* dating all the way back to 2002 listed 55 conditions that were found to be associated with eating gluten.[18] Today this number potentially exceeds 200 and includes virtually all forms of autoimmune disease, currently numbering close to 100, with 40 *additional* diseases that are thought to have an autoimmune component.[19] According to the American Autoimmune Related Diseases Association, as many as 53 million Americans currently suffer from some form of autoimmune disease, as compared with cancer, currently thought to be affecting 9 million Americans, and cardiovascular disease, currently thought to be affecting 22 million Americans: autoimmunity appears to be exceeding both of these combined. Gluten, an indigestible protein found in wheat, barley, and rye, is nearly ubiquitous in processed foods and personal-care products. It is known to potentially initiate or exacerbate essentially all autoimmune processes, and its consumption poses a very high risk factor. The presence of almost any type of symptom should motivate anyone to immediately rule out gluten immune reactivity through accurate (i.e., Cyrex Labs) testing. Among these conditions, numerous psychiatric disorders and cognitive issues that one might not necessarily think of as being associated with autoimmunity can be potentially included here.[20–24]

- An estimated 54.1% of people with depression may have autoimmunity against their own serotonin receptors.[25–27]
- More than 80% and quite possibly more than 90% of all low-functioning thyroid cases (in many cases presenting with depressive symptoms) are actually autoimmune in nature.[28]
- Bipolar–disorder type symptoms are found to be highly correlated with thyroid autoimmunity.[29–31]

As I pointed out in my book, "Depression has been found in 67% of patients with untreated celiac disease (Addolorato et al. 2004)."[32] The same study found that high levels of anxiety are also exceedingly common in such patients (73%). Gluten sensitivity (or the possibility of it) cannot be ignored here as a contributing factor or underlying culprit. In an article in *Alimentary Pharmacology & Therapeutics*, the author stated, "Depression is reported

to be a feature of celiac disease and is ranked as its most common neuropsychiatric disturbance (Hallert et al. 2002)."[33] Food sensitivities in general always need to be considered wherever depression or anxiety is an issue.

Tending to Your Internal Wildlife and the Brain–Gut Superhighway

Among the biggest buzzwords heard in the natural health field today is *microbiome*. Indeed, as 90% of the cells making up the human body are bacterial, fully 99% of the genetic material occupying the human organism at large is fundamentally "alien" (i.e., nonhuman) in nature. These microscopic hoards occupy every nook and cranny of our second brain (i.e., the GI tract) in varying concentrations and types, as well as elsewhere within the human body, be they welcome or not. Without question these vast populations of living organisms within our own have their own agenda, requirements, and varied physiological impact that must be seriously taken into account. The relative health or pathology of these populations has demonstrably pronounced consequences upon our own.

Gut bacteria (over 1000 different species numbering up to 100 trillion) are being discovered increasingly to have a major influential role in brain health and functioning, as well as mood. Gut bacteria both produce and respond to the same neurochemicals – such as GABA, serotonin, norepinephrine, dopamine, acetylcholine, and melatonin – that the brain uses to regulate its moods and cognition. In part, these neurochemicals may align the brain and its behavior to the feedback that it receives from the bacteria living in the gut. Obviously, cultivating and maintaining healthy probiotic colonization of the gut should certainly be a priority with any brain-related issue.

Currently, psychiatric disorders thus far connected with the health of the microbiota include anxiety, depression, autism/ASD, Alzheimer's disease, schizophrenia, and eating disorders, to name a few. The presence or absence of various microorganisms within the gut seems to be able to powerfully influence the action of key neurotransmitters. There is also some evidence to suggest that stress and norepinephrine (NE) can enhance the pathogenicity of certain (gram-negative, rod-shaped) bacteria![34]

The human brain and gut each arise from literally the same common fetal tissue and remain forever connected through a single common thread, running all the way from the brainstem to the abdomen, known as the *vagus nerve* – unique among mammals in humans. This telephonelike "wire" connecting the two aforementioned "tin cans" (brain and gut) provide a communication superhighway from the gut to the brain by our gut bacteria, and to some degree back the other way. An abundance of emerging research seems to show that these minute denizens have a direct and powerful influence on brain chemistry through this pathway. For instance, GABAergic pathways have been shown to be influenced by certain *Lactobacillus* species (*rhamnosus* and at least one other), which in turn may have a positive modulatory effect upon GABA expression in the brain through the vagus nerve.[35]

Less welcome internal riffraff occupying the small intestine in great numbers (a condition known clinically as SIBO, or small intestinal bacterial overgrowth) have been linked to numerous physiological and immunologic consequences, as well as mood symptoms such as depression.

Gut inflammation invariably begets neuroinflammation – again, our key nemesis when it comes to depression. One cannot separate the fate of one end of the vagus nerve from the other. Both gut barrier compromise and blood–brain barrier compromise occur through the same related mechanisms and are each influenced by the production of *zonulin* – either through the ingestion of gluten (whether one happens to have immune reactivity to it or not) or the presence of endotoxin lipopolysaccharides as a result of dysbiosis.

But as sexy as the burgeoning subject and growing body of research into the human microbiome happens to be, other aspects of digestion must also not be ignored – and without question additionally play integral roles in the health of said microbiome. One interesting recent study looking at this issue from a microbiome perspective found that, while the researchers classified humans as omnivores, human stomachs naturally have the high acidity levels normally associated with scavengers.[36] Although plant foods have their decided benefits here, we are undeniably designed to be a meat-eating species, with a hydrochloric acid-based (and not a fermentative-based) digestive system. Such a diet better ensures appropriate HCl production.

Poor hydrochloric acid production and subsequent pancreatic insufficiency may additionally impair the ability to properly digest proteins and may create deficiencies of amino acids needed for hormonal/neurotransmitter production. Low HCl may also significantly impair the proper ionization and utilization of key minerals, such as zinc, magnesium, iron, and others needed for healthy brain, mood, and cognitive functioning. Impaired HCl production additionally impairs production of intrinsic factor, required for digestion and absorption of vitamin B12 (deficiencies leading to macrocytic anemia, eventual neurological damage, severe memory dysfunction/dementia and mental instability, irritability, and/or paranoia).

Furthermore, biliary issues may greatly impair the digestion and absorption of fats and critical fat-soluble nutrients, further impairing mineral absorption and proper protein utilization. Digestion overall ➤

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is a multidimensional avenue ripe for consideration with respect to any presenting mental health issue, and the human microbiome is but a part of this equation – albeit a highly significant one.

In short, it is simply not possible to separate digestive health from mental health issues.

Concluding Remarks

In this limited format, it is nearly impossible to encapsulate the complex etiology surrounding the epidemic phenomenon of depression. I have endeavored to touch upon some key points and issues but did not provide additional information regarding specific nutrient deficiencies, the adrenal–dysregulation connection (which I cover in depth in my e-book, *Rethinking Fatigue: What your Adrenals are Really Telling You and What You Can Do About It*), and the special nutritional requirements accompanying genetic metabolic conditions affecting depression in some, such as pyroluria.[37] I also lacked the space to tie in my experience using neurofeedback training, which I have found to be a profound adjunct to nutritional regimens in helping to synergize the best possible functional improvements. Further information about this subject in a more clinical context can be found in the recently released academic book *Restoring the Brain: Neurofeedback as an Integrative Approach to Health,* to which I was a contributing author.[38]

In summary, with respect to the nutritional side of things from a foundational macronutrient perspective, there is nothing at all more stabilizing to the brain than healthy, natural dietary fat ... and nothing more commonly destabilizing than dietary sugar and starch (followed closely by food–sensitivity related immune reactivity). The underlying bugaboo here (it turns out) is inflammation, and "Ketone body metabolism reduces oxygen free radicals, enhances tolerance to hypoxia, and may prevent organ dysfunction from inflammatory processes."[39]

The bottom line is this: The more you can come to rely on ketones as your brain's primary source of fuel (as opposed to glucose), the healthier, less inflammatory, and more stable your brain will be and the more gracefully it will age.

A cure-all? No. But the most remarkable, solid, supportive dietary foundation upon which better mental (and physical) health may be built or ultimately even restored.

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Fibromyalgia

by Leslie Axelrod, ND, LAc

More patients are being diagnosed with fibromyalgia (FM) since the incorporation of the latest 2010 diagnostic criteria. Previously a diagnosis of FM was based on positive physical exam findings revealing 11 of 18 tender points.[1] The new criteria recognize the wide array of somatic symptoms and multisystem involvement which were neglected in the previous diagnostic criteria. The physical exam component is substituted for subjective reporting as a widespread pain index (WPI). PE and labs are utilized primarily to rule out other conditions, such as myofascial pain syndrome, hypothyroid, inflammatory myositis, and vitamin D deficiency. The combination of the WPI tally and symptom severity scale (SS) are used to confirm the diagnosis of FM when the symptoms are present for at least 3 months and cannot be accounted for by another condition.[2]

FM is a diagnosis of exclusion and may be challenging to treat due to multisystem involvement. Biochemical and functional changes are exacerbated by a lack of sleep and chronic pain, leading to a variety of symptoms. A comprehensive therapeutic approach is essential to treat at the symptomatic level, as well as the underlying dysfunction.

Sleep

The criteria highlight fatigue, waking unrefreshed, and presence of cognitive changes.[3] Hypothalamic-pituitary-adrenal (HPA) dysfunction is a key player in sleep disturbance. Abnormal circadian rhythm contributes to elevated evening cortisol and melatonin dysregulation.[4] A study by Crofford stated that FM patients appeared to have a "loss of HPA axis resiliency."[5] It is essential to restore normal sleep patterns for any chronic patient to heal, especially with FM, which can improve symptoms, and will help restore HPA axis function. **Phosphatidyl serine** (PS) has been shown to decrease cortisol and abnormal ACTH associated with stress and extreme exercise.[6] Clinically, I have seen PS 100 mg be helpful for patients experiencing insomnia associated with elevated nighttime cortisol. However, FM patients are at various stages of adrenal dysfunction and 24-hour cortisol testing is indicated. **Melatonin** 3 mg at bedtime has been shown to be effective in improving sleep, as well as decreasing tender point number and pain level in FM patients.[7] A formula of standardized extracts of ***Valeriana officinalis, Passiflora incarnata*** and ***Humulus lupulus*** was compared with zolpidem (Ambien) in primary insomnia, revealing no statistically significant difference between the two.[8] **Lavendula oil** capsules improved sleep in patients with anxiety as well as depression, both psychological manifestations associated with FM.[9,10] A randomized placebo double-blind study of ***Hypericum perforatum*** (St. john's wort) revealed significant improvement in sleep, fatigue and depression, as well as increasing serotonin levels in depressed patients.[11]

Mood, Pain, and Neurotransmission

Abnormal serotonin, dopamine, and adrenaline metabolism contribute to mood changes, as well as pain in FM. Reduced serotonin precursors such as tryptophan, 5-HTP and S-adenosyl-L-methionine (SAMe) negatively affect the conversion of serotonin to melatonin. Conversion of tryptophan to serotonin involves 5-HTP and may be blunted by stress, and **pyridoxal 5'-phosphate** and **magnesium** deficiency.[12] Studies revealed that supplementation of 5-HTP or SAMe improved sleep, fatigue, mood, and tender point counts.[13,14] A nutrient IV, **Myers cocktail**, which contains magnesium, B vitamins, ascorbic acid, and other nutrients, showed statistically significant improvement in depression and pain with FM. Nutritional IVs are typically included in my FM treatment protocol and I have seen patients dramatically respond to a series of Myers cocktails, 1 per week for 4 weeks, or in some cases just **IV magnesium** (3 ml MgCl 200 mg/ml in sterile water), every 1 to 2 weeks.

Gut

Functional gastrointestinal disorders are found in the majority of FM patients, with one study citing 98%, compared with 39% of controls. Irritable bowel syndrome (IBS) is the most prevalent GI issue.[15] Studies have demonstrated that patients with IBS alone or in combination with FM have hypersensitivity to somatic and visceral pain.[16] Decreased serotonin levels have been associated with functional changes such as constipation and diarrhea.[17] A majority of patients with IBS identified food sensitivities as a trigger for their symptoms. Immune system activation of IgG and IgE has been associated with IBS, as well as migraines, another

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common manifestation of FM.[18] Studies showed that elimination of *all* reactive foods resulted in dramatic improvement in both conditions.[19,20] In my experience, **removal of all reactive foods** found by either IgG testing or a comprehensive elimination diet significantly reduces a number of symptoms, especially pain. The patient will remove the foods for a minimum of 2 to 4 weeks, prior to reintroduction. If symptoms occur upon reintroduction, the food is eliminated from the diet. If IgG food sensitivity testing is chosen, it is essential to find a reliable laboratory with consistent results.

The severity of abdominal pain in some FM patients has been associated with the extent of small intestinal bacterial overgrowth (SIBO).[21] Significant improvement in pain and depression occurred with complete eradication of the dysbiosis with antibiotics.[22] Recurrence rate is high after discontinuation of antibiotic therapy.[23] It is essential to correct predisposing factors which may include disturbances in **gastric, gall bladder, and pancreatic secretions** which are bactericidal and/or bacteriostatic. Improving gut barrier function can help prevent bacterial translocation and can be achieved with **glutamine** supplementation.[24,25] Other contributing factors include reduced **intestinal motility, ileocecal valve** dysfunction, and **secretory IgA** abnormalities.[26]

Herbal therapy was found to be "at least as effective as rifaximin" and "as effective as triple antibiotic therapy for resolution of SIBO by lactose breath test."[27] Studies have shown SIBO eradication with **berberine compounds** and **allium**.[28,29] Researchers found **peppermint and coriander seed oils** more effective than rifaximin, in vitro.[30] Whether the agent used is natural or a synthetic drug, the health and functioning of the gastrointestinal tract must be addressed, or the SIBO will likely reappear.

Mind/Body

The increased prevalence of psychological distress and adverse life events, including abuse in FM patients, must be considered when addressing gut health, as well as pain sensitivity, cognitive dysfunction, mood changes, and insomnia.[31,32] A variety of techniques have been shown to be helpful for this population, including qi gong, mindfulness training, meditation, and pool exercises.[33–36]

Exercise Endurance and Muscle Involvement

Exercise is an important part of a therapeutic plan; however, it is frequently challenging for patients with FM to exercise. Elevated baseline concentrations of inflammatory cytokines including IL-8, and stress hormones cortisol and noradrenaline, which contribute to pain, were found in FM patients, compared with healthy female controls. After 45 minutes of moderate cycling, the inflammatory and stress markers decreased to levels similar to the baseline of female controls, contrary to the expected increase found in healthy individuals post moderate exercise.[37] Increased serotonin levels were also found in FM patients after aerobic exercise (less serotonin release after stretching exercises).[38] Despite the potential for postexercise improvement, patients have a reduced functional capacity to perform activities. Lower oxygen consumption, along with increased pain and perceived effort, resulted after a 6-minute walk.[39] Diminished circulation is associated with presence of tender points.[40] **CoQ10**, involved in aerobic cellular respiration, increases exercise endurance in normal volunteers and when combined with ***Gingko biloba*** improves tissue perfusion and quality of life measures in FM patients.[41,42]

In a case report, a patient who met the diagnostic criteria for fibromyalgia was diagnosed with a mitochondrial myopathy when she was unresponsive to conventional therapies. She exhibited elevated lactic acid levels after a 6-minute walk. The authors prescribed a **compound of CoQ10 200 mg, creatine 1000 mg, carnitine 200 mg, and folic acid 1 mg** 4 times daily, resulting in significant improvement over several months.[43] **Acetyl-L-carnitine** (ALC) is a necessary substrate for ATP production by skeletal muscle during exercise and it can be used alone or with other supplements. A dosage of 1500 mg of ALC significantly improved depression, number of tender points, and musculoskeletal pain in a randomized, placebo-controlled study of 122 FM patients.[44]

Mitochondrial dysfunction is prevalent in FM. Elevated interstitial concentrations of lactate and pyruvate were found in the trapezius muscle of FM patients at rest, compared with controls.[45] This would indicate the likelihood of elevated lactic acid levels also at rest in FM since lactic acid production is a byproduct of pyruvate and precursor to lactate. Conversion from pyruvate to lactic acid is typically associated with insufficient oxygenation during exercise. Lactic acid drops a hydrogen atom to produce lactate, creating a more acidic environment when excessive levels are present. The combination of increased pyruvate, lactate, and likely lactic acid implies poor tissue oxygenation as well as a lower pH in the interstitium. This scenario is associated with increased muscle fatigue. I use **homeopathic L+ lactic acid** (Sanuvis), multiple times daily to help decrease muscle pain and fatigue in FM patients.

Conclusion

Treating FM patients can be difficult due to the multitude of aberrant biochemical pathways, including endocrine, neurotransmitter, circulatory, and structural. The therapeutics discussed are only a few of the many different ways to treat FM patients. The goals are the same no matter what the particular therapy is: to improve sleep, reduce pain, normalize HPA axis, address gut health, increase tissue oxygenation, and improve vitality. Treatment is not restricted to nutraceuticals, botanicals, diet, or

exercise. **Acupuncture** or wearing **woolen long underwear** can improve pain level and tender point count in FM, likely due to increased circulation and oxygenation.[46,47] Addressing basic life functions such as sleep, diet, and digestion is essential and must be part of the therapeutic plan. Etiology is frequently difficult to pinpoint, but may provide clues to a treatment plan. In order to address the wide array of symptoms and systems affected, a multidimensional approach needs to be considered for these complex patients.

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Effective Treatment for Chronic Fatigue Syndrome and Fibromyalgia: An Overview and 35 Treatments for Tough Cases

by Jacob Teitelbaum, MD

Chronic fatigue syndrome (CFS) and its painful cousin fibromyalgia (FMS) represent a severe energy crisis in the body. When energy levels drop below a certain point, the area using the most energy for its size, the hypothalamus, goes off line. In essence, it acts like a circuit breaker that clicks off when a circuit is overloaded.

The hypothalamus controls:

- overall hormonal function via the pituitary;
- sleep, making disordered sleep a hallmark of these syndromes;
- autonomic function. This contributes to the NMH/POTS, irritable bowel syndrome, endometriosis, and other autonomic dysfunctions seen in these syndromes;
- temperature regulation. This is why most people run lower than 98.6 °F. Temperatures over 99 °F suggest an antibiotic-sensitive infection.

Low energy also causes the muscles to get stuck in the shortened position. It takes more energy for a muscle to contract than to expand, which is why our muscles get tight after a heavy workout, instead of going loose and limp. Chronic muscle shortening results in chronic pain (called myofascial pain). The chronic pain then triggers secondary central sensitization ("brain pain") and small fiber neuropathy (SFN). Multiple immune deficiencies are also seen, and the recent clinical experience of Dr. Mark Sivieri shows a possible association between low IgG 3 levels (common in fibromyalgia), autonomic dysfunction, and SFN. These tantalizing data may lead to a better understanding of the "missing link" between our immune and nervous systems.

Because these conditions represent a common end point resulting from many triggers, there are literally hundreds of treatments and theories about what causes CFS/FMS, which can make things very confusing. The purpose of this clinically focused article is to offer a simple but proven framework into which these varying causes and treatments can be placed. We will also give a quick summary of how to institute an overall and highly effective treatment protocol ($p < .0001$ versus placebo with an average 90% increase in quality of life). We have called this protocol the SHINE protocol, addressing the following five areas. As overall treatment has been discussed at length in an earlier *Townsend Letter* article, we will give it a brief summary here. I will then give a checklist of 35 key problems and treatments to consider for more difficult or refractory cases.

S: Sleep

Nonrestorative sleep with insomnia is a hallmark of CFS/FMS.

Helpful natural treatments include the Revitalizing Sleep Formula (a mix of six herbs from Integrative Therapeutics), melatonin, magnesium, the smell of lavender, and sleep hygiene. If the person's mind is wide awake and racing at bedtime, this suggests that cortisol is too high at bedtime, and this may be helped with phosphatidylserine and Ashwagandha.

Helpful sleep medications include Ambien, trazodone 25 to 50 mg, gabapentin 100 to 300 mg, and Zanaflex 2 to 4 mg.

There are over 30 natural and prescription sleep aids that can be helpful. Unfortunately, Valium-related sleep medications tend to keep people in light sleep, worsening sleep quality.

H: Hormones

Because the hypothalamic-pituitary axis controls almost all of the hormones in the body, and most tests rely on normal hypothalamic pituitary function, treatment is based on a mix of clinical signs and symptoms along with actual hormone levels. That a test is in the normal range means very little. Bioidentical hormones should be used, adjusted to optimize function, along with natural support

for the glands (e.g., tri-iodine 6¼ mg for thyroid function, Adrenal Stress End for Adrenal Function, edamame for estrogen support).

I: Infections/Immunity

There are literally dozens of infections that can cause a person to have an energy crisis and "blow a fuse." Most important is treating candida. Considering the presence of antibiotic-sensitive infections such as Lyme disease and a host of others is also important, but only treating with the antibiotics and not addressing the rest of the SHINE protocol is likely to result in only incomplete and transient improvement. Antivirals and immune support (both discussed below) can also be helpful in selected cases.

N: Nutritional Support

This is simplified by using powders and other treatments that keep the pill count down. People do *not* like being part of the "handful club," where they are taking handfuls of pills all day, and are not likely to stick with a protocol when this is required. In addition to improving the quality of their diet, have patients avoid excess sugar, and increase protein, salt, and water intake. I also give those with fibromyalgia the following supplement regimen, which requires only one drink and 3 to 5 pills a day instead of over 50:

1. The Daily Energy Enfusion Vitamin Powder (by Integrative Therapeutics) plus a 5 g scoop of ribose (Corvalen by Douglas Labs) each morning. I simply have them add water and stir with a fork. This simple combination will dramatically and easily optimize energy and health, and I use it in virtually everyone (including myself). The powder supplies 50 key nutrients. Ribose Corvalen, by Douglas Labs) has been shown to increase energy by an average of 61% after 3 weeks. Begin with 5 g t.i.d. for 3 weeks and then drop to 1 to 2 times a day
2. Coenzyme Q10 200 mg, acetyl-L-carnitine 1000 mg daily, and if ferritin is under 60, I add iron. I also give EurOmega-3 (by EuroMedica) one a day for omega-3 support. This is the brand that I use, as 1 pill replaces 8 regular large fish-oil capsules

E: Exercise As Able

Too much exercise will result in what is called "postexertional fatigue" where the person feels bedridden the next day. Not enough exercise will result in deconditioning, which is just as bad. Have the person began a simple walking program, where they feel "good tired" after and better the next day. They can increase by 50 steps a day (a simple $15 pedometer can be an excellent investment) as tolerated. After 10 to 12 weeks on the SHINE protocol, their energy will dramatically increase as well as their ability to condition.

