CARDIOVASCULAR HEALTH

TOC 17

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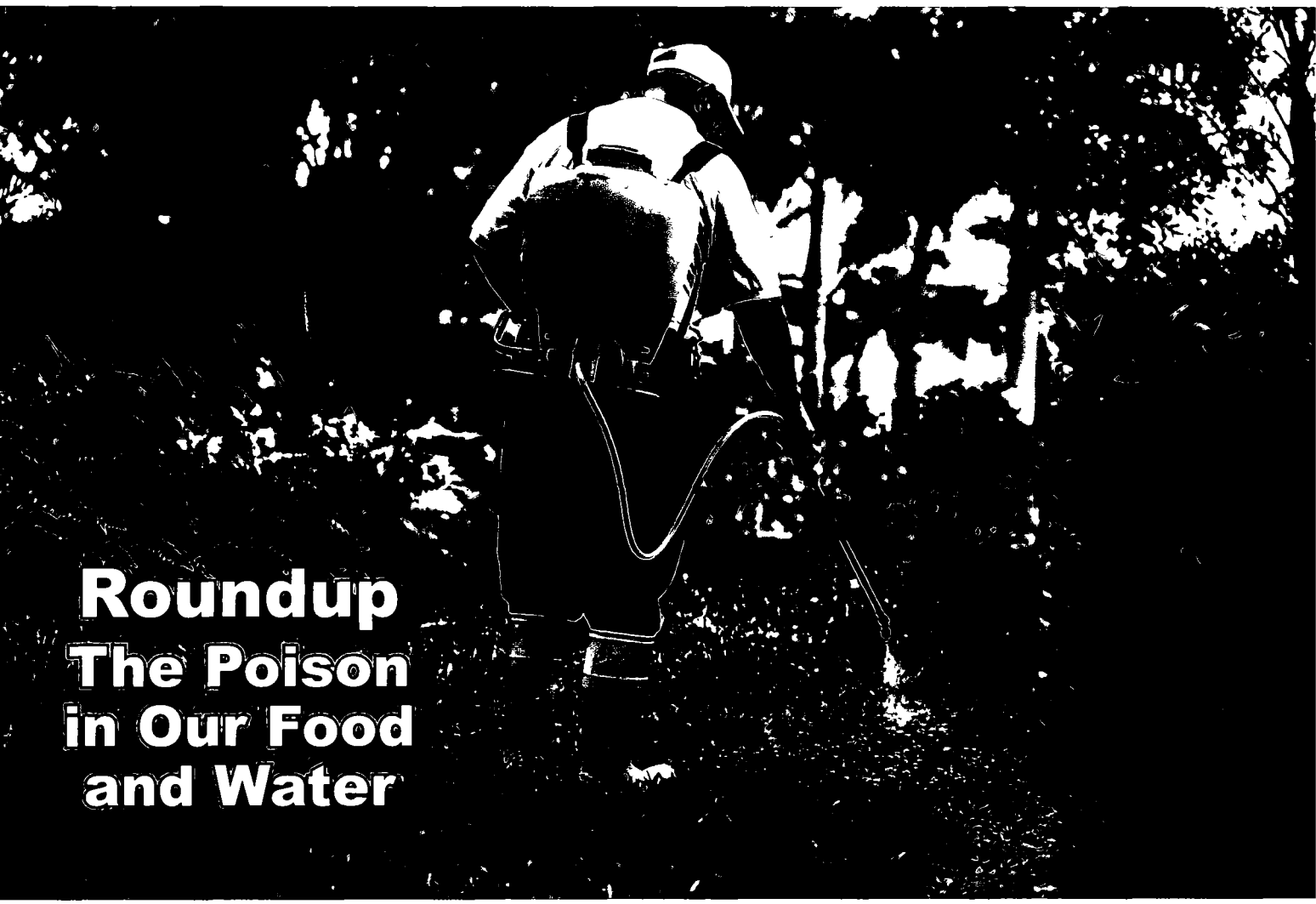

Roundup
The Poison in Our Food and Water

Sugar's Toxic Effects
Its Role in Coronary Artery Disease

Heart Failure Q&A
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P44

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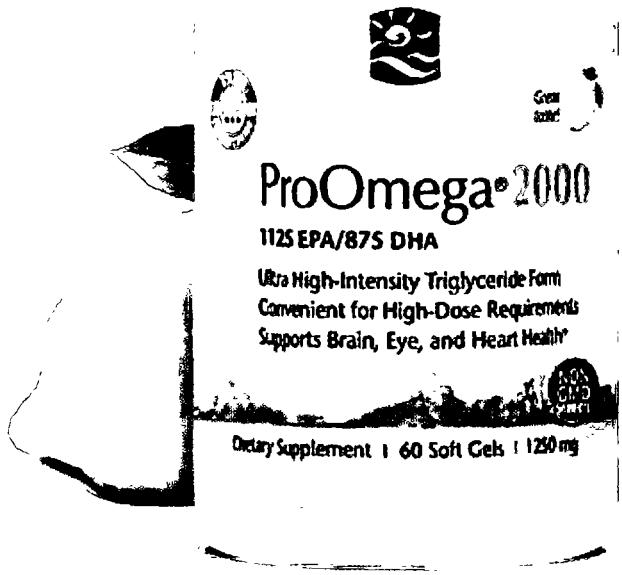

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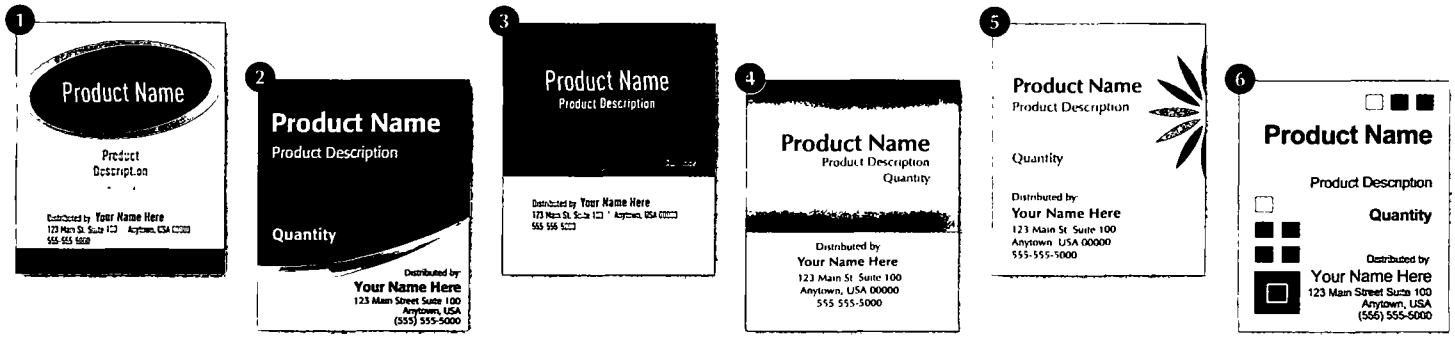

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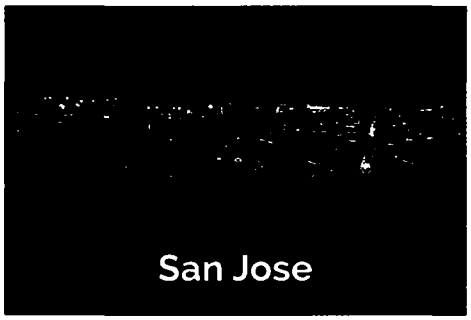
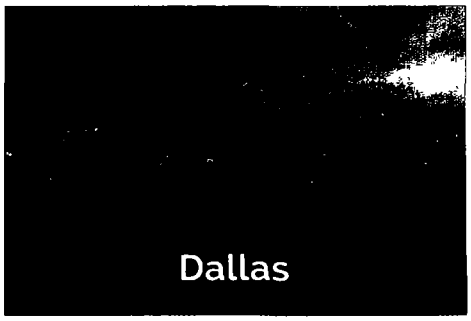


August 6
Organic Acids Testing Workshop

August 7
Genetic Testing Workshop



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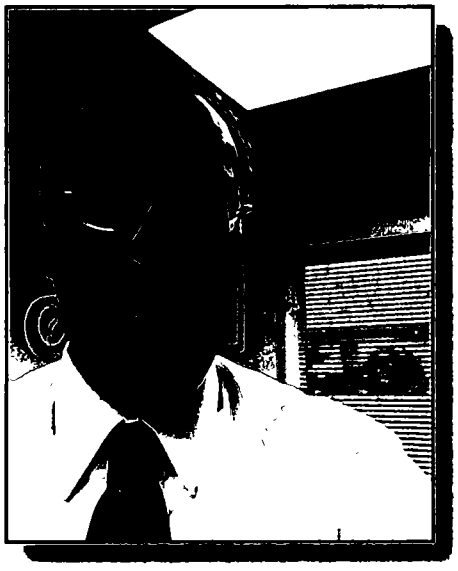

From the Publisher

A Cure for Asthma?