Pain

Like the oil light on your dashboard, pain is your body's way of a saying that something needs attention. Our published research showed that after 3 months on SHINE, pain decreased by approximately 50% ($p < 0.0001$ versus placebo). On the other hand, it is almost never acceptable to leave somebody in chronic pain, and adding treatments for pain can be very helpful. Narcotics are rarely needed, but are much less toxic than the chronic pain when they are needed.

Helpful treatments for pain include:

Natural: structural and energy-based treatments such as chiropractic, osteopathy, acupuncture, and massage can be very helpful but are unlikely to give persistent relief until the underlying biochemical problems are also addressed. People do best when SHINE and the structural/energy treatments are combined. In addition, several herbal combinations are outstanding for pain. My favorites are:

1. Curaphen, a mix of four herbs, plus Traumaplant comfrey cream (both by EuroMedica)
2. Pain Formula, a mix of three herbs (Integrative Therapeutics)

The Curaphen has been a pain relief miracle for people. It works quickly for acute pain, but give natural treatments 6 weeks to see the optimal effect for chronic pain. They can be combined with each other and with pain medications.

Pharmaceutical: Ultram, Neurontin, and Flexeril are good medications to begin with. NSAIDs are generally not helpful for fibromyalgia pain and can be toxic. Acetaminophen can help but depletes glutathione. If it does need to be used, I will add a special highly absorbed form called Clinical Glutathione.

Treatment Tools to Simplify Care

To dramatically simplify care of these complex conditions, I offer free symptom questionnaires and treatment checklists. If you would like me to e-mail you the file, simply request the free treatment tools from me at EndFatigue@aol.com. If you would like a much more detailed treatment checklist with approximately 300 helpful treatments, feel free to ask for the "long protocol" as well. In addition, to simplify evaluation and treatment of anybody with fatigue or fibromyalgia, we have the free "Energy Analysis Program" available at www.EndFatigue.com. This can analyze their symptoms, and even their pertinent lab tests if available, to determine what is draining their energy and tailor a program for that individual to optimize their energy. This will also dramatically simplify your care of people with these conditions.

An 8-hour online CFS/FMS training course can also be found at www.vitality101.com/PAN.

35 Helpful Treatments to Consider in Refractory Cases

The below is a quick checklist to go through and consider when people are not responding to basic treatments:

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1. Rule out sleep apnea and restless legs syndrome. I simply have people videotape themselves to see if they snore and stop breathing (in which case they need a sleep study) or have restless legs syndrome. If the latter is present, I make sure that the ferritin (iron) level is over 60 and supplement with magnesium at bedtime. The medications Neurontin and Ambien both help restless legs syndrome as well.
2. Be sure that the person is sleeping 8 hours a night.
3. Ask about nasal congestion during sleep. Inability to breathe through one's nose while sleeping will cause nonrestorative sleep. Breathe Right nose strips, Max-Air, and/or NoZovent products (all on Amazon) can be helpful, as can treating candida.
4. Consider Xyrem (prescription) if unable to get good-quality sleep by other means.
5. Consider thyroid receptor resistance with the high-dose T3 thyroid protocol devised by the late Drs. Broda Barnes and John Lowe.
6. Try different forms of thyroid if others do not work. Although most people do best with Nature-Throid, some do better with Cytomel or Synthroid. If using T3, some do best taking it in a single daily dose, where others need to divide the dose into 2 to 4 doses daily.
7. Consider a treatment trial of low-dose hydrocortisone (Cortef) up to a maximum of 20 mg a day.
8. Consider and treat for orthostatic intolerance (NMH or POTS) with increased salt, water, support stockings, midodrine, and even Dexedrine (maximum dose 20 mg daily). In severe cases I also consider DDAVP, although this helps in only a small subset.
9. Bioidentical testosterone kept at about the 70th percentile of the normal range helps pain and energy in both men and women.
10. Growth hormone may be helpful in a small subset.
11. If the HHV-6 IgG level is 1:640 (or four) or higher, or if the CMV IgG is >4, I consider a 6-month treatment trial with Valcyte if the person has not adequately responded to other treatments. Otherwise, if there is a history of sudden onset with viral symptoms with the CMV and HHV6 IgG being <4, I consider a high-dose Valtrex trial (1 g 4× day for 6 months). Celebrex 100 to 200 mg 1 to 2× day can augment the antivirals' effectiveness
12. Be sure that the candida has been adequately treated with at least 6 weeks of an azole medication (e.g., Diflucan). Unfortunately, I have not found the natural treatments by themselves to be adequately effective in some cases.
13. If nasal congestion is present, prescribe the Sinusitis Nose Spray (ITC pharmacy) and the silver nose spray (Argentyn 23). I give 1 spray of each in both nostrils b.i.d. for 6 to 12 weeks.
14. Remember to give zinc 20 to 25 mg a day for 3 months. Whenever chronic infection or inflammation is present, the person will become zinc deficient, causing marked immune dysfunction. More is not better, as it can cause copper deficiency. For long-term support, the vitamin powder has 15 mg a day, which is adequate.
15. If bowel symptoms are present despite 6 weeks of anti-candida treatment, especially with foul (sulfur) -smelling flatus (think back to the "silent but deadlies" of your grade-school days), a bacterial gut infection such as SIBO (small intestinal bacterial overgrowth) is likely and needs treatment. Parasites should be ruled out as well, using a lab that knows how to do proper testing (e.g., Genova, Doctor's Data, or Diagnos-Techs).
16. Low-dose naltrexone 4.5 mg at bedtime (from a compounding pharmacy). Give at least 3 months to work. If it initially disrupts

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sleep, begin with a lower dose and give in the morning. See www.lowDoseNaltrexone.org for more info).

17. Consider a 6- to 24-week therapeutic trial with doxycycline or Zithromax.
18. Check a blood test for "Immunoglobulin G, subclasses 1–4, serum." If one of the four subsets is low (most commonly IgG 3 followed by IgG1), treatment with IV gamma globulin can result in a dramatic response after 4 months. This is very expensive and takes a lot of work to get insurance coverage, so I reserve it for the 10% to 15% of people with the most severe and refractory illnesses.
19. Consider Dr. Ritchie Shoemaker's neurotoxin protocol.
20. SQ Heparin may be helpful, but carries significant risk, so I reserve it for the ~5% of people with the most severe and refractory illnesses.
21. Consider the methylation protocol. I do *not* recommend SNP genetic testing, as the majority of healthy people will come out "abnormal." Instead, see the work done by Dr. Neil Nathan.
22. Do a transglutaminase IGA and IgG antibody to check for celiac disease.
23. Check a total IgE level. If elevated, do IgE (*not* IgG) food and inhalant testing to isolate the specific allergies.
24. If food sensitivities are present, do NAET desensitization (see www.NAET.com).
25. A wheat and gluten-free diet trial. Check transglutaminase IgG and IgA to rule out celiac disease
26. Be sure they are on the vitamin powder and ribose. Consider a trial with NADH 20 mg sublingual (called Enada Mojo) each morning for 6 weeks.
27. Be sure that the ferritin is over 60.
28. B1 (thiamine) 600 to 1500 mg a day
29. Rhodiola 100 mg each morning. Increase by 100 mg daily each week to max 400 mg/day.
30. Frequency specific microcurrent (FSM) for persistent pain (see www.FrequencySpecific.com).
31. Atlas chiropractic treatments for those with autonomic dysfunction.
32. Annie Hopper's Dynamic Neural Retraining System (see www.dnrsystem.com).
33. For pain, have the person use woolen long underwear and woolen sheets and pillowcases during cold weather. This has been shown to be as or more effective than pain medications. (Resource: http://us.icebreaker.com.)
34. Dr. Paul St. Amand's guaifenesin protocol.
35. Provigil/Nuvigil 100 mg 1 to 2 each morning (caution: interferes with birth control pills). ◆

Nutrient Supplement Enhances Natural Killer Cell Function in Women with Chronic Fatigue Syndrome and Fibromyalgia: Preliminary Report

by Rita R. Ellithorpe, MD; Robert Settineri, MS; Talon Ellithorpe, BS; and Garth L. Nicolson, PhD

Abstract

Objectives: Chronic fatigue syndrome (CSF) and fibromyalgia (FM) share similarities in sequelae including postexertional malaise, pain, sleep disturbances, neurological and cognitive manifestations, and motor impairment along with reduced natural killer (NK) cell function. This brief clinical report examined the effects of a nutrient dietary supplement, Transfer Factor Multi-Immune, on the functional activity of NK cells in a small number of women with a confirmed diagnosis of either CFS and/or FM. **Methods:** Subjects who met the inclusionary criteria and had reduced NK function were instructed to take two capsules of supplement per day. On Days 0 and 30, blood samples were taken to determine NK cell functional status. **Results:** After treatment, 6 out of the 7 subjects had a statistically significant increase ($p = 0.02$) in NK function ranging from 135% to 4667% after treatment; 1 had a decrease of NK function of −61%. The median increase in NK cell function after treatment was 247%. **Conclusions:** This preliminary study suggests that the administration of a natural supplement can increase NK cell activity in women with CFS and FM with low NK activity.

Introduction

Chronic fatigue syndrome (CFS) is a condition characterized by a variety of signs and symptoms, with postexertional malaise and/or chronic and persistent disabling fatigue being prevalent symptoms.[1–4] Other symptoms of CFS include pain, sleep disturbances, neurological and cognitive manifestations (impaired concentration, mental processing, short-term memory), motor impairments, and altered immune and autonomic responses.[1–4] It is difficult to estimate the prevalence of CFS because of the complexity of its case definition and its overlapping signs and symptoms with myalgic encephalomyelitis (ME).[4,5] The Centers for Disease Control reported a prevalence for CFS of 0.3% with over 1,000,000 adults with this disorder in the US, but the rate could be as high as 2.5% with the use of different case definitions.[6,7]

Fibromyalgia (FM) has overlapping symptoms with CFS and mostly affects adult women.[8–10] FM is a chronic, diffuse musculoskeletal pain syndrome of unknown etiology characterized by chronic widespread pain, abnormal pain processing/heightened pain sensitivity, chronic fatigue, sleep disorders, and emotional distress or depression.[9,10] FM decreases quality of life and productivity and is associated with varying degrees of functional disability, psychological distress, lost work time, and increased use of health-care services when compared with unaffected individuals.[10–12] FM affects more than 5 million Americans and is more prevalent in women than men (3.4% vs. 0.5%).[13] There appears to be more diagnostic variability in FM relative to other coexisting syndromes that have overlapping symptoms, and it is often difficult to diagnose FM separately from CFS due to its overlapping symptom relationship.[13,15–19]

Immune responses are often impaired in CFS and FMS.[20–22] Impaired lymphocyte responses to mitogen and reduced natural killer (NK) cell cytotoxicity are the most consistent findings in a substantial proportion of patients with CFS.[23–26] Indeed, it has been suggested that NK cell measurement may be diagnostic in CFS.[26]

NK cells are cytotoxic lymphocytes of the innate immune system. They are potent effector cells that eliminate tumors and infected cells while providing signals that shape adaptive immune responses. NK cell counts in the high normal range are beneficial for long-term health.[27–29] Since NK

cell deficiency is a consistent finding in CFS patients, we measured NK function in a small group of women with CFS or FM and decreased NK function to see if a nutritional supplement could increase their NK function within 1 month.[25,26]

Methods

Volunteers were recruited (age range, 25 to 60 years). The criteria for acceptance encompassed a confirmed medical diagnosis of either FM or CFS, and current symptoms involving severe fatigue and inability to perform normal activities without unusual exertion.[3,9] Confirmation of a severe fatigue score utilized the Piper Fatigue Scale Survey (PFS) with a fatigue score of 6.5 or above.[30]

Each volunteer was given a general physical exam and asked to fill out a medical intake form. Excluded were those who had been on any immunostimulatory pharmaceuticals or nutraceutical products, especially those containing transfer factor, for 60 days prior to start of the study. As part of acceptance for inclusion in the study, a 20 ml blood sample was taken from volunteers and analyzed for NK activity. A minimum cutoff of a NK blood level activity of 35 lytic units (LU) was set as a requirement for entry into the study. This was based on a midrange stratification of NK functional determination (average LU) of CFS individuals.[31]

Volunteers who met the inclusionary criteria were given a 30-day supply of Transfer Factor Multi-Immune (TFMI), a polyvalent transfer factor preparation supplied by Researched Nutritionals (Los Olivos, CA). TFMI contains a proprietary combination of natural ingredients formulated to support beneficial immune and cellular functions.[32] Subjects were instructed to take two capsules per day on an empty stomach, either 2 hours after or 1 hour before eating, during the 30-day trial period. On day 30, a final blood sample was taken to determine NK functional cell analysis. During the trial, volunteers received weekly dosage and frequency reminders via e-mail to help maintain compliance.

For assessment of NK cell function, 20ml of blood was collected on Day 0 and Day 30, and then expressed-mailed (overnight delivery, with cold packs to Viracor-IBT Laboratories, Lee's Summit, MO). Peripheral blood monocyte cells (PBMC) were isolated from whole blood and mixed at various ratios with fluorescently labeled K562 target cells. Following incubation, the percent of lysed K562 cells was determined by flow cytometry.[33–35]

Results

Seven out of 18 volunteers were able to meet the inclusionary criteria for this study. The 11 other volunteers were excluded either because they did not have a PFS score ≥ 6.5 or their NK functional score was above 35 LU. The qualifying enrollees were all female, ages ranging from 30 to 60 years old (mean age = 49.9 years). Their average PFS score was 8.0, indicating severe fatigue on the PFS rating scale.

At day 30, 1 of the 7 women had a 61% decrease in NK LU functional value, while 6 out of the 7 individuals ranged from a 135% to 4667% increase in NK LU functional values. Using the actual data values, the pretreatment baseline mean was 13.2 ± 4.2, and this increased to 24.2 ± 3.2 in NK functional LUs post treatment. The increase was statistically significant ($p = 0.02$) utilizing a T-test determination. However, there were two outliers, the lowest and highest responders, −61% and +4667% difference over baseline, respectively. Reporting the mean alone could be altered by the influence of the extreme outliers; therefore, using the median (midpoint value of the percent difference) compensates for skewed data resulting from outliers. The median percent increase of NK cell LU within the entire group treated after 30 days of TFMI was 247% (Table 1). The magnitude of the individual percent differences are shown in Figure 1 (p. 62).

Discussion

There are some overlapping symptom and immunological relationships between CFS and FM. Impaired lymphocyte responses to mitogens and reduced NK cell cytotoxicity are the most consistent findings in a substantial proportion of patients with CFS, and a decline in NK cell functionality/activity has also been observed in FM.[25,26] Here we used a natural dietary supplement (TFMI) to increase NK functional activity and found that in 5 of 6 women the product significantly increased NK activity. Although this was a small patient group, the patients with the lowest NK function appeared to be the best responders to the TFMI supplement.

Previously a human herpesvirus-6 (HHV-6) transfer factor preparation was administered to two CFS patients with an active HHV-6 infection, and the treatment inhibited the infection and reduced some of the clinical manifestations of CFS in 1 patient but had no effect in the other.[36] Using an oral polyvalent transfer factor preparation against herpesviruses, De Vinci et al. found that 12 out of 20

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Table 1: NK Levels after Treatment with TFMI in CFS and FM Participants

Initials	Age	Sex	Pre Tx NK LU	Post Tx NK LU	% Difference NK LU	PFS Score
LF	44	Female	31.80	19.60	−62%	8.57
SW	30	Female	20.90	28.30	135%	8.38
CP	56	Female	15.30	23.90	156%	7.52
DA	54	Female	13.70	33.90	247%	8.43
DS	59	Female	7.60	21.00	276%	8.48
SN	60	Female	1.80	9.90	550%	8.48
LD	46	Female	0.70	32.60	4667%	6.76
Mean ± SE	**49.9 ± 4.0**		**13.1 ± 4.2**	**24.2 ± 3.2***	**852.7 ± 639.5**	**8.0 ± 0.03***

* p = 0.02

CFS patients responded within 3 to 6 weeks with reduced symptom scores, but correlation with virus serology was not evident.[37] This exploratory clinical pilot study indicates that a nutrient combination containing polyvalent transfer factor (TFMI) can increase NK cell functional activity after 30 days of administration in individuals with CFS and FM who have depressed NK function. NK function is related to infection control, and individuals with reduced NK function should benefit from the TFMI supplement. CFS and MF patients are known to have ongoing chronic viral and bacterial infections, and the number of such infections correlates significantly with symptom severity.[8,38,39] Thus TFMI should benefit patients with CFS and FM by increasing NK function.

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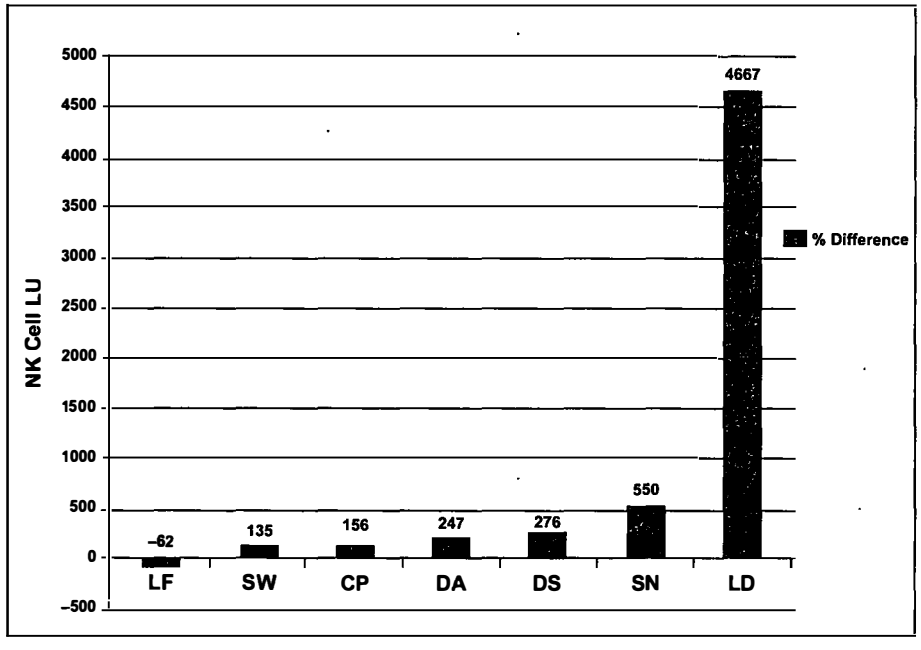
Figure 1: Percent Difference of Pre- and Posttreatment with TFMI



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Pain as a Contextual Experience

by Erik Peper, PhD

Pain is not simply a neurological or biological experience, it occurs in a context. Imagine two scenarios. In one, a child falls, hurts his knee, the mother kisses the knee, and the pain disappears. In the other, an old man lies awake at two in the morning with throbbing pain, wondering if the pain will ever go away.

Similarly, consider the case of an eventful heart attack. Before the attack a man may experience chest pain and simply ignore it. (Historically, men are conditioned to ignore pain, and may even be hardwired with this predisposition.) Once the heart attack is identified that same level of pain may be terrifying, because it raises the possibility that he could die. Later, following bypass surgery the pain could actually be worse, but now it is reframed. Pain is associated with hope because the patient realizes that he has survived the heart attack and the surgery, and he sees the possibility of healing. The pain may be horrible, but the experience has a different quality. It represents hope: I will survive. It is no longer colored by negative images. If he is in a medical environment that he respects, he also feels safe and trusting, and that sense of safety tends to make the pain more tolerable.

The experience of pain is defined by the entire context in which the pain occurs. This is a critical aspect of the phenomenon. The pain of childbirth, for example, may be extreme, but it is understood that the pain is normal and that it will end. This may also be nonverbally communicated by a supportive midwife or doula, especially if she is a mother herself. Without words she is saying, "This is an experience that you can transcend, just as I did." Psychologically, the pain serves a higher purpose, to deliver a child into the world, and in a sense this may also make the pain more bearable.

Personal Insight on Pain

As a researcher in human physiology and performance, I have studied pain periodically over the past 30 years. Here I would suggest that how we interpret the stimuli affects the quality of our experience. Physiologically, there are two components of pain. 1) Pain is a sensory experience and, 2) it is also a reflection of activation in the brain. If we do not attend to that experience, do not put any labels on it, then it is simply sensation.

Several years ago, I observed, monitored, and physiologically recorded the experiences of a Japanese yogi who performed various forms of piercing (piercing his tongue and neck with unsterilized metal skewers) (Peper et al, 2005; Kawakami, Peper, & Kakigi, 2015). Although most of us find it painful to even look at the photos, the physiological data of his pulse, brain waves, and breathing patterns made it clear that he was not experiencing pain per se.

Physiologic Data: Responses to Piercing

A yoga master was psychophysiologically monitored while he pierced his neck and tongue with skewers to demonstrate control of pain and bleeding. Measurements included respiration rate (RR), heart rate (HR), diaphragmatic and thoracic breathing, electrodermal activity (EDA) and electroencephalography (EEG) from Cz and Fz. The yogi reported no pain during piercing and no bleeding was observed. In general he had elevated HR and low unresponsive EDA throughout the session. His respiration rate averaged 7 bpm during the slow breathing meditation prior to and following the piercing. His EEG showed predominate alpha of 10 Hz during meditation. Alpha, SMR, and beta elevated at Cz during piercing with no change in delta or theta. Alpha and beta elevated at Fz during piercing with no change in SMR (sensory motor rhythm), delta or theta. While he stayed in alpha during the piercing, there was broader alpha activation ranging from 10 to 14 Hz. This demonstration suggests a finding of

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conscious self-regulation, as opposed to disassociation, for controlling attention and responsiveness to painful stimuli. It could be hypothesized that clients with chronic pain could be taught how to control pain using the mind/body interface, (Peper, Wilson, Gunkelman, Kawakami, Sata, Barton, & Johnston, 2006).

These findings were reiterated when I had the opportunity to observe, physiologically record, and film the context of pain with a group of Sufi initiates in Amman, Jordan and during presentations at a scientific meeting (2012, 2013). These individuals, led by a spiritual master, take part in a ceremony that involves drumming and chanting, and at the end of that ceremony they pierced their bodies with unsterilized skewers (typically in the face, neck, arms, or chest). Like the Japanese yogi, participants exhibited no experience of pain. There was no bleeding, and the tissues seemed to heal almost instantaneously.

What decreases the experience of pain and promotes rapid healing with the absence of bleeding? In the case of the Sufis, this occurred in a setting in which the piercing was experienced as a totally normal, spiritual phenomenon, one which occurs in a setting of religious faith and trust in the leader. The Sufis reported that they had permission and support from their master, Sheikh Mohammed Abdul Kareem Kasnazani. Thus they felt entirely safe and protected; they had no doubt they could experience the piercing with reasonable composure and that their bodies would heal completely. This was not simply a matter of belief; they knew that healing would occur because they had seen it occur at piercing rituals many times in the past. The faith that healing would occur rapidly was transmitted as a felt sense in the group, the sense that pain would not occur, but if it did, it was not to be feared but embraced. The experience may be modulated by the psychological context of the group, the drumming, and the chanting. (If this seems beyond belief, consider the firewalk which is frequently included in motivational group experiences, filmed and posted for viewing on YouTube.)

My work frequently involves biofeedback measurement of human physiology. At this point I have participated in more than 100 research papers, so I am highly attuned to the phenomena of sympathetic and parasympathetic activation. In the initial Jordan experience, I videoed the ritual of piercing with non-sterilized skewers and knifes but did not employ instruments to monitor brain waves, muscle tension, skin conductance, or heart rate. Based on observation, I saw no evidence of sympathetic activation (stress response) in any members of the group. As a scientific outsider, I noted that none of the participants in the Amman demonstration showed any pain behavior or reported pain, there was no bleeding, and for each participant, the tissue seemed to heal almost instantaneously.

The experience was so normalized that when asked if I wanted to experience the piercing, I agreed to participate. I was in a relaxed, peaceful frame of mind. I also continued to be a scientific observer, and I directed a colleague to make a video recording of me as I experienced piercing for the first time in my life. This, in part, is an account of my own personal experience.

At the moment when the stimuli occurred, when I was pierced, my brain did not anticipate nor evoke any sensation of pain, nor did I experience a sense of stress (sympathetic arousal). I had a sense of safety, because I had observed others in the group, one by one, experiencing the piercing without any sensation of pain or distress. Consequently, the experience did not evoke anxiety, fear, or concern. Although I remained an observer, I felt peaceful and entirely safe. I did not anticipate pain and had no concern that the piercing would be dangerous, and in fact, I experienced no pain. Unlike most of the other individuals there, about two drops of blood formed on the surface of my cheek as the skewer was removed, whereas the others had none. In my case, the wound closed totally within a minute, and an hour later there was no evidence of the piercing. The only sensation I experienced was a slight electrical tingle.

Throughout most of the evening, my role in the group was as outside observer: I monitored a video camera, recording the experience of numerous people being pierced. I did not chant, and I was simply present in their world, so my experience of safety may have occurred as a result of mirror neurons. In that context, it can be proposed that pain is not only a personal experience, it is a social experience. Essentially, there are a number of reasons why I did not experience pain or discomfort, which reflect the contextual nature of pain.

At a later date, we had the opportunity to repeat the piercing demonstrations with the Sufis at a scientific meeting and record their physiological responses. The most impressive finding was that the physiology markers (heart rate, skin conductance, and breathing) were normal and there was no notable change (Booiman, Peper, Saleh, Collura, & Hall, 2015; Peper & Hall, 2013). The QEEG did

show significant differences indicating the inhibition of pain (Collura, Hall, & Peper, 2014).

Thoughts on Pain

If you can isolate pain, the pain has no meaning. This is clearly demonstrated in research involving placebos. We also know that soldiers surviving battle may suffer horrific pain; but typically, they require less pain killer than would be anticipated. In this context the pain is an indication, "I have survived." Whether they were terrified or heroic, they now feel safe.

On the other hand, an isolated individual, alone at night with only the physical sensation of pain, may find the pain tremendously stressful, which can intensify the experience. In this situation there are concerns about the future, "This is going to hurt, it's going to be painful, I'm going to die from this, maybe I'll die alone," and the worry continues. Focusing on the pain alone intensifies it. If one can let go of these thoughts and breathe through the pain that gives hope.

What to Do While Waiting for a Diagnosis...

What are the implications of these experiences in clinical situations in which the patient is in constant pain and yet has not received an accurate diagnosis? Or in cases in which the patient has a diagnosis such as fibromyalgia, but treatment has not reduced the pain significantly? Experiencing pain or illness that goes undiagnosed and is not acknowledged can increase the level of stress and tension, which contribute to pain and discomfort. Acknowledgement validates the patient's experience and confirms that the pain is not psychosomatic (imagined), because that simply makes the experience of the pain worse. Once the patient has a more accurate diagnosis, focused treatment may be possible.

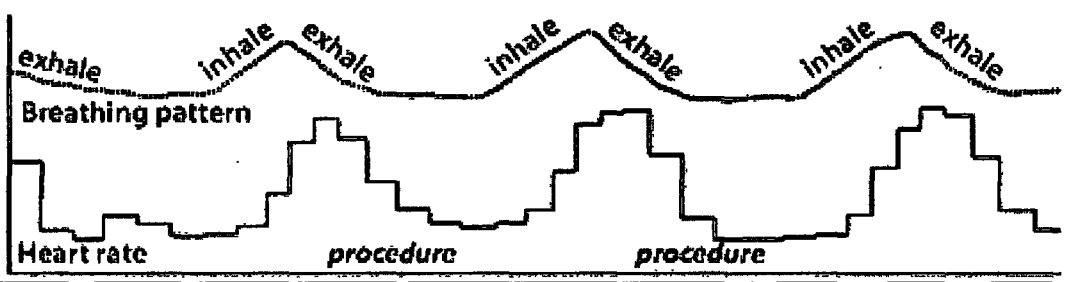
When one has chronic pain, the question is, what can be done? The first steps are for the patient to acknowledge to oneself that unrelenting pain evokes hopelessness, and to remind one's self that this does not mean the situation is unsolvable. With what little energy one has, it is important to focus on other options for diagnosis and treatment. With that limited energy, one needs to also include activities that reduce the pain. In my own work I have seen that activity that is creative, that is emotionally expressive, can reduce pain. The case comes to mind of a woman who had excruciating chronic pain and became a painter. During those moments of painting, when she activated her creativity and her curiosity, the pain and dysfunction took a backseat. In a sense her experience of pain simply was not registering.

There are many strategies to control pain which range from hypnotic induction, self-healing visualizations, changing conditioned response patterns, having one's attention captured by other multisensory experiences, breathing exercises such as exhaling during the experience of pain, and being totally in the present and experiencing the pain just as sensation, and others. Yet there are many components that are unknown.

Overall, pain appears to be reduced when a person can accept without resignation what has happened or is happening. Pain is often aggravated when the person is resentful or wishes that what has occurred could be different. If the patient can accept and then look towards something that has purpose and meaning, pain may still occur; however, the quality is different. As long as one is angry or resentful of the pain, or of circumstances believed to have caused the pain, the pain is often worse. In other words, chronic sympathetic arousal increases sensitivity to pain and also reduces healing potential. ➤

An Exercise for Use During Blood Draws and Medical Procedures: Correlating the procedure with inhalation and exhalation.

A simple breathing technique can be used to reduce the experience of pain during a procedure or treatment, or during uncomfortable movement post-injury or post-surgery. Physiologically, inhalation tends to increase heart rate and sympathetic activation while exhalation reduces heart rate and increases parasympathetic activity. Often inhalation increases tension in the body, but during exhalation, one tends to relax and let go of tension. The goal is to have the patient practice breathing so that the uncomfortable procedure or movement is initiated during the exhalation phase. Applications of this technique include having blood drawn, insertion of acupuncture needles in tender acupoints, or movement that causes discomfort or plain. Patients who use this approach during a procedure report approximately 50% reduction in pain.



A working hypothesis is that if one is sympathetically aroused for too long, then the system becomes exhausted. A fairly good measure of this is heart rate variability. People whose heart rate does not vary (low heart rate variability) are at significantly greater risk for numerous illnesses. If they are exhausted for too long a period of time, they have difficulty mounting a sympathetic response to a stressor. Secondly, people who respond with a primal "freeze reaction" also tend to have lower heart rate variability.

The challenge is to understand what occurs in experiences such as those of the Sufis and how to translate this into clinical practice so that suffering can be reduced. We propose that the first step is to create an atmosphere of safety, trust, and hope. In that context yoga practices to increase slow diaphragmatic breathing while maintaining alpha EEG would teach clients somato-cognitive techniques to refocus their attention during painful stimuli (mindfulness) (Pelletier & Peper, 1977). Using slow breathing as the over-learned response would facilitate recovery and regeneration following painful situations. This approach could also act as structured desensitization to painful stimuli and might be a complementary clinical technique for voluntary pain control. To develop mastery and be able to apply this type of skill under situations of stress requires training and over-learning. Yoga masters over-learn these skills with many years of meditation. With mastery, patients may learn to abort the escalating cycle of pain, worry, exhaustion, more pain, and hopelessness by shifting their attention and psychophysiological responses.

The major lessons I learned from studying the yoga master and the Sufis are that a client has to feel totally *safe* and accepted. It is clear that components of that experience include trust, hope, and faith, qualities that the industrial-medical complex has pushed aside because they are not billable. Yet these qualities form the foundation of humanistic, holistic medical care and are often covert reasons why people are frustrated by their experience with medical care and seek complementary and alternative medicine.

Erik Peper, PhD

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Resources

A link to the Sufi website that has numerous pictures and descriptions is available at: http://www.kasnazan.com/article.php?id=1820

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The Growing Role of Neurofeedback in Integrative Medicine

by Siegfried Othmer, PhD, and Susan F. Othmer, BA

We are at the threshold of revolutionary change in our approach to mental dysfunctions as they come to be seen primarily in the frame of neural network relations. To date, the recovery of brain function has been approached mainly in the frame of neurochemical models, but even this principally involves neurochemistry in the service of neural communication. The medications in common use for mental dysfunctions by and large target the neuromodulator systems that regulate synaptic excitability. But there is another aspect to the problem. Information transport via the action-potential mechanism is subject to tight timing constraints, and this represents a major potential failure mechanism for the brain under duress. This is a particular issue following physical or emotional trauma, or when the brain has been diverted from its proper developmental pathway early in life. In these cases there may be little or no evidence of structural injury to the brain. The deficits must lie almost entirely in the functional realm, and therefore should be accessible to a functional remedy. And yet we know that pharmacotherapy is largely ineffective in application to these conditions. The deficits are more easily understood in the bioelectrical domain of timing and frequency. And when remedies emerge based on an appeal to neural network functioning in the frequency domain, the case for a new departure in understanding mental dysfunctions is consolidated. This is where we now find ourselves.

Progress in brain imaging over the last two decades has brought these issues to the fore. At first we had to make do with the static imagery of PET and SPECT, but this already drew our attentions back to the intact, functioning brain, and elevated our gaze from brain slices in petri dishes and the firing patterns of individual neurons. Such a divide-and-conquer strategy gave us no hope of ever fully understanding the living brain. A complementary systems-level perspective was missing. With the emergence of functional magnetic resonance imaging in the early 1990s, we had our first opportunity to witness brain dynamics, albeit with very poor time resolution, as the process being monitored was glucose uptake. This led in time to the identification of our core connectivity networks, which constitute the foundation of a hierarchy of functional organization in cortex.[1] Follow-on studies revealed that identifications could be made between various mental disorders and dysfunctions in our intrinsic connectivity networks (ICNs).[2] On that basis, Menon proposed that much of psychopathology could be grounded in the failure of our core control networks to coordinate properly. Evidence was cited for several conditions, including schizophrenia, depression, anxiety, dementia, and autism. But the mechanism undoubtedly has more general applicability.[3] Yet other studies demonstrated that conditioning experiments targeting localized features of the fMRI could elicit functional improvement.[4] As an example, deCharms demonstrated benefit for complex regional pain syndrome (CRPS1), yet another relatively intractable condition that does not yield to pharmacotherapy.[5] Jointly, these findings implicate functional connectivity of the core networks as a basic failure mechanism in mental disorders. The full exploitation of these new findings call for an integrative, systems-level perspective on brain function, one that takes both perspectives – the neurochemical and the bioelectrical domains – into account. And on the clinical side, that implies the need for an integrative approach to remediation as well.

Very few scientific novelties burst upon the scene without obvious antecedents, and the same holds true here. Much of what is now being proved out in fMRI-based neurofeedback has been previously demonstrated using feedback with the EEG as a training variable. For example, just 2 years after the publication by deCharms, a similar report was published using EEG-based training with CRPS1, and the results were comparable, if not better.[6] The method used was just 1 year old at

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the time. It was infralow frequency training, the principal topic of this article. However, the antecedents of this method go back more than 30 years.

The EEG was our first noninvasive technique for studying brain dynamics, but its complexity limited its clinical utilization, so the world moved on. It has taken new developments in mathematical analysis and in data acquisition to restore the EEG to its proper place in research. This is also having beneficial fallout for clinical practice, with innovation increasingly occurring at the pace of software development. The history of EEG biofeedback, now commonly termed neurofeedback, is elaborated in a newly published book titled *Restoring the Brain: Neurofeedback as an Integrative Approach to Health*. The book covers recent developments, with particular focus on the rapidly emerging technique of infralow frequency training. The case is made for neurofeedback to play a complementary role in integrative medicine.[7]

The EEG gives us insight into the brain's regulatory activities and how these are organized both spatially and temporally. The argument briefly goes as follows: Cortex is organized for massive parallel processing in the service of pattern recognition. The organization of such patterns must be supported by neuronal assemblies of macroscopic spatial scale, and these must be organized for simultaneity in processing. The principle that "simultaneity defines belonging" is known as *time binding*.[8] Seen in its simplest mathematical terms, the neuron is organized for coincidence detection – on the timescale of milliseconds – by the nature of the action-potential mechanism. Coincidence at the level of the neuron in turn supports simultaneity at the level of the neuronal assembly. Since action potentials are perishable entities that are not self-replicating, the persistence of states must be explicitly organized through repetition. Refresh is supported via a recursive cerebral architecture, thus generating a periodicity that maintains continuity. Simultaneity of action at the level of the neuronal assembly, in combination with periodicity, translates to local synchrony at the level of the EEG. Communication between cortical sites is reflected in synchronous (or at least coherent) activity at those sites. Thus, the regulatory role of neuronal assemblies is reflected in frequency-based organization of sufficient magnitude to become discernible to us in the EEG, giving us exquisite insight into timing relationships at the network level. Hence the EEG distills for us the aspect of neuronal activity that is involved in neuronal regulation (as opposed to information transfer). We don't get to see the text, but rather only the context.

We know that the brain is a highly competent, if not overeager, correlation detector, and in feedback this quality is put to good use. If the brain is allowed to witness selected features of its own EEG, it has no difficulty recognizing its own agency with respect to that signal. Once that loop is closed, the brain inevitably also takes responsibility for the signal and tries to control it. This process is analogous to the brain's taking responsibility for keeping the bicycle properly balanced and the car properly pointed down the freeway. The rider or the driver doesn't have to be engaged on these matters. They can be left to the brain to handle in background. The same principle holds in the case of EEG feedback and fMRI feedback. The process does not necessarily involve conscious mediation. All that is required is that the process not be interfered with. Distraction is the bane of the bicyclist, of the driver, and of the neurofeedback trainee.

When the brain is involved in feedback under conditions in which it is allowed to exercise its discretion, there is a bias in the direction of better regulation. Left to its own devices, but with the benefit of physiologically relevant information, the brain tends to move toward calmer, better-controlled states. It is residence in calm, de-stressed states that presents the therapeutic opportunity for the functional reorganization of the core networks. The brain is entirely in charge of the recovery process that follows. We have simply arranged to provide a propitious context. The client is usually aware of nothing more than the feeling of migration to a state of calmness with which he may not have been previously acquainted. (Even squirrely autistic children may adopt a quiescent, meditative pose while undergoing the training.) The client may also remark about a state of alertness that does not seem congruent with such a state of placid calmness.

What has been described above is the typical experience of someone undergoing neurofeedback in the infralow frequency region of the EEG. There are many other ways of doing neurofeedback, however, and some history needs to be reviewed to provide context for the discussion to follow. EEG biofeedback got its start in the 1960s with the training of the cortical resting rhythms, principally the famous alpha band at nominally 10 Hz, and the sensorimotor rhythm at nominally 13 Hz.[9,10] The alpha band signal at the occiput could be regarded as the resting rhythm of the visual system, and the sensorimotor rhythm (SMR) could be understood as the resting rhythm of the motor system. Since the activity in these bands has an episodic, bursting character, it was trained in an operant conditioning paradigm of challenge (with respect to a threshold) and reward. In both instances, the objective was to move the trainee toward lower levels of arousal; that is, toward calmer states and improved levels of regulation. In the case of the alpha training, this was found to be ameliorative of anxiety states, and the SMR-training was found to be stabilizing against motor seizures and even temporal-lobe seizures, among others.[11,12] These initial findings were vigorously challenged at the time,

but they have been amply validated since.[13,14] A meta-analysis of the work with epilepsy has also been published.[15]

The research on SMR-training for seizure management became the springboard for application to hyperkinesis, which later became ADHD.[16,17] All but one of the ADHD studies that also tracked IQ found significant improvements in IQ score with the training. A 20-point IQ improvement was observed in two 8-year-old mildly mentally retarded twins. The results were published after 5 years of follow-up, over which time the gains held but no further improvements could be elicited.[18] The work with SMR-beta training led to much broader application to psychopathology by the early 1990s.[19] It emerged that the challenge to a single dominant rhythm of the EEG in a training paradigm sufficed to evoke broad functional reorganization of the cerebrum.

Subsequent to the early research, alpha training evolved in three directions. One aimed toward optimum functioning through the broadening of the attentional repertoire via the promotion of whole-brain alpha synchrony.[20] Another used intensive alpha synchrony training in support of psychotherapy and personal transformation.[21] The third and most common application was oriented toward the promotion of deep, internally focused states that facilitated the resolution of traumas and a reprieve from addictive propensities. This came to be known as Alpha-Theta training once theta-band reinforcement was added to the protocol.[22-24]

The next major thrust in the technology was toward the individualization of what came to be known as SMR-beta training (because reinforcement of the slightly higher-frequency beta 1 band (15–18 Hz) was also commonly included in the protocol). The personalization of the training took two forms. The first of these followed immediately upon the availability of affordable full-brain mapping capability on PCs in the early 1990s. This allowed the transient excursions into dysregulation to be detected wherever they occurred on cortex, and the training strategy to be adapted to focus on such excursions. The training brain was cued with respect to such excursions in what was referred to as inhibit-based training. This involved nothing more than the transient withholding of rewards. Brain activity was not actually being inhibited. The other thrust, for which our own group was responsible, consisted of the individualization of the reward frequency, which began after 1995. It was observed that sensitive and unstable brains were differentially responsive to different EEG frequencies, and that for optimal outcomes the target frequency sometimes had to be tuned to within 0.5 Hz or even less.

Such frequency specificity could be readily confirmed because of its repeatability. In the highly responsive individuals at issue here, we were dealing with demonstrable real-time control of their physiological state. For instance, one person might feel hungry at one frequency, and yet experience satiety at a nearby frequency. The therapist could toggle the frequency back and forth and reliably reproduce these feeling states. Another person might feel tearful at one frequency (without having any basis for being teary), and yet feel placid or even upbeat at an adjacent frequency. The transition period could be as little as a minute or two. Yet another person might feel the onset of a migraine aura at one frequency, and observe its subsiding at an adjacent frequency. Again this held true reproducibly. Unsurprisingly, bipolar individuals are particularly responsive, and in some cases can be actively moved between depressive and manic states within a period of minutes with a slight shift in reward frequency. In between these two frequencies lies the optimal target frequency at which the brain can train itself toward stability simply by virtue of lingering there for a number of training sessions. This gives the neural networks the opportunity to consolidate the new configuration.

The implications of this responsiveness are huge. We were in fact effecting real-time alteration of physiological state in the general case. Trainees mainly differed in their awareness of such state shifts. Those with the most sensitive, unstable, or reactive brains were the best reporters on their own state as well as being the most sensitive to the choice of target frequency. For both of these reasons, such sensitive individuals were the "canaries" that guided further development of the method. In the event, we were led to provide training at ever lower frequencies to accommodate them. By 2006, after several years of gradual migration to lower frequencies, this trend caused us to enter the infralow frequency region. Training was performed at frequencies of 0.1Hz and below, the very region in which the intrinsic connectivity networks were first identified using fMRI. In the following, this will be referred to as ILF training.

At such low frequencies, threshold-based training was out of the question. The cycling time was too slow. We had to resort to signal-following, in which the brain is simply exposed to the exceedingly slow undulations of the signal. The brain's interest was captured by the continuity of information flow, and the whole training exercise became more effective than it had ever been before. For the first time, the brain was being trained in accord with its own preferences rather than being regimented like one of B. F. Skinner's pigeons. The brain was in charge of its own journey, based on its own assignment of meaning to the signal that it was observing. (The reader's indulgence is requested for the use of such anthropomorphic language with reference to the brain as an autonomous agent.) The results were so dramatic – and so parametrically specific – that we promptly issued a protocol guide to our practitioner network.[25]

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What, then, can we accomplish with techniques such as this at our disposal? In order to organize the full range of clinical findings, it is useful to have in mind the hierarchy of the brain's regulatory obligations. Considering the brain in its role as a control system, its principal burden is to assure its own unconditional stability. The method is very effective with brain instabilities such as migraines, panic attacks, asthma episodes, seizures, vertigo, night terrors, and even bipolar disorder. The training has been relatively ineffective to date for narcolepsy and sleep apnea, although it can be very helpful in isolated cases.

Remarkably, all of the above conditions respond well to a single protocol, which makes it plain that we are remediating a core vulnerability rather than specific conditions. The placement of choice is T3-T4 (in the international 10–20 system), which indicates that the functional deficit relates to the coordination between the two hemispheres. However, no claim of uniqueness is implied. The above conditions respond to a variety of other protocols as well. For example, a 90% favorable response for migraines was observed by Walker using QEEG-based methods.[26] So the T3-T4 training is usually sufficient for the purpose, but it is not obligatory.

Remediating brain instabilities had been our strong suit from the moment we first adopted the interhemispheric placement of T3-T4 in 1999. Up to that time we were using lateralized placements to target migraines that were typically also lateralized. When a particular migraine simply migrated to the other hemisphere when it was directly targeted, the interhemispheric placement was tried, and the migraine dissipated promptly. The interhemispheric placement soon became standard. It was the brain instabilities that mandated such a precise targeting in terms of frequency, and thus drove the agenda to ever lower frequencies.[27]

Next in the hierarchy is the issue of tonic state regulation, and within this broad category we have a hierarchy as well, one that conforms to our developmental sequence. Foundational in this hierarchy is the regulation of tonic arousal, which is in turn intimately connected with affect regulation, autonomic regulation, and interoception. This is the developmental priority in infancy and early childhood, and it is the primary target in ILF neurofeedback. Fortunately, the deficits in these domains lie largely in the functional realm, quite irrespective of how intractable they may appear behaviorally. They are therefore accessible to us for remediation with neurofeedback.