This provocative question is the title of a book by David Hahn, MD.[1] Unlike some other health books that beckon with titillating headlines, Hahn's book is solid with clinical studies and case histories. Hahn is not a huckster pandering his own-patented formula, nor recommending an expensive wonder drug. Truthfully, I cannot see that he will profit much from this book and his self-funded research, except for the satisfaction that he will offer relief to thousands of adult and children asthma sufferers. The problem is really twofold: First, most physicians cannot accept the fact that asthma's primary cause is not allergy or inflammation; rather, it is infection. Second, without accepting an infection etiology, doctors are disinclined to prescribe an antibiotic, much less a long-term antibiotic. Hahn is infuriated with this collegial resistance to considering an infective element to asthma. Patients are informed that asthma is a lifelong illness, manageable with bronchodilators

continued on page 8 ➤

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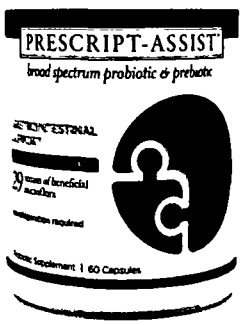

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[1] Pennisi, E (2011) Body's Hardworking Microbes Get Some Overdue Respect *Science, 330* (December 2010), 1619

7

From the Publisher

➤ *continued from page 6*

and inhalers, subject to episodes of exacerbation, even critical events. To have a simple antibiotic, routinely prescribed by most physicians for bronchitis and pneumonia, be ignored when it could play such an important role in arresting and reversing the asthma process, is the basis for Hahn's book.

Hahn is a Stanford Medical School graduate who opted to become a family medicine practitioner rather than a super-specialist or lab bench researcher. Still, he remained very academically inclined and liked the idea of conducting research. Hahn's investigations, however, were clinically based in the community. He liked to study treatment outcomes with patients who are sick but not needing specialist care. Primary care research is different from lab bench research: translational research looks at the efficacy of treatment in a tissue culture, rodent population, or tertiary care population of the hospital; primary care research looks at the effectiveness of treatment with a community-based population. Unfortunately, primary care research is not well funded and does not get the resources available to academic researchers. Still, Hahn has been involved in a number of primary care studies. One of his earliest published studies was published in *JAMA* in 1991, when he made the observation that asthma was seen in patients experiencing bronchitis or pneumonia caused by *Chlamydia pneumoniae*.[2]

Hahn's group had been examining patients with persistent cough and upper respiratory infection. Many of these patients were found to have abnormal IgG and IgM antibodies to *C. pneumoniae*. The serendipitous finding was that among those patients who had positive *Chlamydia* antibodies but no history of asthma, many developed wheezing and frank asthma. The intriguing observation for Hahn was that simple antibiotic therapy eliminated asthma symptoms and need for chronic treatment.

Hahn's book offers extensive accounts of a number of adult and children patients who were suffering with protracted asthma. Of course, case reports are considered weak scientific evidence. However, one patient, "Jim Quinlan," who had on at least one occasion required emergency resuscitation for status asthmaticus as documented in his local newspaper, ultimately was treated by Hahn; and following 4 months of antibiotic treatment, his asthma symptoms markedly improved and went into continued remission. He did not require any further asthma treatment, and the local newspaper reported his mountain-hiking trip with his family 3 years later. Quinlan was so impressed with Hahn's treatment that he posted his story on line and ran a blog for other asthma patients to post their story and share with families (see www.asthmastory.com).

Hahn is not looking to be a primary referral for asthma patients. He would prefer that physicians treat their asthma patients with antibiotic therapy. Although physicians can order testing to determine if their patient has *Chlamydia*, he thinks that even if the antibody testing is normal, the patient deserves a trial of antibiotic therapy. The antibiotic is pulsed,

continued on page 10 ➤

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➤ *continued from page 8*

given in weekly oral doses; Hahn does not see the need to treat the patient daily. He argues that a limited regimen of weekly antibiotic treatment will not create communitywide antibiotic resistance. Still, he would like to see the asthma research community do an appropriate randomized clinical trial to demonstrate the effectiveness of antibiotic therapy. Admittedly the antibiotic might not be just anti-infective, it could be anti-inflammatory as well. The point is that medicine has little justification to delay conducting a study.

Chikungunya: Coming Soon by Mosquito Bite to a Town Near You

Chikungunya, pronounced "chic-kun-gun-yah," sounds as if it may have something to do with chickens, but there is no relationship. It is a virus like the one that brings on dengue fever, except chikungunya's course of febrile illness is complicated by longstanding arthritis and arthralgia. The name comes from the Makonde language; it was originally discovered in southern Africa in 1952, in the region between Mozambique and Tanzania. Chikungunya translates to "drying up" and "become contorted" and refers to the deformity that "bends up." While it was discovered in Africa, the virus carried by the ubiquitous mosquito *Aedes aegypti* has spread *chikungunya* through Africa, Asia, and more recently South America. If the mosquito name sounds familiar, that would be because it is now mentioned frequently when discussing the new viral disease Zika. In fact, some cases of chikungunya may be a coinfection of Zika virus acquired though a bite from the daytime-feeding mosquitoes.