Within the category of arousal regulation we include insomnia, agitation, and hypervigilance, as well as general overarousal. Within the domain of affect regulation we include the anxiety-depression spectrum, the capacity for attachment and empathy, and the personality disorders. Within the domain of autonomic regulation we include dysautonomia, sympathetic/parasympathetic balance, regulation of blood pressure, heart rate, and vasoconstriction, peripheral temperature, galvanic skin response, and even gastric secretions (in connection with reflux). With respect to autonomic regulation there is a substantial correspondence with traditional biofeedback utilizing measures of peripheral physiology.

Within the general category of state regulation we also encounter transient dyscontrol (quite possibly externally mediated) that is subsumed in the general category of behavioral disinhibition. It needs to be distinguished from brain instabilities. This category includes impulsivity, obsessive and/or compulsive behaviors, Tourette syndrome, bruxism, and rage behavior. Among these, Tourette syndrome and OCD present the greatest challenges to neurofeedback in its present state of maturity. Impulsivity, on the other hand, responds more consistently and is more completely resolved than the other conditions. In large group evaluations of ILF training for a general clinical population (5000 participants), the effect size was large (>0.9) and the posttraining distribution in impulsivity was found to exceed the norm. These data have been presented in a professional forum, but have yet to be published.

The above observation illustrates that this kind of training is best regarded in the frame of training toward optimum brain function rather than as a technique to expunge dysfunction. The latter objective is accomplished by virtue of the former. That explains why the approach can rely on a modest number of electrode placements for all trainees. It is basic regulatory mechanisms common to us all that are being targeted in the training, not one or another specific deficit.

Beyond state regulation issues we have the third category of regulatory burden, namely responsiveness to the environment both on the input and on the output side. This category includes sensory processing issues, learning disabilities, maintenance of vigilance, attentional faculties, and working memory. It also includes motor planning and motor function such as speech articulation.

It was executive function that received most of the attention in neurofeedback in the early decades, mainly because this conformed to the interests of cognitive neuroscience. For the same reason, the training for the ADHD spectrum targeted the left hemisphere exclusively because that was the only one for which a cartography was available. The right hemisphere remained terra incognita; there was no point in even showing it in the textbooks (with the exception of the sensorimotor strip).

And yet clinical demands had driven us ever more toward lower frequencies and toward a right-hemisphere priority. Just as the left hemisphere has priority with respect to executive function, the right hemisphere has priority with respect to the foundational regulatory concerns of arousal, affect, and

autonomic regulation. The right insula has a very different life experience from that of the left, so to speak. Since it was our most challenging clients who drove us ever lower in training frequency and ever more firmly onto the right hemisphere, it follows that the most intractable conditions encountered in mental health relate to vulnerabilities of right-hemisphere function first and foremost.[28] Further, since we are driven to attend to the earliest developmental priorities of the developing infant, it follows that we are targeting the residual sequelae of early childhood trauma in much of our work.

Throughout the evolution of the training protocol schema over the last two decades a remarkable consistency has been observed. The frequency at which right-hemisphere training optimizes for any individual differs systematically from that of the left. In the infralow frequency range, the left hemisphere training optimizes at twice the frequency of the right. In biological systems it is the lowest frequency that sets the tone, and higher frequencies coordinate with the basic rhythm. A harmonic relationship is not unexpected. Within the conventional EEG frequency range, the right hemisphere optimizes at 2 Hz lower than the left. Here it is likely that the left hemisphere is taking the lead and the right hemisphere is the follower. The division of labor seems appropriate: The right hemisphere is in charge of our state of being, of our vegetative and our core or intrinsic self; the left hemisphere is in the lead when it comes to reacting to and engaging with the world. This view has recently received support from an evaluation of information flow within microstates.[29]

The implications for brain training are that we should understand the infralow frequency training principally in terms of right-hemisphere priorities, and we should understand training in the conventional EEG range in terms of left-hemisphere priorities. That is indeed how matters have unfolded over the years. The crossover between these two realms is at the only place that it can be, namely at 2 Hz on the right hemisphere, which corresponds to 4 Hz on the left in both the high frequency and the low frequency perspectives. Fleshing out this model are frequency rules that relate interhemispheric training in the frontal and prefrontal region to training on the central strip, and those that relate the parietal and occipital interhemispheric training to that on the central strip. Collectively this model testifies to the specificity – as well as the subtlety – with which brain dynamics are organized on the large scale. It supports the presumption that the integrity of timing and frequency relationships are foundational to the harmonious functioning of the brain.

It should be observed in passing that the sole evidence for the above frequency rules consists of the collective subjective reports of trainees that allow the determination of the optimum training frequency in each case. No independent evidence for these frequency rules yet exists. There is not even any objective evidence for the existence of the optimum response frequency. So on the one hand, the findings fail to meet conventional research standards in terms of objective evidence, and on the other hand the posited relationships are likely among the most firmly established rules governing the dynamic organization of our neuronal networks. The frequency rules have been observed to hold consistently by thousands of clinicians who use them to guide their work. They hold over the entire range of frequencies that has been characterized, some four orders of magnitude.

The Current Status of Neurofeedback in Health Care

Collectively we are still near the beginning of the journey of exploiting techniques such as neurofeedback for physical and mental health. But already much has been well established, and the outlines of what is possible are becoming clear. All neurofeedback methods have their more specific and their more general effects, in that every brain challenge affects not only the specific mechanism being engaged but with it the whole brain as well. The particularity of the different methods means that no single one can be expected to satisfy all of the clinical objectives.

Among the principal approaches, infralow frequency training likely has the most comprehensive clinical footprint. The particular strength of the infralow frequency training is in application to the various trauma syndromes that afflict core state regulation, which must be the clinical priority.[30] This includes in particular developmental trauma and the autism spectrum, wherein systematic remedies have clearly been lacking. It also includes the adult manifestations of early trauma such as dissociative identity disorder, borderline personality disorder, other personality disorders, and chronic pain syndromes. A case series for pediatric epilepsy utilizing ILF training has been published.[31]

The largest documented experience base exists for PTSD among recent combat veterans.[32] In a survey of some 300 trainees in the 2009–2011 time frame, about 25% recovered within 20 training sessions. Another 50% recovered within 40 sessions. The remaining 25% either took even longer or recovered only partially. Recovery meant that symptom severity fell below clinical significance. Some 75 symptoms of dysregulation were tracked. 90% reported recovery from migraines. In 80% of those suffering from depression, scores were cut in half within 2 weeks, or less than 10 sessions. The same was found for anxiety. There was nominally 75% response for most symptom categories. The least responsive symptom was tinnitus, at 50%. These results were presented at a professional meeting but have not been published.

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The ILF training can be profoundly helpful for the degenerative conditions, the dementias and Parkinson's, but a broad distribution in outcomes is to be expected. In all these cases, training has to be maintained at some level to retain gains. The training can be helpful with schizophrenia as well. In one astounding case, the trainee (who was also a 20-year veteran with PTSD) lost his interest in smoking by the fourth session, a signature of progress with respect to the schizophrenia and the nicotine dependency. He had had no intention of quitting when he came for training.

The most commonly used neurofeedback method at the present time is very likely to be a variant of the Sterman/Lubar SMR-beta training, since that has the largest research base behind it, and the largest trained practitioner community. We ourselves taught that method to several thousand clinicians for about 10 years starting in 1990. This protocol has been shown in six formal studies to match stimulant medication, as judged by a continuous performance test. The application is mainly to the ADHD spectrum, likely the largest category of referrals for neurofeedback. A meta-analysis covering this work has been published, and an update that also covers the research history was published four years later.[33,34]

The specific virtue of QEEG-based training is to target brain dynamics in the conventional EEG range of frequencies using mainly inhibit-based training protocols. Remarkable results have been published for application to schizophrenia and Down syndrome.[35,36] QEEG-based training can also be very helpful for the localized deficits that may be found in traumatic brain injury and in cerebral vascular accidents.[37,38]

Multisite alpha band training serves to improve attentional function. It induces states similar to those achieved in meditation, and thus may be used in support of meditation. Alpha-Theta training is used very effectively in addictions treatment, and it also plays a role in recovery from PTSD. Long-term outcomes are very favorable with this method in comparison with standard treatments.[39]

Infralow frequency training is not the only technique that relies on the slow cortical potential for training. In Europe, a challenge-based method has been under development since the 1980s. It is called slow cortical potential (SCP) training and involves challenging the trainee to alter the slow cortical potential at Cz by several microvolts within a period of 8 sessions. The objective is to train the mechanisms of cortical activation.[40,41]

It is estimated that currently some 20,000 practitioners of neurofeedback are active in some 50 countries. Over 50 professional licenses are engaged in the practice of neurofeedback, and the work has been published in over 275 different refereed journals. In the US, most of the services are on a self-pay basis because third-party reimbursement remains marginal. The cost burden can be moderated in cases of long-term training by means of supervised home training by parents who have received a modicum of instruction in the method. Clinical decision-making remains in professional hands. Application to sports performance and to the performing arts is a growing interest, one that is not constrained by the bounds of licensure.

One can already project that in their mature implementation neurofeedback technologies will have significant impact on the mental health status of the population and at the same time decrease the overall medical cost burden, much of which is secondary to brain-based disorders.

Supportive Materials and Additional Reading

Those who wish to see more specifics on the above treatment may find the following publication helpful:
Othmer S, Othmer SF, Kaiser DA, Putman J. Endogenous neuromodulation at infra-low frequencies. *Semin Pediatr Neurol.* 2013;20(4):246–260.

See also the following Web-accessible monograph:
Othmer S. *A Rationale and Model for Infra-Low Frequency Neurofeedback Training.* http://www.eeginfo.com/research/researchpapers/A-Rationale-for-InfraLow-Frequency-Neurofeedback-Training.pdf.

Look for an extended version of this article with charts, with the November 2015 contents, on our website: townsendletter.com.

Dr. Siegfried Othmer and Susan F. Othmer have been involved with neurofeedback since 1985. The initial impetus was the brain-training of their son Brian for his seizure disorder. The training was life transforming for their son, and this redirected their professional lives to the further development of neurofeedback as well as to the promotion of its public acceptance.

Dr. Othmer is currently chief scientist of the EEG Institute and president of the Brian Othmer Foundation. Susan Othmer is clinical director at the EEG Institute, located in Woodland Hills (Los Angeles). The Othmers have pioneered a number of novel applications of neurofeedback over the years. The Othmers provide professional training in EEG biofeedback and sponsor a professional network of neurofeedback therapists, the EEG Associates. The Othmers have been developing premier instrumentation for neurofeedback continuously over the last 22 years, and this development is ongoing.

Notes

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Neurofeedback

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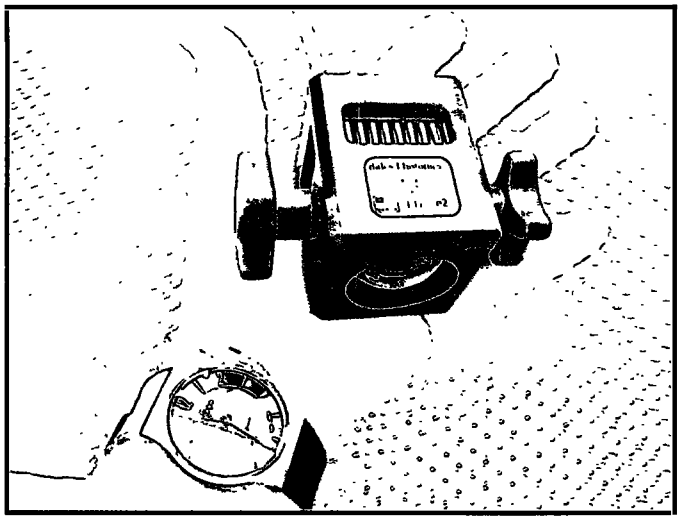
A Breakthrough in Using Light Therapy to Treat Neuropathies

by Len Saputo, MD



BioPhoton light emitter on hand.

This article describes the successful treatment using light therapy of three patients with peripheral neuropathy. The etiology of neuropathy for each of these patients was different, as were the patients themselves in age, sex, and general condition. All of the patients were significantly disabled and had previously undergone extensive conventional treatment without significant relief.

I have used light therapy to treat over 2000 patients with a variety of painful health conditions since 1999, when I first met Maurice Bales, who had extensive experience with the development and manufacturing of infrared light devices, beginning in the 1970s with his work at NASA and the Lawrence Livermore Lab. Maurice trained me to treat a wide range of painful conditions that included neuropathy, neck and back pain, TMJ disorders, headaches, fractures, and sports injuries. I have found that if something hurts, chances are that treatment with light will help.

Despite its remarkable effectiveness, safety profile, and affordability, light therapy remains for the most part underappreciated and underused. This lack of utilization of light therapies is not just by mainstream medicine but also by the alternative and integrative medical communities. This situation exists despite the fact that more than 70,000 peer-reviewed articles have been published on light therapy and listed on PubMed going back to 1899. Since then light therapy has been documented to relieve pain, increase circulation, reduce inflammation, speed up wound healing by an average of 40%, increase lymphatic drainage, attract stem cells, and stimulate mitochondrial production of ATP – among other things.[1–15] This sounds a bit like Star-Trek medicine!

I have selected three case histories that demonstrate the range of peripheral neuropathies that can be treated using light therapy.

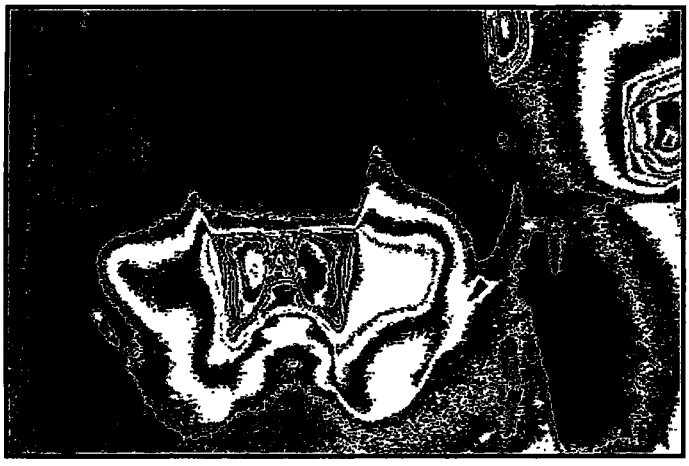
Case #1: Chemotherapy-Induced Peripheral Neuropathy

J. K. is a 69-year-old female referred by her oncologist for treatment of advanced peripheral neuropathy caused by chemotherapy. She was diagnosed in 2010 with colon cancer and was treated with surgery, chemotherapy, and radiation. She felt well and remained in remission until December 2014, at which time she was found to have stage IV disease based on diagnosing metastases to her lungs. She was started on chemotherapy with Erbitux.

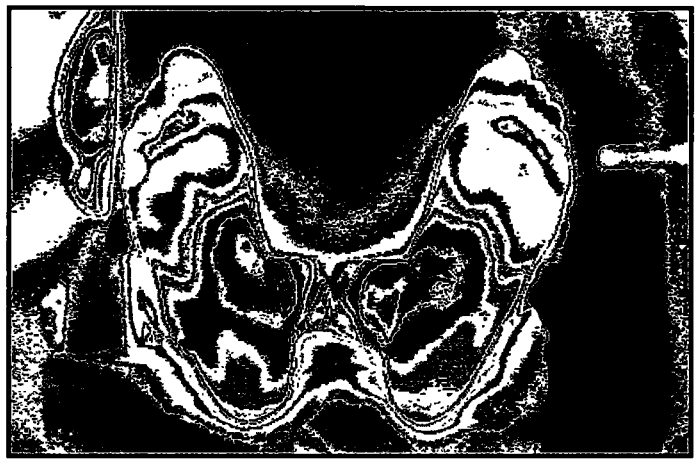
Her cancer responded to this treatment, but within a few months she developed progressively worsening numbness in her hands and feet. By June 2015, she had such dense numbness that she could not feel the accelerator or brake in her car and was unable to button her clothing. She became depressed because she was for the most part confined to her home. Her oncologist referred her to me for treatment of her neuropathy because it had become so severe that chemotherapy had to be discontinued.

She was treated with 11 15-minute light treatments to her feet, legs, and hands from July 29, 2015, through August 20, 2015. She regained enough sensation in her fingers and

Pre-Tx Plantar Feet



Post-Tx Plantar Feet



Pretreatment thermographic image of soles of feet show lack of circulation as blue and green colors. Posttreatment shows significantly increased circulation as red and orange.

feet that she can now drive, walk normally, and button her clothing without assistance. She is now much more active socially and is back on her chemotherapy treatment. She remains in remission and is enjoying life once again.

Case #2: Trauma-Induced Neuropathy

T. S. is a 39-year-old woman who was in a tornado three years ago, when a large uprooted tree fell on her geodesic dome and crashed her to the ground. Ever since that event, she could not raise her arms above her neck; has been walking with a wide-based gait to maintain her balance; has been weak in both legs; tires easily; and developed numbness, burning pain, and tingling in her feet and lower legs.

Her podiatrist referred her to me to treat her peripheral neuropathy with light therapy.

The patient's examination revealed dense numbness extending from the bottoms of her feet to the midcalf. She had normal pedal pulses and no Babinski sign, but her knee and ankle reflexes were absent. Her lumbar spine had very significant bilateral pain to direct pressure from L3 to S1. The range of motion of her neck was restricted to 45 degrees bilaterally and there was moderate tenderness to palpation in the suboccipital portion of her neck. She also suffered from both lumbar disc disease and neuropathy.

She received seven treatments on her feet, low back, neck, and TMJ with light from July 15 through August 21, 2015. The patient reported, "Photonic stimulation has been a miracle for me. I no longer have pain when I stand or walk, and am able to straighten my knees. I walk with balance and at a normal speed, which I never imagined I would be able to do again. I am dreaming of getting a bike and returning to yoga and dance."

Case #3: Diabetic Neuropathy

R. S. is a 56-year-old male with a history of type 2 diabetes, hypertension, obesity, hyperlipidemia, and being a "wine connoisseur." He was referred by his chiropractor

Posterior pre-Tx

Posterior post-Tx

Pretreatment image shows inflammation in orange and red from a posterior radiculopathy. The posttreatment image shows a reduction of inflammation and more symmetrical pattern of heat distribution. (The white spot is an artifact of the BioPhoton treatment.)

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for treatment of his neuropathy with infrared light. His symptoms began in 2008 and included numbness and mild burning nighttime pain that had been progressive and assumed to be caused by type 2 diabetes. It is noteworthy that he was being treated with glipizide, amlopidine, hydrochlorothiazide, pravastatin, and nortriptyline, all of which have an association, albeit weak, with peripheral neuropathy. Odds are that the most likely cause in this case was a combination of diabetes and alcohol.

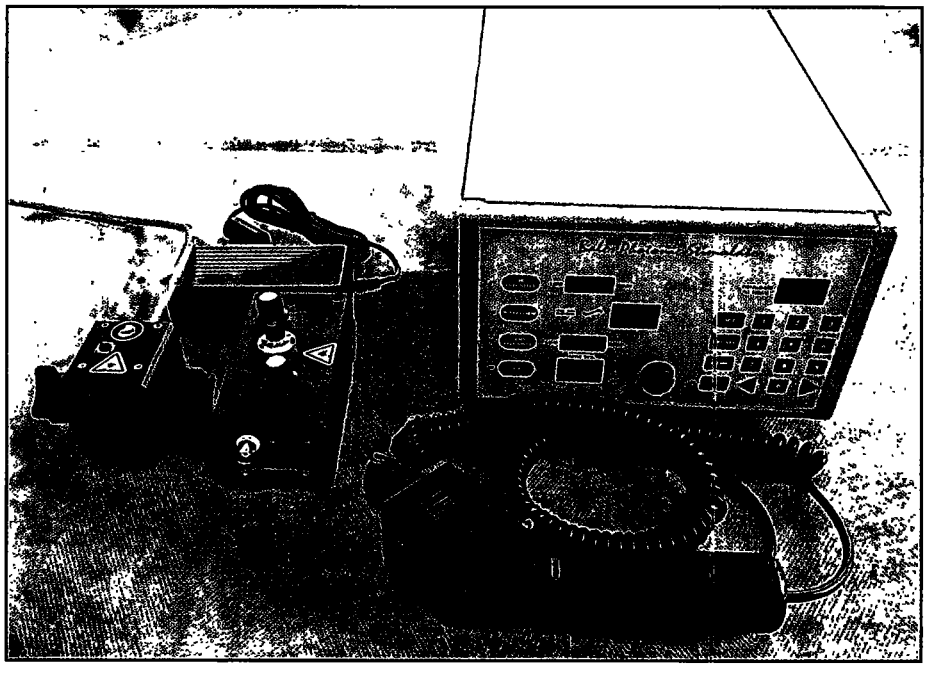
He was treated from January 2014 through June 2015 with 31 infrared light therapy treatments to his feet. The combination of gradually reducing his alcohol consumption and employing light treatments had a major effect on improving his neuropathy symptoms. At the present time has no pain and only mild numbness in his feet. His gait is normal. In addition to using light therapy, we have successfully focused on improving his lifestyle factors including stress, insomnia, diet, exercise, weight management, and reduction in alcohol consumption. Because of his compliance we have been able to discontinue all of his medications.

Pain management has become a very sophisticated discipline that tends to be complicated and often associated with challenging side effects. Light therapy is another story, because it is simple, effective, safe, and affordable. In contrast, in mainstream clinical practice, it is typical for patients with severe pain to be treated with a polypharmacy that usually includes drugs for pain, anxiety, depression, insomnia, and a wide range of additional drugs to manage their side effects. Many people take 10 or more drugs and, not unexpectedly, simply cannot function very well. These are often those patients who come to my office!

For some neuropathies, light treatment alone is sufficient to relieve even the most severe pain. I have been able to wean more than a thousand patients off their medications. For other painful conditions, it can be helpful to use an integrative team approach that can include chiropractic, Chinese medicine, bodywork, imagery, psychotherapy, pulsed electromagnetic field therapy, and so on.

I have found that the safest and most effective way to use light therapy is to use the right device under the guidance of infrared imaging in real time. The Bales Thermal Image Processor (TIP) that we employ is a high-resolution infrared camera which is highly stable and sensitive. It allows us to use light devices that can deliver the right wavelengths with enough power that we usually get impressive clinical improvement in just a single 15-minute office visit. This approach also allows patients to observe their infrared images in real time and see for themselves the impressive changes that occur during a treatment. So patients get great clinical results not only from the effects of light itself, but also from the effects of visualizing how the treatment changes the thermal patterns on their skin.

We have learned that with certain conditions, it is critical to follow the thermal effects of light during treatment so that we visualize what we're doing and also minimize any chance of making symptoms worse. This is especially important in people with fibromyalgia and other forms of neuropathic pain such as complex regional pain syndromes, shingles, certain vascular headaches, and several other conditions.



The light emitter, computer, and power supply of the new BioPhoton 100 on the left, compared with the original Photonic Stimulator on the right.