Before Zika made headlines as the putative cause of the recent epidemic of microcephaly in Brazil, chikungunya was being closely watched by the CDC. The virus has been slowly making its way through the Caribbean, into the southern US, and spreading northward. While chikungunya may be limited to 2 weeks of a flulike illness, it readily enters the synovia of joint spaces. Once the virus is ensconced in the joints, it is very difficult for the immune system to remove it. Patients are faced with treating joint pain with anti-inflammatories and the potential of more disfiguring arthritis. The virus may be readily diagnosed with IgM serology, PCR, and cell culture. There is no specific treatment and no vaccine prevention. As with Zika and dengue, prevention is accomplished by wearing clothing covering the extremities, applying insect repellant,

continued on page 12 ➤

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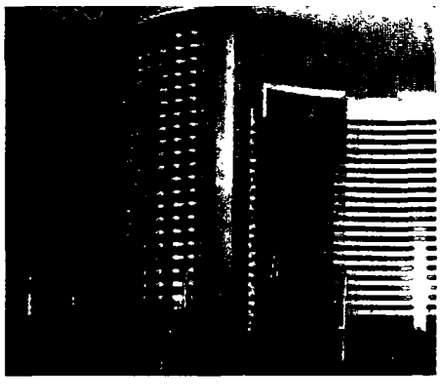

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➤ *continued from page 10*

and not traveling in areas ridden with mosquitoes. Of note, chikungunya, like Zika and dengue, may be transmitted from mother to fetus and may be transmitted sexually as well.

Sugar Toxicity – A Silent Epidemic

If you have been paying attention to Dr. Gaby's many discourses, you know that your diet should not be centered on caramelized foods. While these foods are "mighty tasty," or "good eatin'" (in some circles), they are replete with glycation, what Dr. Gaby refers to as AGEs (advanced glycation end products). A plant-based diet, filled with vegetables and fruits, avoids AGEs, unless one caramelizes the onions. Here the emphasis is on glycation brought about by eating animal proteins that have been barbecued or seared; the higher the temperature, the more AGEs. However, Drs. Edwards and Malik, authors of this issue's "Sugar Toxicity" article, are interested in a very different glycation process – the glycation that occurs within the body brought about by overconsumption of sugar and refined carbohydrates.

We all know about the perils of eating sugar and fructose to excess. Obesity, metabolic syndrome, and diabetes are the obvious concerns. Less obvious is how excessive sugar plays a pivotal role in progressive cardiovascular disease. Of course, in terms of basic physiology, sugar excess leads to fat deposition, abnormal hormone balance, insulin resistance, hypertension, and hypertriglyceridemia. Edwards and Malik make the case that excess sugar plays a direct role in glycation of our cellular membranes, particularly the endothelial cells of our arteries, arterioles, and capillaries. The authors describe the "glycocalyx" as a "polysaccharide sugar polymer coating that surrounds all cell membranes." They consider it a functional biofilm that is responsible for controlling the endothelial vascular tissue. When a person consumes excess sugar, the glycocalyx is subject to major glycation modification. The disruption of the glycocalyx leads to localized fluid imbalances and edema. Inflammation brought about by glycocalyx glycation is the primary factor leading to plaque formation.

Edwards and Malik argue that it is not the large vessel arterial plaque and endothelial dysfunction that cause major vascular events; instead it is the glycation taking place in the "microcirculation," the capillary beds in every body tissue and organ, that eventuates in massive cardiovascular events. The authors question whether cholesterol is truly the fundamental pathology. Glycation is not only problematic for individuals who are obviously overconsuming sugar, especially in the obese, but also in thinner individuals whose sugar habit is

continued on page 14 ➤

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From the Publisher

➤ *continued from page 12*

not so obvious. Edwards and Malik advise keeping the blood glucose below 85 mg% and having a hemoglobin A1c of less than 4.6. When these numbers are high, Edwards and Malik would call for a strict reduction in sugar and carbohydrates as well as appropriate supplementation to reduce them. They would also advise the use of EDTA chelation to remove toxic element burden, as well as to decrease glycation in the microcirculation.

Skin Detoxification for Kidney Disease

Dr. Jenna Henderson is a naturopathic physician who specializes in treating patients with kidney disease. I am very happy that she contributes her knowledge and experience writing articles for us. (It would be worthwhile to read her previous articles; go to www.townsendletter.com, roll over the "Article" tab, go to "Search recent indices," and then search for *Jenna Henderson*.) One of the major difficulties in managing patients with chronic kidney disease is that when prescribing intravenous therapies and recommending supplementation one may aggravate the kidney pathology – after all, the damaged nephrons must remove the vitamins, minerals, amino acids, and other chemicals. Henderson has established guidelines for working with kidney patients to be able to safely support them naturopathically. The bottom line remains whether or not the BUN and creatinine worsen with treatment. Any treatment worsening those indices must be prohibited.

Henderson's discussion of kidney skin detox is a variation of hydrotherapy. Benedict Lust and other old-timer naturopaths employed hot and cold water treatments as a mainstay of their healing therapies. As conventional medicine adopted the "new" wonder drugs early in the 20th century, allopaths reached for the prescription pads and operated on patients, abandoning dietary approaches and hydrotherapy. Still, water treatment remained a mainstay for naturopathy through much of the past 100 years until more recently, when NDs have been compelled to utilize "evidence-based" medicine.

Soaking in a bath of Epsom salts and apple cider vinegar does not seem very scientific. Yet Henderson argues that the skin is a major excretory organ, eliminating a significant amount of urea and other waste products. A lengthy bath would be very useful for the patient having chronic renal failure especially when dialysis is not available. Henderson notes that even when dialysis is available, the additional bathing would be useful for the renal patient's quality of life. And I would imagine it would benefit most of us who do not have kidney problems as well.

Jonathan Collin, MD

Notes

1. Hahn D. *A Cure for Asthma*. People's Pharmacy Press; 2013.
2. Hahn DL, Dodge R, Golubjatnikov R. Association of Chlamydia penumoniae (strain TWAR) infection with wheezing, asthmatic bronchitis and adult-onset asthma. *JAMA*. 1991;166:225–230.

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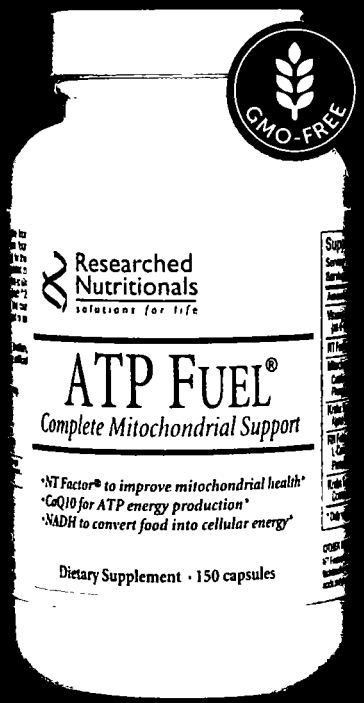

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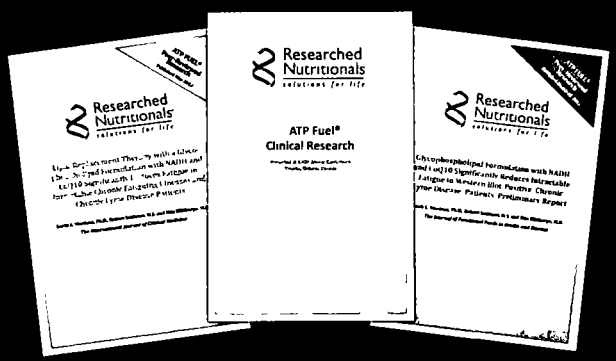

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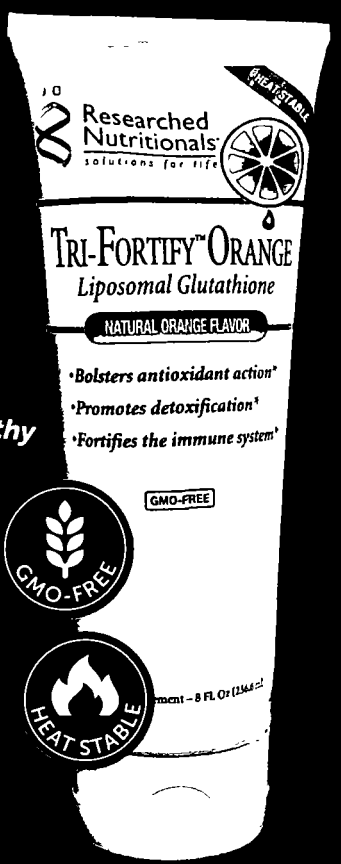

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IN THIS ISSUE May 2016 | #394

ON THE COVER: The True Dangers of Roundup (36), Boosting Kidney Function (44), Heart Failure Q&A (48); Treating Cardiovascular Disease (54); Sugar's Toxic Effects (62)