There are hundreds of light therapy devices available, greatly varying in their respective prices, mechanisms, and efficacy. The device that I began using in 1999 was the Bales Scientific Photonic Stimulator, in conjunction with the Bales TIP camera. When its inventor, Bales, worked for NASA and the Lawrence Livermore Labs, he was developing equipment used for the space shuttle. Starting in 1985, he began to adapt his work to the medical field, creating his thermographic camera in 1990 and the Photonic Stimulator, which was approved by the FDA as a medical device to treat pain in 1997. Bales has made dozens of incremental improvements to photonic stimulators over the past two decades. What is especially noteworthy about the three cases I discuss in this article is that I used a revolutionary new

model introduced only this year, now called the BioPhoton 100. This device is significantly more powerful than its predecessors, offers variable wavelengths and frequencies, is considerably smaller, and costs less.

Here are some of the specific differences:

Power: Output power has been increased from 0.250 watts to 8.9 watts. Output power is a very important factor for permeation depth. While lower-powered devices may benefit cells at the superficial level, they fail to penetrate deeper tissue, which is often the root problem of a chronic disease. The BioPhoton can target tissues deep within the body and penetrate the skull to reach the brain. More power equates to more photon energy being transmitted to the cells, which also reduces the duration and number of treatments.

Spectrum wavelengths: The previous model had a fixed wavelength of 850 to 880 nm, while the BioPhoton 100 has mixed-spectrum blue light at wavelengths from 450 nm and red and far-infrared light up to 940 nm. Blue light only penetrates superficial tissues but can treat cutaneous conditions such as traumatic injuries such as burns, cuts, contusions, and even infections such as MRSA.[16–18] Increasing the power of blue light can deliver substantial amounts to the deeper tissues. It should be noted that blue light has greater ability than red or infrared in releasing nitric oxide to cause vasodilation.[19,20] Infrared wavelengths include 850 nm and 940 nm and have the actions mentioned earlier.

Modulation (waveform) options: The BioPhoton 100 Professional model can accept external input from other devices. This provides the practitioner with the ability to replicate other frequency protocols that can be customized to meet individual treatment goals. These protocols may include square, triangular, sine, or audio waveforms at varied frequencies. It has been theorized that different waveforms are beneficial in the treatment of various diseases.

Smaller size and lower price: The size of the device has gone from 14.5" × 10" × 6" down to 5.5" × 2.5" × 2.75." The price of the original Photonic Stimulator was $9320 (in today's dollars), while models of the BioPhoton 100 range from $2200 to $7000. These improvements make it possible for practitioners to devise a treatment protocol and then rent the device to patients to use in their homes for a specified period. This allows for daily use, which equates to faster healing, and more satisfied patients. Home treatment allows for more regular treatments at a lower cost while freeing up more time for other patients.

I believe that the BioPhoton 100 is a significant breakthrough not just in light therapy in particular but in medicine in general. We are now involved in research in conjunction with the National Institutes of Health at UCSF. Light therapy often provides superior results than do conventional treatments for a variety of illnesses and is completely noninvasive and, used correctly, free of side effects. The clinical applications of photon therapy are expanding at the speed of light!

I'm even more enthusiastic today than when I was first introduced to light therapy by Maurice Bales. It has been very rewarding to see the surprised look on the faces of so many of my patients after just a short 15-minute treatment. Because the word spreads fast when there's an effective, quick, safe, and affordable solution to managing painful conditions, I've had to devote more than half of my practice to light treatment. The vast majority of my patients come to me through word of mouth from other patients. I encourage my medical brethren to see how they might incorporate light therapy into their practices. They will not only be able to help a lot of patients who don't need to suffer, but can also make it a profitable undertaking.

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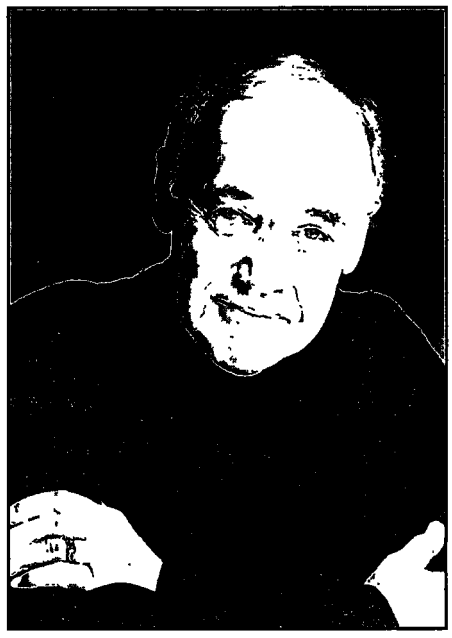

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Tummo Meditation Versus Autogenic Training: Visceral Nervous System Self-Regulation, East and West, and Implications for Integrative Psychotherapy

by Gérard V. Sunnen, MD

Introduction

Tummo (inner fire) meditation is an ancient technique of personal enlightenment centered on the creation of bodily warmth. Autogenic training, some 100 years old, is a system of self-control, centered on the creation of sensations of heaviness and bodily warmth. Both techniques implicate conscious entry into nervous system networks, because heaviness and warmth are sensory modalities. Both techniques also aim to create higher states of well-being derived from greater body/mind alliance yet suggest that dedicated practice opens doors to dimensions of the self hitherto unknown.

Holistic psychotherapy embodies a concept that invites the engagement of the body in any meaningful personal transformation. This approach incorporates, by any number of methods, the expansion of awareness into the workings of bodily organs, resulting in experiences of inner harmony and of centering of self.

Many contemporary therapies, from classical psychoanalysis to cognitive therapy, seek to engage the mind, yet the mind only, to satisfy one's quest for personal evolution. This is insufficient and can only have limited success. Attaining a sense of wholeness necessarily engages the body/mind interface.

In this article, two mind/body techniques are selected for their ability to activate multilevel personal transformation. These techniques can be integrated within most psychotherapeutic methods. Melded into the psychotherapy process, mind/body practices can offer physical and psychological benefits that can turn out to be far more substantial than would be seen from either modality used alone.

Several practices have shown usefulness as activators of personal transformation within the framework of psychotherapy. Added to the mission of self-discovery and self-actualization that psychotherapy embodies, techniques such as hypnosis, and its autoadministered modification, self-hypnosis, yoga, meditative disciplines in their various forms, and autogenic training can be utilized to activate the push to coveted personal change.

Increasingly appreciated is that the therapy of the mind becomes more comprehensive, and its mission most successfully attained, when the deeper workings of the body are more fully explored and, in a sense, mastered. Cliché and true: harmony of body resonates profoundly with harmony of mind.

Visceral Regulation: Relationship to Spiritual Development.

The human psyche generates a vast array of emotions, from the most primal, such as fear, hunger, anger, and libido, to the most subtle, as with empathy, love, and gratitude. Emotions drive self-adaptation and change; without them, life would remain strangely static.

Primal emotions, however, are not only the strongest and most pervasive in the mind's emotional repertoire; importantly, they also usurp much of the psyche's energy reserves, and this mostly subliminally.

Primal emotions are mainly experienced in the brain, and specifically in the ancient limbic system and its extensive ramifications, but for the most part, they biologically take place in the body. Emotions in the anxiety/fear/worry spectrum, and the in the anger spectrum (irritation, annoyance, resentment, rage), recruit vast conglomerations of nerves connected to the spinal cord – including the celiac (solar) plexus – and further relayed to organs of the chest, abdomen, and pelvis, and to the entire musculature.

Much of all this activity occurs below the threshold for consciousness, churning organs all the more because inhibitory signals originating in higher brain centers temper the full expression of primal emotions. Energies spent in this process are simply that: spent, and unavailable to those dynamics that would otherwise awaken personal evolution and higher order states of experiencing.

The dissolution of stress, in all its myriad physical and psychological manifestations, is the primordial indication for the practice of autogenic training and Tummo Meditation.

Executive Awareness

Executive awareness is herewith defined as the experiencing of the ➤

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immediacy of personal existence. Translated into the fabric of emotions, executive awareness is the feeling of "I," the ongoing perception of "I am, here and now."

Awareness – much like human memory – is located ubiquitously in the brain, involving the activities of all neurons. Various cerebral areas contribute selectively to awareness's intensity and configuration. Although there is no single brain locus housing the core entity of awareness, the brain's frontal cortex illuminates the largest component of willful intent, a fundamental component of executive awareness. Will, as a penultimate human faculty, incorporates clarity, direction, and determination, all essential ingredients for meditation.

Executive awareness can exercise several decisive functions, amongst them a capacity to project itself into and through the brain's outflow conduits that, via their most distant tendrils, reach the totality of the organ systems they energize.

The fact remains, however, that although science can explain many dynamics of awareness as it travels within nervous system circuitry, its true and fundamental nature is yet totally unknown.

Autogenic Training in Clinical Practice

Autogenic training, a healing modality developed by a psychiatrist in the last century (and further perfected by many other clinicians over the decades; Luthe 1969), offers a process of self-development leading to improvements similar to those achieved via hypnosis and meditation. The impetus for the creation of this technique came from the ambivalence some people voiced about hypnosis as it was viewed at the time, implicating some abdication of self-control. Today, clinical hypnosis, and its modification, self-hypnosis, are viewed as skills leading to enhanced self-knowledge and fluid self-control.

In the beginning stages of this training, in the context of comfortable body positioning, sensations of relaxed heaviness are elicited in the extremities, mentally amplified, and then progressively channeled into the entire body volume. Soothing sensations of warmth are subsequently evoked in the same bodily spaces. Care is taken to avoid tensing muscles, and generating motion of any kind, except for respiration. The expansion of awareness into hitherto autonomously functioning bodily processes gradually takes place.

Autogenic training's beneficial sensations can be brought on more quickly by creating verbal reflexes. During practice, the inner voicing of selected words or phrases, such as "calm, relaxation, energy" engage the brain's extensive language networks, eventually eliciting heaviness and warmth with their verbal prompts.

Autogenic training may be suggested to someone experiencing symptoms of visceral imbalance due to stress. Talk of "stress" is often brought out early in the initial interview of individuals who thus show a capacity for insight that tends to make them good candidates for mind/body training. Stress is invariably described as involving any number of organ systems: cardiovascular, respiratory, gastrointestinal, skin, urinary, and immune, among others.

Tummo Meditation in Clinical Practice

Tummo meditation derives its name from the nature of its meditative focus. Most meditation practices offer a direction for meditative centering. An exception may be Zen meditation, which seeks to banish all thought forms, so that meditating on nothingness allows new perceptions to emerge.

Tummo is a Tibetan word whose meaning approximates "inner fire." In this practice, the meditator focuses on the creation and amplification of imagery that, in the realm of the senses, belongs to the experiencing of bodily warmth, if not outright heat, and inner light.

The description of the benefits of Tummo meditation features the attainment of special abilities for confronting cold environments with physiological grace. While this capacity may be useful in milieus commonly encountered by developers of these techniques, namely the Tibetan monks of the Himalayas, the true intent of Tummo meditation lies far beyond cold tolerance. Indeed, the attainment of the "inner fire," even in its beginning stages, yields far-reaching rewards of enhanced mind/body capabilities, and in more advanced stages, offers pathways to higher order transcendental experiences.

Tummo meditators invite heightened sensations of bodily heat, often coupled with the imagery of symbols designed to summon spiritual knowledge. Heat, paired with light in the mind's eye, may initially be visualized as emitted by a candle radiating from the abdomen's center. The visualization of this inner flame is coaxed to expand in its intensity and configuration, eventually infusing the totality of the body schema. Rising from the abdomen's center and becoming more brilliant with every breath, it is beckoned to rise into the crown of the head. Heat and light, as metaphors for life energies, thus rise from the body to flower in the mind.

Documented are the abilities of seasoned Tummo meditators for reducing their oxygen consumption, and for raising their bodily temperature (Benson 1982, 1990; Kozhevnikov 2013). Beyond the attainment of physiological harmony – such as cardiovascular and circadian rhythm regulation – Tummo meditators invariably report experiences that may be described as transcendent (Sunnen 2013).

In clinical practice, Tummo Meditation is suggested when the visceral nervous network shows signs and symptoms of dysregulation referable to cardiovascular, respiratory, gastrointestinal, skin, urinary, and immune systems, among others. The art of meditative focusing, at times problematic in practice, can be developed via clinical strategies tailored to the proclivities of meditators.

The Neurology of Autogenic Training

In the beginning phases of autogenic training, awareness is directed to sensitizing the sensory circuits of the extremities. One or both arms, then both legs are invited to amplify sensations of relaxed heaviness, maintaining all the while an awareness connection to the flow of respiration. The sensation of heaviness then diffuses outwardly, ever further into the spaces of the chest, abdomen, and pelvis.

Subsequently, and melded with sensations of heaviness, is the elicitation of sensations of warmth. The heaviness-warmth combo is then progressively disseminated into the entire body space.

The signals initiating autogenic training start within executive awareness.

continued on page 82 ➤

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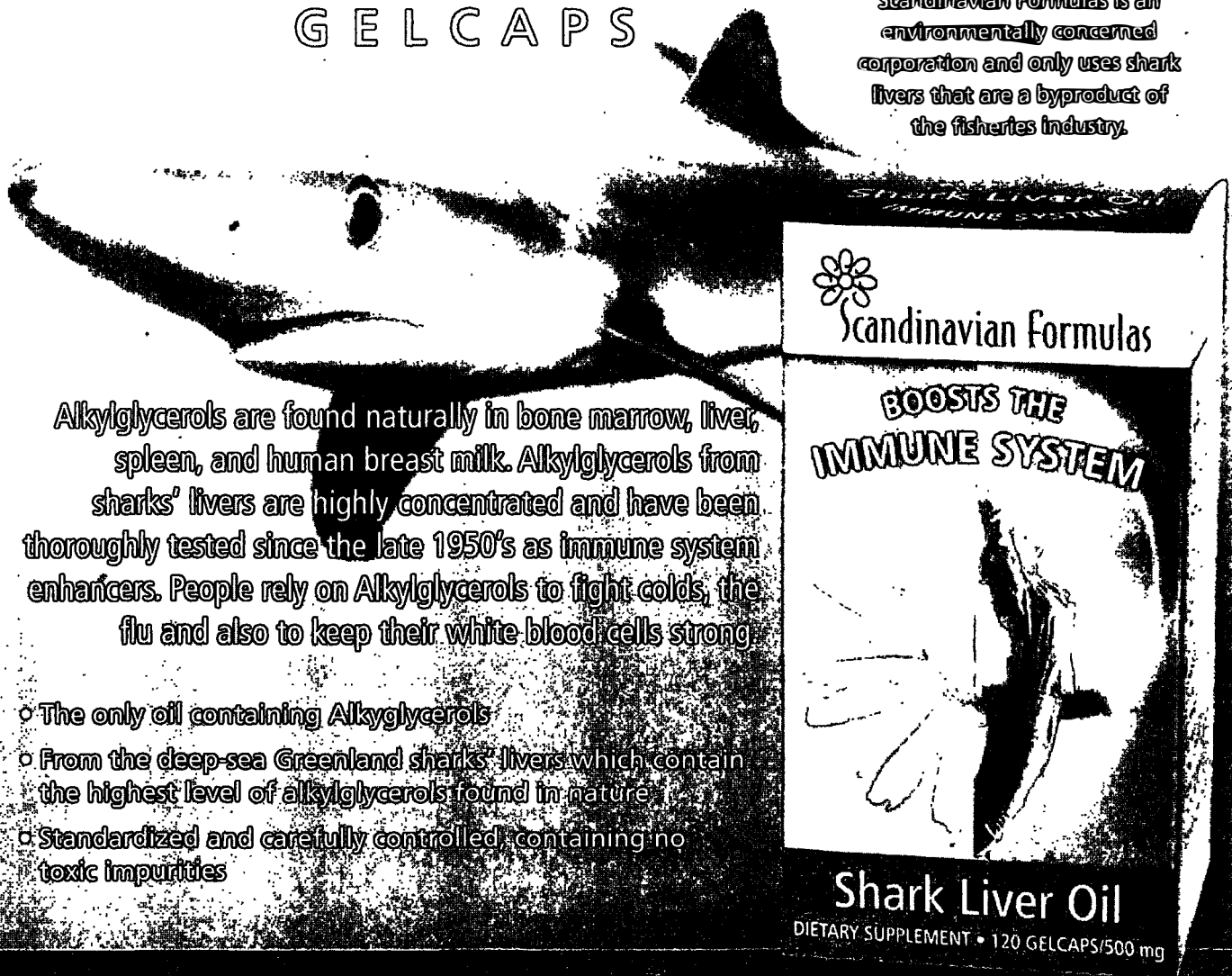

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Tummo Meditation

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They are then channeled into the domain of the somesthetic cortical areas where bodily sensations are experienced in all their nuances. Awareness, continuing in its exploratory journey, reaches more primal sensory centers in the thalamus, then onward into the nerve conduits that, from the spinal cord, receive signals from receptors in the skin, muscles, and joints, including those for touch, pressure, and heat.

The sensations of bodily heaviness and warmth elicited in autogenic training are correlated with muscular relaxation. As training progresses, finer awareness develops for microtensions as they are generated deeply within the body, giving rise to stress. This new internal sensitivity offers the realization that stress can be un-created as easily as it is created.

In autogenic training, the body's voluntary muscles become ever more relaxed, often far beyond ordinary experience. Pushing onward beyond voluntary muscles, the smooth muscles are then imbued with calming awareness, as the ultimate gateway to the dissolution of stress.

Smooth muscles function within the jurisdiction of the visceral nervous system and therefore are ordinarily beyond voluntary influence. Smooth muscles regulate the functions of the heart, vascular tension, digestive peristalsis, respiratory rhythm, urination, sexual function, the eye's workings, and numerous basic reflexes.

As stress reactions are transcended in autogenic training, other sensations may be manifested. Beyond heaviness, there can appear a pervasive lightness of being; and beyond warmth, there sometimes comes a sensation of refreshing global coolness, first appearing around the forehead and temples.

The Neurology of Tummo Meditation

Tummo meditation entrains the participation of several major mental functions, recruiting the action of vast nervous system networks, implicating visual, somesthetic, and visceral systems. Participating, as well, are higher-level cortical functions because they draw on Tummo's spiritual significance.

The experiencing of warmth and eventually heat in the abdominal, thoracic, and pelvic bodily spaces implies an involvement of the rich conglomeration of nerve plexuses inhabiting these areas. Indeed, it is said that the number of neurons in the peripheral nervous system rivals those in the brain.

Heat and light from the image of a lit candle in the abdomen's center activate nerve plexuses in visceral regions. Participating plexuses include those sprouting from the spinal cord (cervical, brachial, lumbar, and sacral), and the diffuse networks innervating the visceral organs (cardiac, celiac, gastric, mesenteric, phrenic, hepatic, and pelvic).

Conclusion

Techniques that develop heightened alliance between mind and body can easily complement contemporary psychotherapies. The benefits include new levels of well-being that incorporate multilevel relaxation, visceral organ harmony, and hitherto unknown (and higher) states of experiencing.

Autogenic training and Tummo mediation originate from different paradigms. While autogenic training derives from Western neurological concepts, Tummo strives to tap into energies conceptualized as resonating with a parallel dimension of a universal kind.

This article proposes two disciplines of body/mind development, autogenic training, and Tummo meditation. Each can be practiced alone or within the context of psychotherapy. The meditator has the choice, not only of developing either method according to one's capacities and preferences, but also to incorporate elements of both in the creation of a unique personal meditative blend.

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Succinate Retention: The Core Krebs Dysfunction in Immune-Inflammatory Disorders

by Majid Ali, MD

In 2004, in my first "Oxygen Homeostasis" column in *Townsend Letter*, I presented evidence to establish respiratory-to-fermentative (RTF) shift as the molecular basis of chronic fatigue in chronic inflammatory disorders.[1] Specifically, I presented data concerning 24-hour urinary excretion of Krebs cycle metabolites in 236 patients. Succinic acid was the metabolite of greatest interest, since its increased excretion occurred with the highest frequency.

In 2014, Chouchani et al. reported that ischemic accumulation of succinate controls redox dynamics of reperfusion injury through mitochondrial reactive oxygen species.[2] They recognized that this finding may have clinical significance for patients with inflammatory disorders. This report fully validated the two main conclusions drawn from my 2004 study: (1) respiratory-to-fermentative shift as the mitochondrial dysfunction in inflammatory-immune disorders; and (2) succinate retention as the Krebs cycle dysfunction of highest clinical interest.

Prompted by the report of Chouchani et al., I reviewed Krebs cycle data for an additional 315 patients seen since my 2004 *Townsend* report. My two sets of data (2004 and 2015 studies) were published online in *Nature* (Table 1).[3] These data are concordant and consistent with the succinate findings in the 2014 *Nature* report. They also support the inference of Chouchani et al. concerning the clinical significance of succinate retention.

In subsequent columns on oxygen homeostasis, based on the respiratory-to-fermentative shift model, I put forth my oxygen models of aging, inflammation, pain, diabetes, coronary heart disease, renal failure, insulin toxicity, hormone disorders, adrenal dysfunction, osteoporosis, allergy, and environmentally induced osteoporosis.[4–14]

Chouchani and colleagues specifically demonstrated that: (1) ischemic succinate accumulation develops due to reversed activity of succinate dehydrogenase triggered by fumarate overflow from purine nucleotide breakdown; and (2) succinate retention occurs partly due to reversal of the malate/aspartate shuttle.[2] These findings, as the investigators anticipated, will lead to the development of a novel class of drugs – "succinate drugs" seems to be good term for them – for preventing and/or or treating reperfusion injury. Undoubtedly, they will also shed light on the mechanisms of action of oxystatic therapies, nutrients, spice, herbs, and enzymes.

The following five distinctions between the 2004 and 2014 reports are noteworthy: (1) the subjects of investigation were human and mice respectively; (2) mitochondrial function was investigated in chronic disorders among humans and acute lesions in mice; (3) the pathologic entities under study were inflammatory disorders and reperfusion ischemic

Table 1: Frequency of Increased* Urinary Excretion of Krebs Cycle Metabolites In Chronic Inflammatory Disorders

Krebs Cycle Metabolites	2004 n = 236	2015 n = 315
Citric acid	194	315
Succinic acid	40	55
Aconitic acid	24	45
Fumaric acid	2	2
2-oxo-glutaric acid	1	2

*Levels of Krebs metabolites measured in mmol/mol creatinine. The mean values of 24-hour urinary succinate excretion of patients and 20 control subjects were 80.3 and 8.7 mmol/mol creatinine, respectively.

injury respectively; (4) the intended approaches to restoration of oxygen homeostasis were integrated non-drug protocols and pharmacologic agents respectively; and (5) the seminal studies of Chouchani et al. dramatically advanced our understanding of impaired succinate pathways in reperfusion ischemic injury, whereas no evidence for similar impairment was developed in the 2004 study.