In Memoriam
Merrill E. 'Ed' Torrance
Kalamazoo, Michigan

Merrill "Ed" Torrance, age 87, loving husband, father, grandfather, and great-grandfather, passed away February 8, 2016. Ed graduated from Western Michigan University with a bachelor's degree. He was one of the founders of the group Great Lakes College for Advancement in Medicine, a precursor to International College of Integrative Medicine. His business, the Torrance Company, was one of our three original corporate partners, along with Miller. For over 69 years, the Torrance Company has supplied vitamins and supplements to physicians and offered quality pharmaceuticals, IV infusion therapy products, hypodermics, and exam room products to health-care professionals. It specializes in products for prolotherapy. Ed's two sons, Mark and Scott, continue to run the family business.

For Ed's obituary, please visit http://www.langelands.com/obituaries/Merrill-Torrance.

Wendy Chappell, MBA
Executive Director
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National Fibromyalgia & Chronic Pain Association Conference, October 9–10, 2015: A Review

by Emily Kane, ND, LAc

About 120 people who work daily to alleviate chronic pain gathered in Crystal City, Maryland, just across the bridge from the nation's capital, for a jam-packed weekend of continuing education October 9 and 10, 2015. Organized by the NFCPA (National Fibromyalgia & Chronic Pain Association), this was a unique gathering open to researchers, health-care professionals, and patients. The attendee mix not only served to galvanize researchers to stay committed but also provided cutting-edge information to patients and helped unify stakeholders in advocacy work to remove bias against chronic pain sufferers.

Day 1 started off with an exciting presentation by keynote speaker Daniel Clauw, MD. Clauw is an internationally renowned chronic pain researcher and a professor of rheumatology at the University of Michigan. He updated us on how to think about fibromyalgia. "Forget about the 18 tender points." Any part of the body can be tender, and it's not a local, but a central phenomenon. Previously, we had thought of FM as a discrete illness with focal areas of tenderness and related psychological and behavioral factors.

The new thinking is that there is a final common pathway for the constellation of symptoms, namely the central nervous system. Clauw admonished us to think of FM as part of a larger continuum with many somatic symptoms that create diffuse tenderness. Further, FM is not about just pain but also impairments in memory, sleep, and mood. These other issues can actually be more problematic than the pain. Here's a tidbit of information: many FM patients feel that they have dry eyes; however, they have negative Schirmer's tests and do not test positive for Sjögren's disease (both known causes of chronic dry eye syndrome). However, FM patients are far more sensitive than nonaffected people, and a small breeze across the eyeball will cause pain in the FM patient but not in a person without chronic pain. Artificial tears can help quite a bit. FM patients who learn to "push through" living with pain do better because of maintaining a positive outlook. Clauw also started a small chain reaction over the weekend in using the analogy of an electric guitar to understand the new model of FM. The brain is the amplifier, and in FM patients this is turned way up. The body of the guitar is the body of the patient, and the strings are the nerves that connect the periphery (skin) with the spine and brain. Strumming on the strings of an FM patient will create a lot more "noise" (pain) than in the average person. Folks that have long-history central pain (for example dysmenorrhea in teen years, IBS in the 20s, low back pain starting in the 30s) clearly have the amplifier set high. They have central issues. The work in FM is to learn to turn down the amplifier and not pluck the strings so hard. I'm not sure if the speakers coordinated this point (I suspect not), but we heard about electric guitars from Dr. Wolfgang Bauermeister and Dr. Frank Rice on Sunday as well! Clauw recommended that we all avail ourselves of 10 empowering modules for reducing chronic pain at the website FibroGuide (www.fibroguide.com).

Alyssa Wostrel, MBA, of the DC-based Integrative Health Policy Consortium gave a brief update on section 2706 of the ACA (Affordable Care Act, or "Obamacare"), which has been law since 2010 and will eventually open many venues for reimbursable integrative care, such as acupuncture, trigger point therapy, health coaching, and cognitive behavioral therapy. The law empowers state insurance commissioners to require state-based insurers to comply with the nondiscrimination language, which forbids discrimination against provider types, as long as the providers are properly licensed in their state. Wostrel encouraged us to contact our state insurance commissioners if our health insurance has not been covering a certain type of provider – because technically this is now illegal. Consider this talking point: The US has the most expensive, and one of the least functional, health-care systems on the planet. There is excellent evidence that patients who engage with integrative care have better outcomes, and cost less. Check out the consortium's booklet "Integrated Health and Medicine: Today's Answer to Affordable Healthcare," available online. (See also Pathways to Healing on page 23.)

Next up was Dr. Lynn Webster, who presented on the impact on patients of the FDA's moving oxycodone from a Schedule III to a Schedule II drug. Although overdose deaths have gone down, patients have suffered because the higher schedule requires much closer physician monitoring, which of course increases costs and delays in refills. Some prescribers are "narcophobic," meaning that they are loath to be seen as too free with the prescription pad. This has left some patients high and dry, and suffering. The reschedule is important nevertheless as part of the solution for reducing

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opioid addiction, which is rampant in the US, and for driving us all to find better pain solutions. One such solution may come in the familiar weed grown by many of the founders of this country: hemp. Webster gave a brief overview of the state of phytocannabinoids in the US today and emphasized that while medical marijuana won't solve all our problems, the non-"high" portion of the plant, CBD (cannabidiol), holds significant promise for not only pain but also immune regulation and even improving cancer prognoses. In the states (23 plus Guam) that have legalized marijuana to some degree, a recent survey shows that there has been a 25% reduction in deaths by opiate overdose, and also significantly less use of the ER for pain, despite the lower availability of oxycodone, the most prescribed pain narcotic in the US by far.

After a quick stretch break, we were treated to what was for me the most novel information at the conference, which is the role of neck problems in chronic pain syndromes. A sleep specialist (neurologist Victor Rosenfeld, MD), a rheumatologist (Andrew Holman, MD), and a cervical spine specialist (Cory Kingston, DC) helped us understand how a kink in the neck creates hyperarousal of the central nervous system, with concomitant lowering of the pain tolerance threshold. Rosenfeld led us through normal and disordered sleep architecture, and we could see from the graphs that FM patients have much more "alpha intrusion," which basically means less, often much less, deep delta-wave, restorative sleep. Deep sleep is where tissue repair can occur. Holman explained that it's not good enough to image a neck in a neutral upright position only. What's required to assess spinal compression are neck images (plain X-ray or MRI) in flexed and extended positions as well. If you feel bad or dizzy, or get a pain flare from tilting your head back or forward, it's quite likely that you have some impingement on your spine which inhibits optimal cerebral spinal fluid (CSF) flow, thus chronically sending pain signals to the brain. Kingston described an all-too-common modern poor-posture stance, forward head posture, which he dubs a syndrome; and he aptly demonstrated the unfortunate biomechanics which result from poor posture. *Text neck* is a term that he coined for a common activity that throws our spine out of alignment and ultimately causes chronic tightening of the upper back and neck muscles.

After lunch, NFMCPA board member and passionate pain prevention advocate Dr. James Fricton (a dentist by trade) presented an overview of the prevalence and impact of chronic pain in the US, as well as his innovative work to empower both providers and patients.

Dr. William Collinge spoke about how mindfulness, cognitive behavioral therapy, and self-awareness can reduce pain symptoms, especially when used as part of a comprehensive, holistic approach to ameliorating pain.

Dr. Kim Dupress Jones, nurse practitioner, PhD, and associate professor at OHSU (Oregon Health & Science University), led us through ideas for exercise modification so that we don't give up but keep movement in our lives every day. The basic idea is to start low, go slow, but keep going.

The day wrapped up with two more informative speakers with lots of practical tips on modifying your kitchen and bathroom or even car; how to find community exercise classes that work for you; and how to ration your energy sensibly, so you don't crash early in the day. Barbara Kornlau, JD, OTR, and certified pain educator presented on "Living and Buying with FM and Chronic Pain"; and Mary Biancalana, MS, CMTPT, LMT, and owner of the Chicago Center for Myofascial Pain Relief, cheerfully demonstrated dozens of trigger-point releasing tips using simple tools such as a tennis ball.

Day 2 started early with a series of presentations followed by breakout sessions. First we heard from researcher Dr. Frank Rice, one of the world's leading experts on skin innervation and epidermal chemistry. Rice definitively expanded our thinking about what part of the body can feel pain. His research has uncovered "small fibers" capable of sensory transmission (nerve activity) in all cells: skin cells, even the pigment producing keratinocytes, and hair follicles and blood vessels, even the tiniest in the capillary beds. These small nerve fibers affiliated with all cells not only sense pain, but also can respond to light, thermal cues, and nutrient detection and cause reflexive movement away from pain via neurotransmitters and other chemicals within the adjacent cells' environment, which responds 24/7 to threatening or helpful stimuli through a constant feedback mechanism.