Scientific Basis of Holism in Healing

In my 2004 report, I noted that a report published in *Nature* established succinate and α-ketoglutarate as important signaling molecules.[15] Cells sense their environment through proteins in their membranes. One of the most important family members of such proteins is that of G-protein-coupled receptors (GPCR). GPR91, a member of GPCR family, serves as the ligand for succinate, while another member (GPR99) is the ligand for α-ketoglutarate. Through their dynamics with GPCRs, succinate and α-ketoglutarate serve important signaling pathways, including those that affect renin functions in the kidney. In an animal model, hypertension was produced by an increase in such signaling. These findings also underscored the importance of succinate retention in mitochondrial dysfunction and shed light on the broader clinical significance of RTF shift.

The Philosophy and Science of Holism in Healing

In 1980, I recognized the crucial need for ecologic thinking in clinical medicine and published a monograph titled *Altered States of Bowel Ecology* to focus on the centrality of the bowel in all deliberations of health/dis-ease/disease continuum.[16] In this volume, I described my seed-feed-and-weed guidelines for restoring bowel ecology disrupted by heavy sugar intake, frequent use of antibiotics, neglect of mold and food allergy, and chronic stress.

In 1983, I published a monograph titled *Spontaneity of Oxidation in Nature and Aging*, in which I proposed my oxidative theory of aging.[17] This spontaneity seemed to initiate and drive the redox dynamics in the body – the human equivalent of the second law of thermodynamics, so to speak – and appeared to be a highly plausible primal mechanism for disease initiation and progression. Within this evolutionary context, in 1987 I summarized my observations and reflections concerning the gating functions of biomembranes in a monograph titled *Oxidative Leaky Cell Membrane Disorder*.[18]

Human evolution may be visualized within the broader context of trillions of energetic events – steps, missteps, and countersteps – inevitably constituting the pathways of molecular complementarity and contrariety. A study of the history of oxygen on planet Earth led to my recognition of oxygen as the king of human biology (recognition of insulin as its minister of energy and metabolism would come 15 years later). In 1998, that work led to the publication of *Nature's Preoccupation with Complementarity and Contrariety*, the first volume of my 14-volume textbook, *The Principles and Practice of Integrative Medicine*.[19]

In closing, I point out that 30 years after I published *Altered States of Bowel Ecology*, the journal *Nature* fully endorsed that position in a 2010 article with the following words: "By 2020, personalized health care could involve doctors monitoring the metabolic activities of a patient's gut microbes and, possibly, modulating them therapeutically."[20]

Next, consider the following words, again from *Nature*: "World Health Organization warns that world may be heading into a 'post-antibiotics era.'"[21]

One day, let us hope, the science and philosophy of holism in healing traditions will rise to yet a higher level – of the whole-body ecology – which looks at the body microbes as an integral part of the whole, which also needs to heal.

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Letters to the Editor

Thank You for Mitochondria Article

[In response to "Mitochondria: Overlooking These Small Organelles Can Have Huge Clinical Consequences in Treating Virtually Every Disease" (June 2015)]

Our daughter after a lifetime of health issues was diagnosed with a mitochondrial depletion syndrome at age 16.

A few things over the years: sensitivity to medications (or severe reactions), bad reactions to vaccines, food allergies and food intolerances, sensitivities to environment.

When we were told that it was "impossible" that any type of environmental toxin affects her health, it brought me to a complete stop.

About 3 years ago we started weeding out corn, soy, gluten (finding that most foods that were the worst for her were also either GM or crops heavily treated with Roundup). No medications, no vitamins – she tolerates none; any cause severe proteinuria. (We have spent thousands, and used compound pharmacies all over the country.)

Through our food and environmental efforts, she is stable. The progression that we saw before the changes has slowed and often stopped and shown small improvements in various body systems. Her kidney labs unless she is in a reaction are great.

She is still sick, and while we hold hope that she will get stronger, we have learned she is damaged and it is "our" fault, as humans. We opt to take responsibility and try to help prevent this from happening to others.

Epigenetic damage. Generations of heavy toxic exposures and dwindling nutrition via medications, foods, environment.

Both of my daughters are exceptionally bright, but not as healthy as my husband and I. My husband and I aren't as healthy as our parents, and our parents aren't as healthy as their parents. Cue the beginning of the Wonder Bread generation.

Mainstream medicine spends outrageous amounts of time and money trying to find a "cure" when prevention for many is possible. Not only do they not make any efforts to teach prevention, they tell patients it is "impossible." They refuse to explain to patients that all those new genetic mutations don't just happen, that we make them. Incredibly frustrating.

Nearly every cancer center in our country now offers dietary advice for patients to avoid toxins (some better than others). The doctors who practice mito medicine also know that mitochondria play a critical role in cancer – yet what is common sense in cancer patients is ignored. Highly frustrating.

Every day on the mito support groups, I see patients on buckets of meds, on elemental formulas (corn sludge), and then more meds to treat that ... not using good-quality supplements ... eating junk foods, but they won't listen – because Doctor knows best.

Thank you so much for this – it really gives me hope every time I see an article that addresses prevention.

Kind regards,
Diane Neuman

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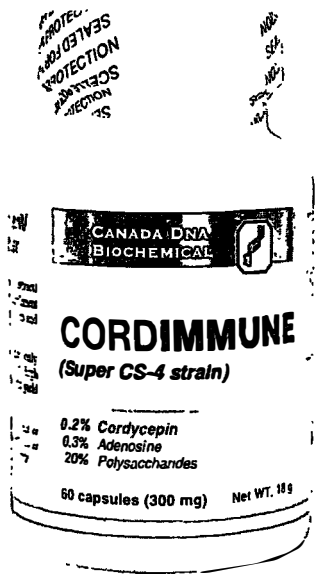

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Taking Charge of Back Pain

review by Jule Klotter

Watch Your Back! by Richard A. Deyo, MD
ILR Press, Cornell University Press, Sage House, 512 East State Street, Ithaca, New York 14850
© 2014; $21.95; hardback; 212 pp.

When I came upon *Watch Your Back!* by Richard A. Deyo, MD, I anticipated a well-researched book revealing the little-discussed shortcomings of back pain treatment. I wasn't disappointed. Deyo coauthored the provocative exposé *Hope or Hype: The Obsession with Medical Advances and the High Cost of False Promises.* In *Watch Your Back!*, Deyo examines the back pain industry and questions the increased use of scans and the effectiveness of many interventions. He also educates readers about the nature of pain and about informed decision-making.

Contrary to expectations, abnormalities found on MRI scans or X-rays are not necessarily the cause of pain. Deyo cites studies that show a sizeable percentage of people who *never* experience pain or sciatica exhibit vertebral abnormalities. In one study, a herniated disc was found in about one-fourth of these pain-free folk, degenerated discs in over half, and bulging discs in about 60%. He says, "... the percentage of 'abnormal' findings in 'normal' people is pretty consistent."

Moreover, scans fail to predict who will experience back pain in the future. When neuroradiologist Jerry Jarvik performed a second MRI three years after first scanning pain-free adults, he found very few new abnormalities. Furthermore, he could not find a correlation between the initial scans and the development of pain. Interestingly, depression at baseline "was a stronger predictor of who would get back pain that the MRI results were," writes Deyo.

MRI scans provide more detail (finding more abnormalities) than X-rays and are more likely to lead to surgery, but more surgery does not mean better results. The patients who were randomly assigned to receive an MRI in another study led by Jarvik were twice as likely to have back surgery within a year, compared with those who were X-rayed only. Yet, both the MRI group and the X-ray group improved to the same degree. The MRI patients, however, were more satisfied with their care – reflecting the cultural belief that technology gives the best results. Deyo recommends avoiding scans unless back pain is accompanied by overt clinical symptoms, such as weakness in a leg or foot, or other factors including unexplained fever, a history of cancer, a history of injection drug abuse, or unexplained weight loss. "Surgery works best when there's a clear-cut anatomical abnormality [such as severe curvature] that explains clear-cut findings on an office examination," says Deyo.

"You can't stand by passively while you wait for a doctor or other health profession to bestow The Cure upon you."

In many cases, the actual cause of pain – despite the finding of common abnormalities – is unclear. Deyo gives examples of people who underwent surgery in the belief that it would end their pain – most notably President John F. Kennedy and Jerome Groopman, author of *The Anatomy of Hope*. Both experienced years of severe pain and limited activity after having surgery. Both found relief with rehabilitative exercise programs. Exercise, combined with cognitive behavior therapy, provides the most successful treatment for back pain.

Pain, explains Deyo, is extremely complex: "When nerve impulses arrive in the brain, they don't stimulate just one spot. Instead, they tickle a complex network that involves many parts of the brain. Memories, anticipations, and moods get linked up with the pain." Stress, fatigue, anxiety, and frustration increase pain. As pain escalates, people limit activity. Cognitive behavior therapy give people tools for managing factors that increase pain so that they can regain function and stay active. Deyo writes, "It appears that this combination of cognitive-behavioral therapy and exercise can literally change your brain. It appears to 're-program' the pain circuitry, perhaps like rebooting your computer when it acts up. Only this is a slower process, and requires more work." Work that only the patient can do.

Watch Your Back! is a highly useful decision-making aid for people with back pain. It explains the complexity of cause and treatment and offers a noninvasive method for retaining and improving quality of life. This is a must-read book for anyone with back pain. ◆

Refocusing Our Efforts Against Cancer

review by Ira L. Goodman, MD, FACS, ABIHM, FAARM
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Tripping over the Truth:
The Return of the Metabolic Theory of Cancer Illuminates a New and Hopeful Path to a Cure, by Travis Christofferson
CreateSpace Independent Publishing Platform
© 2014; paperback; 296 pp.

This is a very important book that could reframe the War on Cancer and establish a new paradigm. Mr. Christofferson is not an MD, but it would be a mistake to ignore this book based on that. There have been several other non-MD authors who have contributed much in the scientific literature, including Ralph Moss on cancer, Robert Whitaker and Kirsch on psychotropic drugs, and Norman Cousins. The book was well written and at times read like a detective novel; I could not put it down. It will be difficult to do it justice in this short summary.

The book's fundamental message is that cancer is not primarily caused by somatic mutations in the nuclear DNA as the current research and theories propose. The DNA damage noticed in many cancers (although not all) is the result, rather than the cause, of the disease, which, according to the author, is primarily from damage to the cells' respiration apparatus. Cancer cells use fermentation instead of the normal oxidative phosphorylation. In other words, the mitochondria and cytoplasmic environment are the common ground where all cancers start and where we should focus.

As Warburg said decades ago, the primary cause of cancer is the cells' replacement of normal respiration (oxidative phosphorylation) with fermentation and cancer cells' voracious appetite for only glucose as opposed to normal cells' ability to utilize ketones as well as glucose. There are many secondary causes of cancer (pollutants, X-rays, etc.) but they all result in the primary defect ➤

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just mentioned. The author carefully takes you through the research of Otto Warburg starting in the 1920s and progresses through the discoveries of Pedersen, Ko, D'Agostino, and Seyfried at Boston University. Detailed bios of these giants, as well as the evolution of their thinking, add to the logic and intrigue of their work.

The fact that the death rates from cancer are about the same now as they were in the 1950s and that chemotherapy directed against targeted mutations has been an abysmal failure in terms of survival benefit (only Gleevec out of the 700-plus targeted drugs has shown real clinical and durable efficacy). Even Herceptin only works in a minority of select cases with modest results in terms of survival. A nice summary of the history of the evolution of chemo is present in the book.

Yes, we are getting better at poisoning , burning, and cutting, but only minimally and not enough to affect overall survival statistics significantly. That is because, according to the author, with the exception of the above-mentioned scientists, we are on a multibillion-dollar wild goose chase after the wrong target (nuclear DNA). The fact that the intratumoral DNA mutations vary considerably (DNA analysis of the same tumor from different locations within the primary tumor) and intertumoral DNA analysis (DNA samples of the same type of tumor from different patients) also varies significantly should make it clear to the most casual observer that we are barking up the wrong tree. This is also proven by the high degree of intrametastatic DNA variability (DNA differences between metastases and the primary tumor in the same patient). In other words, if you take two biopsy samples from the same tumor, the DNA mutations will not usually be the same! The same is true if you take biopsies from different patients' primary tumors even if they are the same kind of cancer, or if you take biopsies of individual metastases and compared them to the primary tumor. The mutations are all over the board, which proves in my mind that these mutations are secondary to the primary cause and it is foolish to try and go after this moving target.

Does the pharmaceutical industry think that we should design multiple targeted drugs for each person's individual cancer when it is well known that the mutations change over time in the same cancer? DNA mutations are clearly a moving target.

What is driving these mutations is the mitochondrial health in the cytoplasm. Seyfried proves this with his elegant nuclear transfer studies that he outlines in his 2012 book *Cancer As a Metabolic Disease*. His experiments have been duplicated. He replaces the nucleus of a normal cell with that of a cancer cell and transplants that clone into a mouse. If the DNA mutation theories were correct, this new cell should become malignant, but it does not! He then replaces the nucleus of a cancer cell with a normal nucleus, and what happens? Cancer grows anyway, since the mitochondria and cytoplasm are still defective in the resulting clone. The nucleus appears to be irrelevant, and only the damaged cytoplasm rules. There is much more detail about these experiments in the book.

The development of drugs such as 3BP (3-bromopyruvate), which inhibits hexokinase 2 and corrects the abnormal functioning of the mitochondria, show great promise; but the funds are not there for phase III trials. There are other drugs being looked at as well. Mention is also made of the ketogenic diet as a method of starving cancer cells, which cannot metabolize ketones as can normal cells. This has been used with great success in some forms of cancer. It makes you wonder if the cachexia seen in advanced cancer is the body's final attempt to induce ketosis as a defense against the tumors.

This book clearly has too much detail to properly describe here, but I think that this author has hit the nail on the head in regard to refocusing our efforts against the disease that is killing more people than ever in spite of the billions dollars spent on the War On Cancer. I am sure that Pharma would be happy to continue to develop more downstream targeted treatments with their big price tag whether it be immunotherapy or mutation intervention. The cancer surgeons would be happy to continue as before, and the entire cancer industry needs to be fed. The name of the game is clearly prevention and treatment against cancer's common-denominator defect: that of the mitochondria and cytoplasm. As Louis Pasteur said on his deathbed: "The microbe is nothing; it's the soil." In the case of cancer, I believe that the cells' mitochondrial and cytoplasmic health are the primary common-denominator defect which leads to downstream DNA mutations at times. Remember, there are times when no mutations can be found in the nuclear DNA in spite of cancer's being present. The cells' "soil" is the cytoplasm, and once that is damaged, the mitochondria send signals to the nucleus which result in nuclear mutations. It is well known that the more aggressive cancers have the most disrupted mitochondrial appearances and function. Directing pharmaceutical treatments against the nucleus in one way or another is missing the point. It may work and has worked transiently, but the overall result has been bad. Treatments against cancer should bolster all your cells and make you feel better, not worse. Hyperbaric oxygen, adequate cellular nutrition, perhaps exposure to ketones, drugs that target the aberrant respiration of cancer cells, and certain electrical treatments that can increase cellular voltage (Ondamed, Tennant, etc.) should be used primarily in an effort to address the root cause before the big guns of chemo, radiation, and surgery are unleashed. Sometimes a bird's-eye view of this disease helps more than continued efforts down the same reductionist tracks. ◆

Mental Health Care Is Evolving

by James Lake, MD

A growing number of psychiatrists, psychologists, social workers, nurses, and other mental health professionals around the world believe that existing conventional treatment approaches such as prescription medications and psychotherapy do not adequately address the mental health needs of people everywhere. There are many reasons for this. Even though prescription medications are often effective and safe, they are not available in many parts of the world, and where they are available they are often too expensive for many people to afford. The potential value of prescription medications for people who suffer with mental illness is also limited by the fact that many medications are no more effective than sugar pills and sometimes cause serious adverse effects. The limitations of prescription medications have resulted in renewed interest in complementary and alternative therapies and in efforts by mental health professionals, researchers, and our patients to find more effective, safer, and more affordable ways to treat many common mental health problems and prevent them from returning.

The rapid growth of CAM is being driven by consumer demands for a wide range of treatment choices, growing dissatisfaction with conventional medical care, and increasing openness to new ideas in the leading institutions of Western medicine. Trends that are interfering with the ability of Western medicine to provide adequate health care include restrictions on the kind and quality of treatments available under managed care, private insurance contracts, and Medicare; concerns over the efficacy and safety of conventional pharmacological treatments; and the increasing cost of medical care in general.

It is a significant fact that individuals who use CAM to treat any medical or mental health problem are generally more educated compared with those who use only conventional treatments. Approximately two-thirds of all adults in the US currently use a variety of CAM approaches to treat a medical or mental health problem. At the same time that patients are demanding more choices in health care, mainstream medicine is becoming more open to change. Courses on complementary and alternative medicine are now offered at most US and European medical schools, and increasing numbers of physicians are becoming certified to practice Chinese medicine, herbal medicine, homeopathy, and other established world healing traditions. Approximately one-half of US physicians refer patients to acupuncturists, naturopaths, homeopaths, chiropractors, and other nonconventionally trained practitioners because they believe that these approaches are safe and effective. Together these trends are stimulating evolution of medical care in the US toward an eclectic network of perspectives, skills, and services addressing the patient's body, mind, and spirit.

The Increasing Use of CAM in Mental Health Care

Approximately one-third of the adult population in the US and Europe uses at least one CAM therapy annually. In this context, more and more people are using CAM and integrative therapies to treat or self-treat mental health problems, and as many as 10% of US adults take prescription medications for depression, anxiety, schizophrenia, and other mental health problems. Ten percent of US adults who visit an alternative medical practitioner have a psychiatric diagnosis, and half of these seek care specifically for their mental health problems. While over 50% of individuals diagnosed with an anxiety disorder and 60% of individuals diagnosed with a mood disorder use a CAM therapy, few disclose this information to their family physician or psychiatrist. The majority of individuals who use CAM therapies also see a conventionally trained physician for the same problem. Among individuals hospitalized for a severe mental health problem, almost two thirds had used a CAM therapy within the past year and fully 80% had not disclosed this information to their psychiatrist. The increasing rate of self-treatment in the context of nondisclosure of CAM use raises significant safety issues

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because many individuals who use vitamins, herbs, or other natural substances also take prescription medications, resulting in potentially serious toxic interactions.

Integrative Mental Health Care Uses Approaches from Western Biomedicine and CAM

Medications will probably continue to play a central role in mental health care – especially in Western countries and especially for managing symptoms of severe mental health problems such as bipolar disorder, dementia, and psychosis; however, nonmedication treatments will play an increasingly important role in mental health care as research evidence accumulates showing that many CAM therapies are both safe and effective. Integrative mental health care is a rapidly emerging field that focuses on maintaining optimal wellness and managing symptoms of each unique person, keeping in mind their values, preferences, and circumstances. Advantages of integrative mental health care over the conventional biomedical model include:

- improved response to treatment
- reducing the dosage of a prescription medication
- reducing adverse effects of prescription medications
- saving money on treatment costs
- having greater control over your symptoms
- greater emphasis on maintaining wellness
- developing a more personalized plan for treatment and prevention

Integrative practitioners often prescribe medications and recommend psychotherapy to clients but go beyond this *limited* model of care. In addition to recommending conventional biomedical therapies, integrative practitioners also recommend a wide range of nonmedication treatment approaches such as herbals, vitamins, and other natural supplements, whole-body approaches such as exercise and massage, changes in the diet, mind-body practices, and energy therapies such as acupuncture and healing touch. Because integrative mental health care focuses on each person's unique needs and circumstances, treatment is often highly individualized.

Introducing a Series of Books on Integrative Mental Health Care

In an effort to address the limitations of the current biomedical model of mental health care, I have written a series of e-books on integrative mental health care with the goal of creating a practical and affordable resource on safe and effective nonmedication and integrative treatments for common mental health problems. The series covers the following mental health problems:

- alcohol and drug abuse
- anxiety
- attention-deficit hyperactivity disorder (ADHD)
- bipolar disorder
- dementia and mild cognitive impairment
- depression
- insomnia
- posttraumatic stress disorder (PTSD)
- psychosis

Visit my website (http://www.theintegrativementalhealthsolution.com) to learn more about my books and order them. ◆

Douglas Laboratories Launches New Line of Vision Health Supplements

Healthy aging is a hot topic today, particularly as the Baby Boomer generation enters its 50s. While attention is frequently given to strong bones and maintaining cognitive health as people age, little consideration is given to vision health. Now, three new nutritional products from Douglas Laboratories are available to support healthy eye function during the aging process, all utilizing the latest research.* This suite of ocular formulas includes Ultra Preventive Vision, Macu-Support, and Eye Moisture Support.

"Science continues to emerge regarding the role nutrition plays in eye health," said Stuart Richer, OD, PhD, FAAO, codeveloper of the new suite of vision health products for Douglas Laboratories. "We've utilized the latest research to create three new nutritional supplements to support healthy eye function."*

Ultra Preventive Vision is a comprehensive multivitamin/mineral formula with phytonutrients and carotenoids specially designed to help support a healthy macula, retina, and visual performance for all ages that are affected by excess blue-light exposure and free radical damage.*

Macu-Support supplies a well-balanced spectrum of key antioxidants that are important in maintaining normal retina and macula function in the eyes. As we age, the ability of the macula to function properly can decline. The nutrients found in Macu-Support have been studied for their ability to help maintain and support macular function and health.*

Eye Moisture Support is a unique dietary supplement featuring QÜELL Fish Oil, organic borage seed oil, and astaxanthin, among other nutrients, for healthy production of tears and moisture in the eyes.*

"At Douglas Labs, we strive to offer a comprehensive line of nutritional supplements for healthy aging," said Andrew Halpner, PhD, vice president, Product Development and Technical Services at Douglas Laboratories. "The ocular formulas that were codeveloped with Dr. Richer are a great addition to our existing line of products to support vision health as we age."*

For more information on Ultra Preventive Vision, Macu-Support, and Eye Moisture Support, please visit www.douglaslabs.com.

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

Anti-Aging Medicine

by Ronald Klatz, MD, DO, and
Robert Goldman, MD, PhD, DO, FAASP
www.worldhealth.net

An Anti-Aging Perspective for Stroke Prevention

The fifth leading cause of death in the US and a major cause of adult disability, stroke afflicts approximately 800,000 Americans annually. One American dies from a stroke every 4 minutes, on average.

A stroke or transient ischemic attack (TIA) by age 50 at least triples mortality risk over the subsequent decades. Frank-Erik de Leeuw and colleagues from the Radboud University Nijmegen Medical Centre (Netherlands) assessed long-term outcomes in the prospective Follow-Up of Transient Ischemic Attack and Stroke Patients and Unelucidated Risk Factor Evaluation (FUTURE) study, which included 959 consecutive patients, aged 18 through 50 years, admitted to a single academic medical center for a first-ever transient ischemic attack (262), ischemic stroke (606), or intracerebral hemorrhage (91) from 1980 through late 2010. In the first 30 days after the event, the fatality rate was 0.4% for TIA, 3.6% for ischemic stroke, and 22% for hemorrhagic stroke, or 4.5% overall. At 1 year, the cumulative mortality rate for 30-day survivors was 1.2% for TIA, 2.4% for ischemic stroke, and 2.9% for intracerebral hemorrhage. While the annual mortality risk after TIA didn't rise significantly, if any, over time, the cumulative mortality of these "mini-strokes" was substantial at 9.2% after 10 years and 24.9% after 20 years. Further, while the smaller number of hemorrhagic stroke patients who survived to 30 days resulted in a more variable annual mortality risk ranging from less than 1% to nearly 3%, their long-term cumulative risk was lower than in the first 30 days, at 10.3% after 10 years and 13.7% after 20 years. The mortality risk over the entire follow-up period compared with an age-, sex-, and year-matched cohort from the no-stroke general population in the Netherlands was consistently elevated after ischemic stroke (26.8% versus 7.6%), though only significantly higher after 10 years post TIA (24.9% versus 8.5%). The study authors warn: "Among adults aged 18 through 50 years, 20-year mortality following acute stroke was relatively high compared with expected mortality."

As well, a stroke can steal 8 years of brain power overnight. Deborah A. Levine and colleagues from the University of Michigan (US) analyzed data collected on 4908 black and white men and women, aged 65 years and older, who were enrolled in the Health and Retirement Study. The team assessed for changes in global cognition – before and after incident stroke. Data analysis revealed that having a stroke ages a person's brain function by almost 8 years, as reflected by slower memory and thinking speeds. The lead investigator urges: "These results show the amount of cognitive aging that stroke brings on, and therefore the importance of stroke prevention to reduce the risk of cognitive decline."

With stroke's potential to gravely compromise quality of life, as well as shorten lifespan, prevention via risk reduction is key. This column reviews recent studies that suggest simple and natural approaches that may help you reduce your stroke risk.

Levine DA, Kabeto M, Langa KM, et al. Does stroke contribute to racial differences in cognitive decline? *Stroke*. May 21, 2015.
Rutten-Jacobs LC, Arntz RM, Maaijwee NA, et al. Long-term mortality after stroke among adults aged 18 to 50 years. *JAMA*. 2013 Mar 20;309(11):1136–1144.
Stroke [Web page]. US Centers for Disease Control & Prevention. http://www.cdc.gov/stroke. Accessed 28 July 2015.

Purpose in Life Reduces Stroke Risk

A number of studies have suggested that having a purpose in life – the sense that life has meaning and direction – may reduce a number of adverse health effects. Lei Yu and colleagues from Rush University Medical Center (Illinois, US) studied autopsy results on 453 older adults, who participated in the Rush Memory and Aging Project. All of the participants underwent annual physical and psychological evaluations, including a standard assessment of purpose in life – where purpose in life was judged on a 5-point scale (higher scores indicated a greater purpose), with the average score at 3.5. Participants were followed until they died, at an average age of 90 years. At the study's start, 114 subjects were affected by stroke. At autopsy, 154 individuals had macroscopic infarctions (areas of stroke damage visible to the naked eye) and 128 had "microinfarcts" (areas of damage visible with a microscope). The team observed that for every 1-point increase in the score of purpose in life, the likelihood of having one or more macroscopic infarctions decreased by about 50%. The study authors write: "Purpose in life may affect risk for cerebral infarcts, specifically macroscopic lacunar infarcts.

Yu L, Boyle PA, Wilson RS, Levine SR, Schneider JA, Bennett DA. Purpose in life and cerebral infarcts in community-dwelling older people. *Stroke*. 2015;46:1071–1076.

Protein May Prevent Stroke

People with diets higher in protein, especially from fish, may be less likely to have a stroke. Xinfeng Liu and colleagues

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Anti-Aging Medicine

from Nanjing University School of Medicine (China) completed a meta-analysis of 7 studies with a total of 254,489 participants who were followed for an average of 14 years. The data revealed that the participants with the highest amount of protein in their diets were 20% less likely to develop a stroke, as compared with those with the lowest amount of protein in their diets. For every additional 20 grams per day of protein consumed, the risk of stroke decreased by 26%. The team advises, however, that the protein of choice be fish and red meat consumption should be limited, in accordance with other published studies associating it with increased stroke risk. The study authors conclude: "These findings suggest that moderate dietary protein intake may lower the risk of stroke."

Zhang Z, Xu G, Yang F, Zhu W, Liu X. Quantitative analysis of dietary protein intake and stroke risk. *Neurology*. June 11, 2014.

Cut Stroke Risk with Fruits and Veggies

Fruits and vegetables are rich in key micro- and macronutrients that contribute to healthy blood vessels. Yan Qu and colleagues from Qingdao University (China) completed a meta-analysis of 20 studies published over the last 19 years to assess the effects of fruit and vegetable consumption on risk of stroke globally. The combined studies involved 760,629 men and women who had 16,981 strokes. The data revealed that stroke risk decreases by 32% with every 200 grams (7 oz) of fruit consumed each day and 11% with every 200 grams (7 oz) of vegetables consumed daily. The study authors conclude: "Fruits and vegetables consumption are inversely associated with the risk of stroke."

Hu D, Huang J, Wang Y, Zhang D, Qu Y. Fruits and vegetables consumption and risk of stroke: a meta-analysis of prospective cohort studies. *Stroke*. 2014 May 8.

Skip the Salt to Slash Stroke Risk

Dutch researchers report that up to 6% of the nation's strokes could be avoided if residents adhere to World Health Organization (WHO) guidelines of a maximum daily salt intake not to exceed 5 grams (equivalent to about 2000 mg of sodium). Marieke A. H. Hendriksen and colleagues from the Dutch National Institute for Public Health & Environment (Netherlands) observe that the average salt intake among Dutch adults is about 83.4 grams per day – markedly higher than the WHO guidelines. The team calculated that up to 6% of strokes and up to 5% of the nation's heart attacks could be avoided if residents complied with the guidelines. The study authors urge: "Substantial health benefits might be achieved when added salt is removed from processed foods and when consumers choose more for low-salt food alternatives."

Hendriksen MAH, Hoogenveen RT, Hoekstra J, Geleijnse JM, Boshuizen HC, van Raaij JMA. Potential effect of salt reduction in processed foods on health. *Am J Clin Nutr*. December 11, 2013.

Exercise May Help with Prevention

Finally, keeping active may lower stroke risks. Australian researchers confirm the importance of regular physical activity for stroke prevention. Analyzing data collected in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study involving 30,239 Americans, aged 45 years and over, with follow-up every 6 months for stroke events, Michelle N. McDonnell and colleagues from the University of South Australia found that 33% of the subjects reported a lack of physical activity, which associated with a hazard ratio of 1.2. While there was no significant association between physical activity frequency and risk of stroke by sex groups, there was a trend toward increased risk for men reporting physical activity of 0 to 3 times a week, as compared with those who were active 4 or more-times a week. The study authors warn: "Self-reported low [physical activity] frequency is associated with increased risk of incident stroke."

McDonnell MN, Hillier SL, Hooker SP, Le A, Judd SE, Howard VJ. Physical activity frequency and risk of incident stroke in a national us study of blacks and whites. *Stroke*. 2013 Jul 18.

To stay updated on the latest breakthroughs in natural approaches that may help you to reduce your risks of stroke, visit the World Health Network (www.worldhealth.net), the official educational website of the A4M and your one-stop resource for authoritative anti-aging information. Be sure to sign up for the free Longevity Magazine e-journal, your weekly health newsletter featuring wellness, prevention, and biotech advancements in longevity.

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Monthly Miracles

by Michael Gerber, MD, HMD
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HCG and Pain Management

HCG has many uses besides weight loss and post–steroid use hormonal normalization.[1-4] It has several potential mechanisms of action for pain management. It stimulates the production of testosterone, progesterone, estradiol, and thyroid, all of which should bring obvious benefits to some pain patients.[2-4] HCG may also achieve pain reduction through neurogenesis and tissue healing.

Intractable Leg Pain

A 62-year-old farmer presented with a 1-year history of intractable leg pain after being suspended in an unusual surgical position during total prostatectomy. The pain was constant, sharp, stabbing, and aching in nature and ran down the anterior aspect of both legs. He was also very toxic to aluminum, arsenic, and cadmium and complained of erectile dysfunction, hypertension, polycythemia, hypogonadism, hypothyroidism, and a cough when he put food in his mouth. During his postsurgical course, he had been tried on many opiate analgesics, gabapentin, and muscle relaxants to no avail. The side effects of the drugs inhibited his ability to work.

I thought that it was a clear case for neural therapy injections with procaine and ozone to address the pain and did a Frankenhauser injection above the prostate and Prolozone with Zeel, triamcinolone, procaine, and ozone to the lumbar spine. This was repeated twice with no improvement in his pain. Referrals were made for chiropractic with ABS back stretching (the computerized rack), massage therapy, physical therapy, and stress reduction techniques. IV chelation therapy and oral chelation therapy were commenced, and we found an infected root-canalled tooth, which was removed with much pus exuding from the wound. He was started on thyroid replacement, cortisol replacement, neurotransmitter precursor therapy with 5-HTP, tyrosine, and cysteine, Pandan for erectile dysfunction, homeopathic remedies, parasite treatments, viral detox, parent essential fatty acid replacement, and other anti-inflammatory nutrients.

After 2 years with no improvement in his pain, I referred him to a pain management clinic which started him on a morphine pump and a spinal electrical stimulation device. This approach made him nauseated and dizzy and wasn't helpful for his pain, and he couldn't work.

Upon reading an article in the *Townsend Letter* on pain relief with HCG, I decided to try it. It took us some time to adjust the dose. At first we tried 1/10 cc sub Q daily of 1000 IU/ml with a little improvement in his pain and then increased to 1 cc three times per week, and he has been stabilized for 2 years on ½ cc six days per week. This has resulted in nearly total relief of his pain. He notes a slight twinge upon going to bed but otherwise is completely pain free all day. A side effect of this therapy has been a 75-pound weight loss. The pain relief commenced before the weight loss, and he has no more erectile dysfunction with a PSA of <0.1. HCG has been life transforming for this gentleman.

Rheumatoid Arthritis

A 51-year-old woman body builder with a many-year history of RA had utilized HCG for weight loss and athletic performance in the past and noted that her joint pain improved. Now using 1/10 cc of HCG, 1000 IU/ml sub Q daily, she has had no arthritis pain for several years.

These successes give me hope for HCG's use in fibromyalgia and other chronic pain syndromes.

Notes

1. Tennant FS. Hormone treatments in chronic and intractable pain. *Pract Pain Manag.* April 2005;5(3):57–67.
2. Matura S, Okashi M, Chen HC, et al. physiochemical and immunological characterization of an HCG-like substance from human pituitary glands. *Nature.* 1980;286:740–741.
3. Odell WD, Griffin J. Pulsatile secretion of human chorionic gonadotropin in normal adults. *N Engl J Med.* 1987;317:1688–1692.
4. Braunstein GD. Human chorionic gonadotropin. In: *Williams Textbook of Endocrinology.* 10th ed. Philadelphia: Saunders; 2003:800–803.

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War on Cancer

by Ralph Moss, PhD
www.cancerdecisions.com

ECTO-NOX Proteins: Growth, Cancer and Aging

Once in a rare while, a scientific book comes along that, while highly technical in nature, also contains information of urgent importance to patients and their caregivers. Such a book is *ECTO-NOX Proteins: Growth, Cancer and Aging* (Springer 2013). This astonishing book offers a detailed and well-organized record of five decades of research by the husband-and-wife team of D. James Morré, PhD, and Dorothy Morré, PhD, which they mainly conducted as professors at Purdue University in West Lafayette, Indiana. James Morré, the Dow Professor of Medicinal Chemistry, was the founding director of Purdue's cancer research center.

In this groundbreaking book, the Morrés explain the global significance of a class of proteins called ECTO-NOX, commonly abbreviated ENOX. The "ECTO" prefix means that these various proteins, regardless of where their originating genes reside, are ultimately expressed on the surface or exterior of cells (from the ancient Greek *ectos*, "outside"). There are presently three known classes of ENOX proteins. ENOX1 is a normal constituent of most cells. ENOX2 is found in cancer of many kinds. ENOX3, also called arNOX, is an age-related class of proteins. These various ENOX proteins are crucially involved in cell growth, biological timekeeping, cancer, aging, and even viral infections. They also share some similarities to prions, proteins that are responsible for a number of human illnesses (such as "mad cow disease").

These proteins are unique in a number of ways. For instance, their expression depends on a particular biological clock, or circadian rhythm, that (depending on the form of ENOX) varies from 22 to 26 minutes. They alternately carry out two separate physiological functions in rapid succession. The book's explanation of these peculiarities is very clear and will strike most readers with a background in science as revolutionary in its implications for basic biology.

Particularly thought provoking are the Morrés' discussions of ENOX2 and ENOX3. ENOX2 is specific for cancer and plays an indispensable role by allowing an immature cancer cell to enlarge to a normal size. The Morrés spent decades perfecting a practical test for ENOX2, now called ONCOblot. This test can reputedly differentiate among 26 different types of cancer. According to the website oncoblotlabs.com, the test can detect tumors as small as 1 mm in diameter, which represents about 2 million cells. This makes it about 10 times more sensitive than a typical positron emission tomography (PET) scan. If cancers can be detected at this early stage, and differentiated as to tissue of origin, then this alone represents a huge advance in the cancer field. It would allow for the possibility of early detection and then medical intervention to eliminate small tumors before they become increasingly difficult to treat.

James Morré told me that he and his wife refused to release the ONCOblot test to the public until they had discovered a way to convert an elevated test score back to normal, presumably by curing very early-stage cancers (personal communication, July 2015).

The practical upshot of this is a pill called Capsol-T. This is a 25:1 mixture of decaffeinated green tea powder and a low-heat guajillo chile pepper. The chile potentiates the activity of the green tea 10- to 100-fold. In a clinical trial involving 110 participants, 40% of them tested positive for ENOX2 on ONCOblot. They then took Capsol-T for around 4 months. They took it around the clock, every 4 hours (using a sustained-release form before bedtime). The result was that 94% no longer showed as positive for ENOX2 on a repeat test. They were presumably cured of early-stage, nonclinical cancer.

Green tea is no stranger to the world of medical research. There are presently about 2000 articles on the topic in PubMed, 1337 of which involve the main catechin, EGCG. But while Capsol-T might sound like just another empirical cancer remedy, its use is based upon a prolonged and intensive scientific study, focused on its ability to inhibit ENOX2. There was nothing haphazard about the way that these food constituents were put together. It turns out to be

the most effective natural inhibitor of ENOX2 in cancer cells. Its own activity is enhanced between 10 and 100 times by the concurrent administration of a small amount of red pepper. In fact, in the laboratory this combination is almost as effective as the powerful (and toxic) chemotherapy drug Adriamycin at inhibiting ENOX2.

I hope that the reader now senses the enormous potential of this line of research, the fruit of more than 50 years of determined work at Purdue and elsewhere. (James Morré himself has published 399 PubMed-indexed scientific papers.) If we now truly have a way to detect very early cancers, differentiate their tissue of origin, and then treat and eliminate them in their preclinical stages, I believe that the Morrés have gone a long way to solving the cancer puzzle! This proposition of course requires further testing. But, at this point, the burden of proof shifts from these individuals to the large and well-funded government and private agencies, which have the capacity to carry out large-scale tests. The fact that they have not done so is both puzzling and frustrating. One hopes this is not another instance of the determined suppression of a generic and nontoxic approach for the benefit of entrenched medical interests.

ENOX3 and Aging

The Morrés' discussion of aging will be revelatory for those who are concerned about the ravages of time on the human organism. The Morrés also identified a substance called ENOX3, also called the age-related ENOX (abbreviated arNOX), which is similar in its fundamental structure to ENOX2, although it originates from genes on different chromosomes. ENOX3 begins to appears at around age 30, and then increases into one's 60s or 70s. The amount of ENOX3 in blood or saliva correlates quite strongly with one's apparent age. In other words, the more ENOX3 one has, the older one looks.

In the laboratory, the Morrés have discovered that certain readily available, nontoxic substances strongly inhibit the destructive effects of ENOX3, thus suppressing one of the mainsprings of the aging process. Key among these is coenzyme Q10. CoQ10 is made in the human body but is also widely available as a food supplement.

Another surprising fact in this book is that certain herbs are protective against ENOX3. These are especially the famous French mixture *herbes de Provence*. But the Morrés discovered that the most effective and beneficial of these herbs is summer savory (*Satureja hortensis*). These herbs are very active in human biology, even at the minute levels used in French cooking. I presently use both the dried and fresh forms of these herbs and intend to keep cultivating them, especially savory, indoors throughout the winter months.

In sum, since 1960, the scientists James and Dorothy Morré have produced an amazing body of scientific work, which they have summarized with admirable clarity in this 500-page text. The book contains more than 1000 scientific references, many of them by the Morrés and their students and coworkers at Purdue University, as well as a very useful and detailed index. Hats off also to the publisher, Springer, since I could not find a single typographical error in the entire book (a rare publishing achievement these days).

Some of the explanations in *ECTO-NOX Proteins* are by necessity very detailed and specialized, and so nonspecialist readers may find themselves skipping over some technical discussions. But the general thrust of the argument is not hard to follow. Once you understand what is at stake in this line of research, you will read this book as the great scientific detective story that it is. If you have an intense interest in questions of growth, cancer, or aging, or want to learn more about the anticancer and antiaging potential of ENOX protein inhibitors, you definitely will not want to miss this groundbreaking book.

Note: My only caveat about this book is the price, which is $267 on Amazon ($219 on Kindle). However, readers of this column can obtain a hardcover copy of *ECTO-NOX Proteins* from the Harvey H. and Donna M. Morré Foundation for Cancer Research, 1112 Cherry Lane, West Lafayette, IN 47906 by enclosing a check for a donation of $100 to the foundation and providing a mailing address.

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Study Supports Metabolic Approach to Cancer

Sugar (i.e., blood glucose) is a well known "rocket fuel" for many cancers. Cancer cells have a "propensity to metabolize glucose to lactic acid at a high rate even in the presence of oxygen" (Mathupala 2009). This is generally known as the "Warburg effect," after the great German biochemist and Nobel laureate Otto Warburg, who first demonstrated this fact in the 1920s. His intellectual heir, the Johns Hopkins biochemist Peter L. Pedersen, PhD, has shown that cancer cells have only half the number of normal energy-generating mitochondria. To fulfill their huge energy requirements, cancer cells turn to "aerobic glycolysis," the direct breakdown of glucose through the process of fermentation.

This fundamental fact about cancer has generated a number of approaches to the disease, collectively called the metabolic approach. Now, a research team at the University of California, Los Angeles (UCLA), has proposed an ingenious new way of inhibiting cancer growth by blocking the tumor's access to glucose. Prof. Claudio Scafoglio and others at the David Geffen School of Medicine, UCLA, published their results in the July 2015 issue of the prestigious *Proceedings of the National Academy of Sciences* (PNAS).

"Cancers require high amounts of glucose to grow and survive," the authors wrote. Passive glucose transporters (GLUTs) facilitate some of the uptake of glucose by sugar-hungry tumors. But the UCLA team has identified an additional mechanism that pancreatic and prostate cancers, at least, use to import glucose. This is called "active glucose transport mediated by sodium-dependent glucose transporters" (SGLTs). They then propose a way to block this uptake.

The Food and Drug Administration (FDA) has already approved several SGLT inhibitors to treat type 2 diabetes (T2D). These are the so-called SGLT2 inhibitors. These drugs lower blood sugar by causing the kidneys to remove sugar from the body through urination. Some of these approved inhibitors are canagliflozin (sold as Invokana or when combined with another drug Invokarnet), dapagliflozin (Farxiga and Xigduo), and empagliflozin (Jardiance and Glyxambi).

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According to the lead author of the study, UCLA Professor Ernest Wright, the new finding on SGLT2 and cancer "is exciting because it provides strong evidence that SGLT2 inhibitors, such as those currently approved by the FDA to treat diabetes, could potentially block glucose uptake and reduce tumor growth and increase survival in pancreatic and prostate cancers" (Scafoglio 2015).

Wright and colleagues mapped the distribution of SGLT2 in human tumors, then measured glucose uptake in fresh tumors using a form of glucose that is specifically transported by SGLTs. They then confirmed that SGLT2 was indeed present in pancreatic and prostate cancer and that this substance "assisted in delivering the glucose that is vital to cancer growth and survival," according to Wright. The use of these drugs may help to increase patients' survival instead.

The UCLA doctors intend to begin a clinical trial to investigate the importance of sodium-dependent glucose transporters in delivering glucose to sugar-hungry tumors. They hope this will lead to the use of the current FDA-approved SGLT2 inhibitors to reduce the viability of pancreatic and prostate cancer cells and increase patient survival.

Seyfried's Comments

I asked Professor Thomas Seyfried, PhD, of Boston College, for his comments on the UCLA study. Seyfried is a strong proponent of the use of very low carbohydrate, or ketogenic, diets in the treatment of cancer, which he outlined in his book *Cancer As A Metabolic Disease* (2012). Here is what he wrote:

"This approach of targeting glucose transporters could be interesting. ... Cancer patients would first need to be transitioned to a ketogenic diet before targeting any glucose transporter. This is the strategy used to treat children with inherited mutations in glucose transporters. Ketone bodies can serve as an alternative fuel for brain and other organs when glucose levels become very low." However, he cautions, "glucose transporter targeting could be highly toxic to normal cells if keto-adaptation is not applied first." He added, in a huge understatement, "I am not sure if all oncologists are aware of keto-adaptation" (personal communication, 2015).

(Ketosis is a state in which the body generates energy from the burning of fat, rather than from the utilization of carbohydrates. The human body can become accustomed to this method of energy generation, even over prolonged periods of time, a condition called *keto-adaptation*. Seyfried advocates both a low-carbohydrate and restricted-calorie approach to cancer.)

Similarly, in my visit two years ago with James Watson, PhD, Nobel laureate and codiscoverer of the DNA "double helix," he told me that he believed that metabolic, which are essentially biochemical, approaches to cancer were more promising than the genomic approach that he himself pioneered for half a century.

"My own solution is to identify people who have ideas about drugs that will attack the uniqueness of the biochemistry of cancer cells," he has said.

Strategies that reduce the availability of glucose to cancer cells are likely to benefit most cancer patients (although of course a state of unintended weight loss can complicate matters). This could include very low-carbohydrate, low-calorie, and/or ketogenic diets, drugs that block glucose uptake, such as Metformin, or these SGLT2 inhibitors now under study at UCLA.

New Evidence for Effects of Amygdalin/Laetrile

According to ancient texts, apricot and peach kernels have long been used as a treatment for lung diseases in China (Smith 1871). The question of amygdalin's effectiveness was the subject of the film *Second Opinion*, which detailed the cover-up of positive data on laetrile at Sloan-Kettering Institute, New York, which led to my firing in 1977 (Merola 2014). Scientific evidence continues to accumulate for the efficacy of the apricot kernel-derived chemical amygdalin (Laetrile) in cancer. In just the past two years there have been experiments showing that amygdalin inhibits the proliferation of liver (Yang 2014), cervical (Chen 2013), and bladder cancer (Makerevic 2014a and 2014b).

The latest such study comes from the First Affiliated Hospital of Bengbu Medical College, Bengbu, China. It concerns non-small cell lung cancer (NSCLC), a disease of increasing importance in China. In this study, the authors obtained the highly metastatic NSCLC cell lines H1299/M and PA/M. They then treated these cells with amygdalin. Liyu Qian and coworkers found that the proliferation of both the H1299/M and PA/M cell lines was inhibited with high concentrations of amygdalin. At lower concentrations, they observed that the invasive and migration capacities of these cell lines were also significantly inhibited.

"These results strongly suggested that amygdalin was likely to have anti-metastatic NSCLC effect. This study offers information of the role of amygdalin that may be useful as a therapeutic target in lung tumors," the authors wrote in the *International Journal of Clinical and Experimental Pathology*.

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Ralph W. Moss, PhD, is the author of 12 books on cancer-related topics. The former science writer at Memorial Sloan-Kettering Cancer Center, for 35 years Moss has investigated the validity of many cancer treatments. He currently directs the *Moss Reports*, a library of reports for patients on over 200 different cancer diagnoses.

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Editorial

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in swine. Although this research was preliminary, it should have alerted us to the possibility that recommending trans fatty acids as a heart-healthy alternative to other types of fat is unwise."[9,10]

I present this historical perspective hopefully not as an ego-driven "I told you so," but to point out that people who are recognized by the mainstream as authorities do not necessarily have the knowledge, big-picture viewpoint, or wisdom to get things right. This point is important, because it reminds us that we should not automatically accept everything that the "experts" tell us. For example, while historical fears regarding dietary cholesterol were probably overblown, so likely is the new official position that dietary cholesterol is of no concern at all. Cholesterol is an unstable molecule, readily oxidized in the presence of air to form highly atherogenic cholesterol oxides. These toxic molecules are less likely to be produced when an egg is boiled inside its shell than when it is scrambled, when meat is cooked at low rather than high temperatures, and when butter is kept covered in the refrigerator rather than left uncovered on the table. The simplistic evolution of cholesterol from a nutrient of concern to one of no concern ignores these nuances. Similarly, the many "experts" who claim that micronutrient supplementation of nondeficient persons is not beneficial seem unable or unwilling to evaluate the scientific literature in its entirety and in an unbiased way. As always, we should evaluate scientific claims not by the status of the person making the claims, but by the strength of their arguments.

Alan R. Gaby, MD

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Women's Health Update

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Omega-3s and Mental Health

Effects of Fish Oil and Vitamin B1 on Primary Dysmenorrhea (Menstrual Cramps)

This double-blind, randomized, placebo-controlled clinical trial was carried out in 240 high school females with dysmenorrhea. They were divided into four groups with 60 in each. The first group received vitamin B1 tablet 100 mg/day starting at the beginning of the menses and taken for 2 months, the second group a fish oil capsule500 mg/day for the same period of time, the third group a mixture of both, and the fourth croup received a placebo, also from the beginning of the menses period for a duration of 2 months.

The inclusion criteria were: those who had primary dysmenorrhea (menstrual pain without pelvic pathology), agreed not to take any rescue medication for their cramps, had regular menstrual cycles, had no other health problems, and consumed not more than one serving per week of fish.

The intensity of the pain was significantly reduced in all three treatment groups vs. placebo. Duration of pain also significantly reduced in all three experimental groups compared with placebo. The results were better at the end of the second month than the first month, in all treatment groups. The severity of pain was measured by the Visual Analogue Scale (VAS) and duration was measured by the Cox Menstrual Scale. Participants recorded their points at the beginning of the study, after the first month, and after the second month. They also completed a detailed questionnaire assessing their menstrual pain and duration.
Here are the results in table form:

Pain Intensity (higher numbers = more painful)

	Before study	After 1 month of treatment (Tx)	After 2 months of Tx
B1	7.49	4.11	2.38
Fish oil	7.59	5.22	3.14
B1/fish oil	7.39	4.01	2.29
Placebo	7.49	7.31	5.02

Duration of Pain (higher numbers = longer duration)

B1	37.98	20.23	22.26
Fish oil	11.00	7.21	9.81
B1/fish oil	38.02	11.36	7.256
Placebo	38.45	25.32	24.38

Comment: This study had some problems, perhaps in the English translation as well as with some of the decimal points. I took the liberty to make the corrections based on other comments in the text. Other studies have shown a reduction in primary dysmenorrhea using fish oils as has vitamin B1. In treating primary dysmenorrhea, it is important to have a strategy that reduces menstrual pain over time, but also treatments that reduce acute pain within 30 to 120 minutes. The current study shows that we can use vitamin B1, fish oil, or a combination and expect improvement over 1 to 2 menstrual cycles.

Hosseinlou A, Alinejad V, Alinejad M, Aghakhani N. The effects of fish oil capsules and vitamin B1 tablets on duration and severity of dysmenorrhea in students of high school in Urmia-Iran *Global J Health Sci.* 2014;(7).124–129.

Vulvar Lichen Sclerosus: Treatment with Topical Avocado and Soybean Extracts

Lichen sclerosus is a chronic inflammatory dermatosis condition that has no certain etiology. Treatment options are few, and topical corticosteroid creams are the mainstay of conventional treatment, although not the only treatment. Evidence-based natural treatments are essentially nonexistent, although many anecdotal and case reports reflect attempts at reducing inflammation with dietary changes, supplements, and topical herbal preparations such as licorice, MSM, and others. None of the natural medicine approaches has a very robust track record. Topical steroids are often needed to reduce itching and/or pain, reduce ulcerations/fissures, and slow or halt the progression of the disease.

The current single-center, prospective cohort, open-label study was designed to assess the efficacy of a topical product containing avocado and soybean extracts (ASE) along with several antioxidant, softening, and emollient ingredients. Patients in the study were those with mild to moderate disease related clinical signs of lichen sclerosus, lichen sclerosus relapse, or recurrence after at least one previous treatment with topical steroids, or intolerance to topical corticosteroids. Patients were excluded if they were taking systemic and/or topical lichen sclerosus treatments during the 4 weeks before enrollment, or had active vulvar infections or other

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vulvar dermatoses or cancer. Women were also excluded if pregnant or breast-feeding.

After screening, 23 women met the eligibility criteria and entered the study, applying ASE cream on the affected vulvar area twice daily for 24 weeks. The product used was Repasine cream (Pharmaday, Italy). It contains extracts of avocado and soybean, hyaluronic acid, vitamin E, sodium carboxymethyl beta glucan, dimethylmethoxy chromanol, and trimethylglycine. During the first 12 weeks, patients also took two ASE capsules daily between meals, containing 300 mg extracts of avocado, soybean, vitamin E, para-aminobenzoic acid, and phytosterols.

By the end of the 24 weeks of treatment, 12 (70.5%) of symptomatic patients and 13 (72.2%)of asymptomatic patients but those who had objective signs of lichen sclerosus, achieved an improvement of at least 75% in subjective and objective global scores, respectively.

Comment: The authors of this study reported in the discussion that the rates of partial to complete symptom and sign remission is not easily comparable to rates with topical corticosteroids. But, while the ASE-containing products did not achieve as rapid a response of at least 75 % as is seen with topical steroids, after the 24 weeks, the improvement attained was essentially the same as a 12-week course of the potent topical corticosteroids. Of note though is that the patients in this study were those with mild to moderate disease.

It appears that the topical and oral ASE products exerted anti-inflammatory, antifibrotic, emollient, and soothing effects on patients with mild to moderate lichen sclerosus.

Borthi A, Corazza MinghetiG, Toni G, Virgili A. Avocado and soybean extracts as active principles in the treatment of mild-to-moderate vulvar lichen sclerosus: results of efficacy and tolerability. *J Eur Acad Dermatol Venereol* 29;2015:1225–1230

Knee Osteoarthritis and Sesame Seeds

Osteoarthritis (OA), also known as degenerative arthritis, is the most common form of arthritis and involves the joint cartilage. The inflammation and degeneration can result in pain, swelling, decreased range of motion and mobility, and even changes in the shape of the joint and abnormal bone growth. The knees are one of the most common joints affected by OA, especially in women.

The current study was conducted in Iran and involved 50 patients (40 women and 10 men) aged 50 to 70 years old who had knee OA with mild to moderate disease severity based on accepted criteria of the American College of Rheumatology (ACR).

The patients were randomly divided into 2 groups: sesame-treated and control. The control group received standard drug therapy of 500 mg acetaminophen twice daily and 500 mg glucosamine once a day. The study intervention group (25) received 40 g of sesame seeds, ground into a powder, per day along with the standard drug therapy, for 2 months. Patients in both groups maintained their usual diet and physical activity during the study.

The Knee Injury and Osteoarthritis Outcome Score (KOOS) and Timed Up and Go (TUG) and the Visual Analog Scale (VAS) tests were used for clinical assessments. VAS measures subjective characteristics or attitudes. In this study, VAS was used to measure the rate and intensity of the pain. 0 represents no pain and 10 represents the maximum pain tolerated. The TUG is used to assess a person's mobility. It uses the time it takes to rise from a chair, walk 3 meters, turn around, walk back to the chair, and then sit down again. Scores of 10 seconds or less indicated normal mobility, 11–20 seconds are within normal limits for elderly and disabled individuals, and > 20 seconds means that the person needs assistance. A score of 14 seconds or more may indicate that the person is prone to falls. The KOOS is a test specific to the knee and assesses a person's opinions and problems associated with the knees. It measures pain, swelling, restricted range of motion and mechanical symptoms, activities of daily living, recreation function, and knee-related quality of life. The KOOS scores for each of the areas measured are transformed to a 0–100 scale, with 0 representing extreme knee problems and 100 representing no knee problems.

After treatment, there was significant difference in pain intensity between the two groups. The mean score of KOOS in both treatment and control groups was significantly increased compared with baseline. The mean score of the TUG questionnaire in both treatment and control groups was significantly decreased from baseline. There was no significant differences in pretreatment scores of KOOS and TUG between the two groups. There was significant difference in posttreatment scores of the KOOS and TUG between the two groups.

Comment: This study showed a positive effect of a rather simple dietary addition of 40 g/day of ground sesame seeds in improving clinical signs and symptoms in patients with osteoarthritis of the knee. It should be considered a good adjunct to acetaminophen and glucosamine.

Sesamin, a lignan derived from sesame seeds, has been shown to inhibit pro-inflammatory cytokines involved in inflammatory factors. Oxidative stress also has a role in OA, and sesame oil can increase antioxidant capacity, superoxide dismutase (SOD), and serum antioxidants, including vitamins C and E. Improving antioxidant enzyme activity and improving oxidative status with sesame is a possible mechanism in improving symptoms and signs of OA.

Possible methods of delivery of could be in smoothies, in yogurt, on fruit or vegetable salads, and on top of cooked vegetables. A tablespoon is approximately 9 g, so this would be 4-plus tablespoons per day: simple, safe, tasty, healthful, and hopefully a way to help with mild to moderate osteoarthritis of the knees (and maybe other joints).

Sadat E, Haghighian K, et al. Effects of sesame seed supplementation on clinical signs and symptoms in patients with knee osteoarthritis. *Int J Rheum Dis.* 2013;16(5):578–582.

Dr. Tori Hudson graduated from the National College of Naturopathic Medicine (NCNM) in 1984 and has served the college in many capacities over the last 28 years. She is currently a clinical professor at NCNM and Bastyr University; has been in practice for over 30 years; and is the medical director of the clinic A Woman's Time in Portland, Oregon, and director of research and development for Vitanica, a supplement company for women. She is also a nationally recognized author, speaker, educator, researcher, and clinician.

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Told You So

In 1980, the US Department of Agriculture (USDA) and the US Department of Health and Human Services (HHS) published the Dietary Guidelines for Americans. These guidelines encouraged people to eat a diet that promotes good health and prevents chronic disease. As mandated by Congress, an updated version of the Dietary Guidelines is published every 5 years. These updates are influenced primarily by a report prepared by the Dietary Guidelines Advisory Committee (DGAC). This committee consists of a group of "nationally recognized experts in the field of nutrition and health," who are commissioned to review the scientific literature and provide recommendations to USDA and HHS.[1]

Two of the recommendations in the new DGAC report represent a major change from earlier versions of the Dietary Guidelines.[2] First, dietary cholesterol is no longer listed as a "nutrient of concern." This change is based on recent studies indicating there is no significant association between dietary cholesterol intake and serum cholesterol or risk of cardiovascular disease. Second, in contrast to previous versions of the Dietary Guidelines, which recommended limiting fat intake to 20% to 35% of total calories, people will no longer be advised to restrict their fat intake. Instead, the new recommendation is to emphasize the use of healthful fats (such as olive oil and nuts), while avoiding harmful fats (such as trans fatty acids).

For half a century we were told to avoid cholesterol and fat (mainly saturated fat), because they will give us heart disease. These recommendations spawned foods such as egg substitutes which, despite being low in cholesterol, destroyed the health of experimental animals and led to their early death.[3] Fat-phobia helped create a huge market for fat-free and low-fat yogurt, which is typically loaded with added sugar and frequently contains no probiotic organisms. People were all too willing to believe that these sweet-tasting, addictive quasi milkshakes were good for them because they were low in fat. And over the years, many other foods of questionable nutritional value pervaded the marketplace, as consumers happily ignored the fact that low-fat junk food is still junk food.

It is encouraging that the new Dietary Guidelines will promote healthful foods such as nuts and fish (despite their relatively high fat content), as well as fruits, vegetables, and legumes, while recommending lower intake of sugars and refined grains. However, the satisfaction of knowing that these sensible recommendations are about to become official is tempered by the awareness that it took the "experts" so long to accept what some scientists and nutritionists have been saying for decades. As early as the 1960s, John Yudkin presented both epidemiological and biochemical data to support the concept that sucrose, not fat, is the key dietary contributor to cardiovascular disease.[4-6] In his 1970 book, *Nutrition Against Disease*, biochemist Roger Williams cited evidence that trans fatty acids and fats heated to high temperatures are harmful, whereas there is little evidence that dietary fat per se is dangerous. Others, including this author on multiple occasions, have emphasized the dangers of refined carbohydrates while arguing that dietary cholesterol and saturated fat are less of a problem than is commonly believed. Yet, the "experts" generally ignored the dissenters and the research they cited.[7] Instead, they clung to the "lipid hypothesis," even, ironically, while acknowledging that their dogma was indeed merely a hypothesis.

And when they did come around to the dissenters' point of view, they did so in such a way as to protect their position of authority. For example, an editorial in the *New England Journal of Medicine* in 2014 about trans fatty acids stated, "In the early 1990s, studies began [italics mine] revealing negative health effects of trans fats, and by the mid-2000s, it was clear beyond doubt that trans fats increase the risk of coronary heart disease. ..."[8] That statement is not accurate. A more accurate statement would have been something like, "Research as early as the 1950s indicated that consumption of trans fatty acids can exacerbate a deficiency of cardioprotective essential fatty acids, and a 1975 study demonstrated that trans fatty acids are atherogenic

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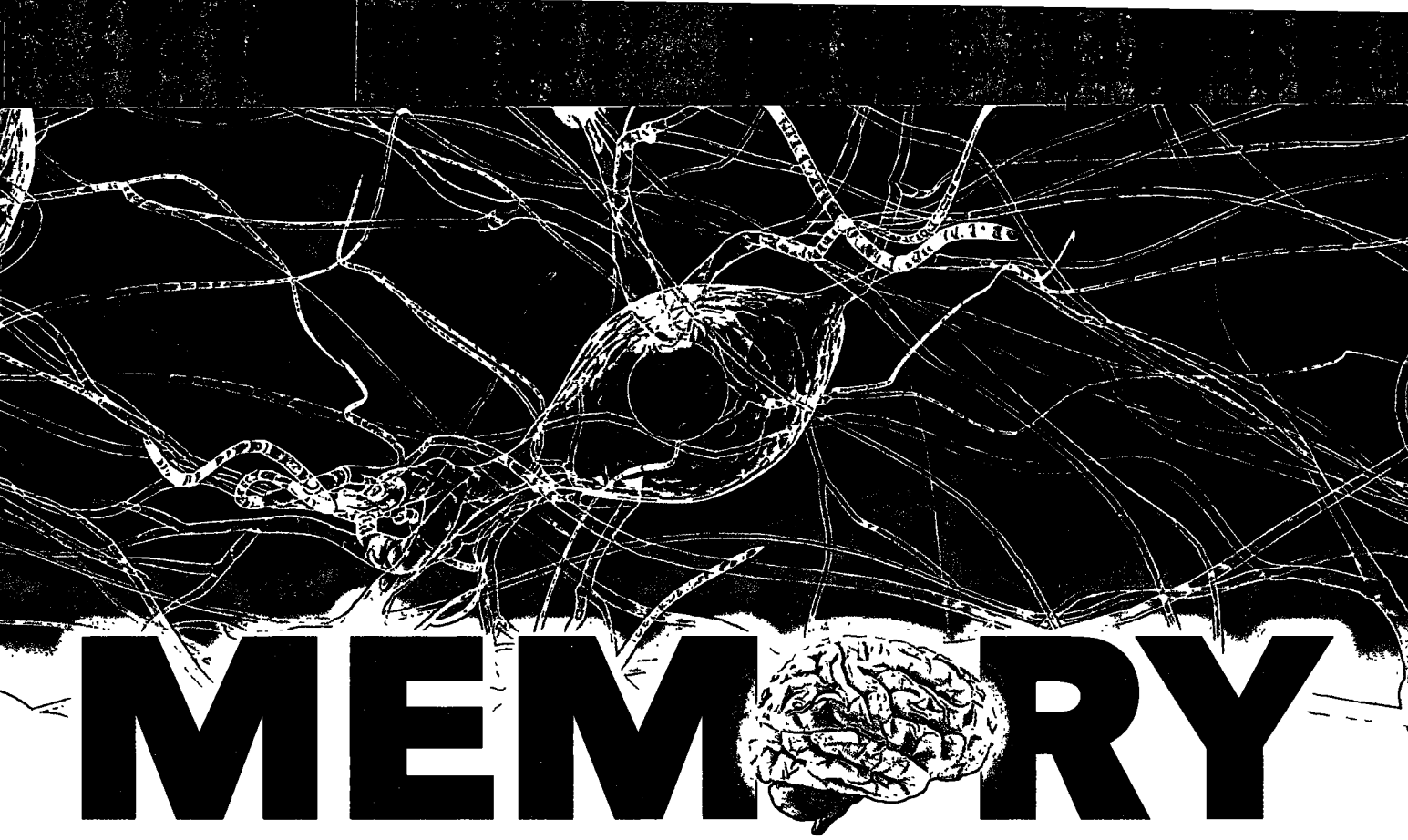

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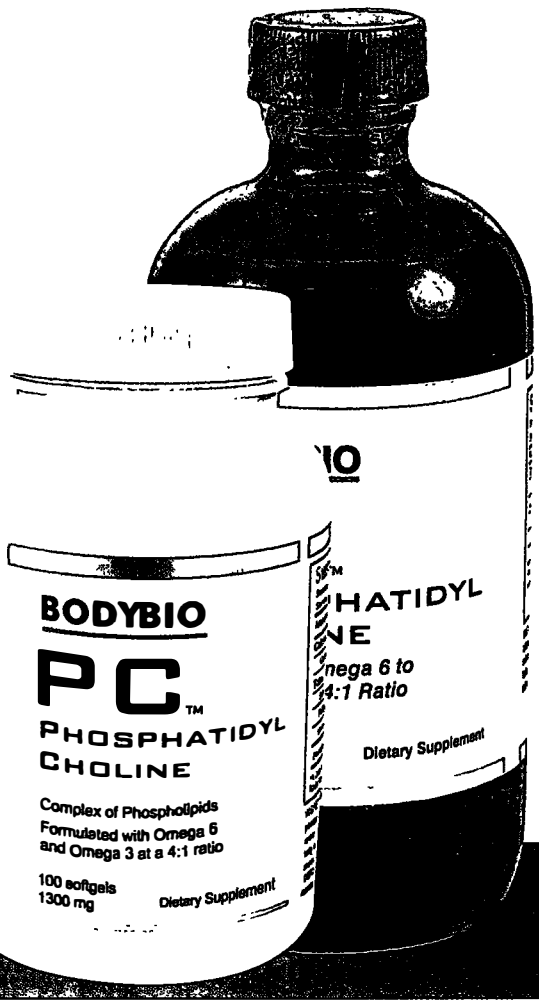

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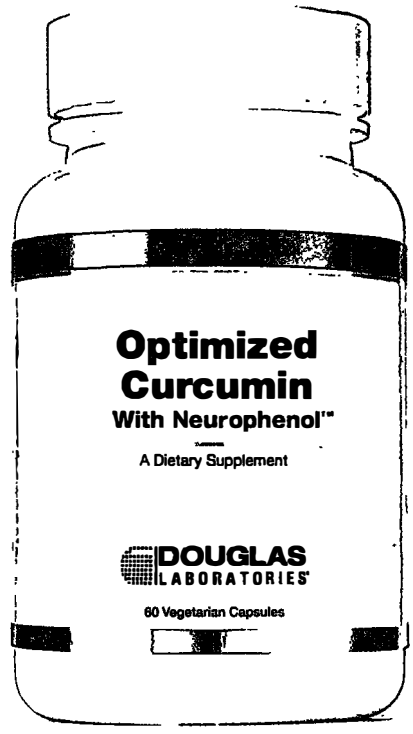

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Disilvestro et al. The Ohio State University. Nutr J. 2012 26;11.79.

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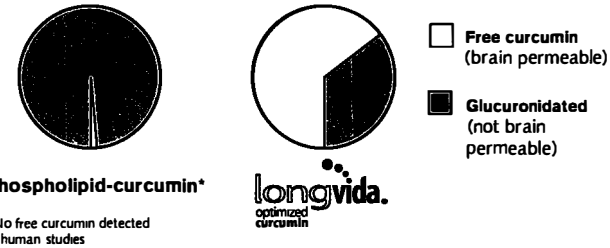

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