Rice differentiated beneficial acute pain, which is transient and due to mechanisms that are responding appropriately to a transient noxious condition, from nonfunctional chronic pain. Chronic pain is inappropriately prolonged pain due to "neuropathic" alterations in the widespread tissue sensory mechanisms. Again, every part of the body has neural fibers (axons) that react to pain. Peripheral nerve cells bring sensory information to the dorsal root ganglion cells, which then feeds into the dorsal cortex of the spinal cord, then up to the somatic sensory cortex in the cerebrum. Small fibers are the thinnest fibers within larger fibers (axon chains) that are not immediately involved with gross pleasurable sensation but often involved in painful stimuli. Some fibers respond to all sensation; say, warmth. Separate fibers (the small fibers) give different signals when the warmth intensifies to dangerous levels of heat. Our bodies interpret pain as an obvious threat to homeostasis.

Chronic pain patients are often frustrated by negative EMGs because small fibers don't have sufficient signal strength to be picked up with this testing. With more sophisticated tools, we now know the skin is loaded with small fibers. Paradoxically, chronic pain conditions are typically associated with a loss of epidermal nerve endings. Small fiber neuropathy by definition means loss of epidermal axons. However, the remaining fibers are apparently overly sensitive.

Small fibers are associated with the vasculature, which converge with the sympathetic nervous system. The sympathetic nervous system (fight or flight) fibers regulate the sensory fibers. Maybe drugs such as SNRIs work not on the brain, but in the periphery? Rice postulates that FM may involve a pathology of the convergent sensory and sympathetic innervation on cutaneous arterioles. Women have twice as many

sympathetic fibers along their blood vessels than do men, and these fibers seem to be estrogen sensitive, which could explain why many more women than men have chronic pain and Raynaud's syndrome.

What started this mismanagement of vascular flow which characterizes Raynaud's and other pain syndromes? Likely stress to the brain, which creates more sensitive sensory input.

There is normally a finely tuned interaction among the CNS, peripheral nervous system, and the body that maintains homeostasis and normal perceptions.

There is increasing evidence that there are measurable biological pathologies occurring in peripheral tissues. This offers potential new targets for therapeutic intervention and to improve diagnostics.

There is a tremendous capacity for the nervous system to find a solution to solve adverse physical and psychological challenges. We are lucky to have such a dedicated pain researcher as Frank Rice.

Next we heard Michael Sorrell, MD, a veteran NIH researcher, who presented on myofascial pain. Pain is caused by disturbance of myofascial trigger points (TPs), which are hyperirritable spots in skeletal muscle or in the fascia associated with skeletal muscle. We know that TPs are electrically different from surrounding tissue. They have spontaneous electrical activity. If you stick a needle in, more response is generated than if stimulating a non-TP area. TPs have altered biochemistry; reduced pH, higher levels of bradykinin and acetylcholine. TPs are usually located in taut bands of muscle. When a taut band is stimulated (plucked or strummed), it often contracts, causing a local twitch response, which is a spinal reflex. TP pain can mimic radiculopathy, migraine aura, bony, abdominal, or cardiac pathology, and other symptoms. If the TP does not respond to myofascial therapy, look again for a primary source of the pain.

Sorrell presented several case studies. One concluded that 85% of patients with migraine without aura improved at least 50% with myofascial therapy.

Next on the agenda we were captivated by German physiatrist Wolfgang Bauermeister, MD, PhD, who started his lecture by emphatically proclaiming his love of rock and roll (and electric guitars). Dr. B. gave us a sneak preview of his innovative work using a special ultrasound technique (elastography) to identify tissue texture changes and confirm the very real presence of TPs.

The last segment before lunch and the break-outs was a more in-depth look at the work of Fricton. He presented a dynamic, colorful PowerPoint full of cartoons, quotes, and humor – but also many dire facts. For example, pain is the No. 1 driver of cost in the US health-care system, according to a 2012 American Pain Association analysis, costing $635 billion or more annually. Pain is also the main cause of disability. As part of how to address these huge problems, Fricton directed us to a free, online class called "Prevention of Chronic Pain: A Human Systems Approach," available through Coursera (www.coursera.org).

I chose to learn more about Kingston's approach to correcting cervical stenosis for the first breakout after lunch. The weather in DC was beautiful, sunny with just a touch of a fall breeze.

Kingston said we could contact him (his practice is in Logan, UT) with questions about referrals: Coryk73@yahoo.com.

Our first exercise was to assess a patient visually for compensation around optimal alignment.

Eyes will always want to be level with horizon so the body will find a way to make the eyes stay level. The ear holes should line up directly over the shoulders in a side view. Shoulders should be equally level. Hips should be level. The ability to rotate head left and right should be equal.

Conference Review

Good frontal alignment puts the sternal notch directly below the middle of the forehead. FM is not just muscle pain; it's a whole raft of comorbid symptoms. The neck is so important because it's where the brain connects to the body. The function of the bony vertebrae is to keep us upright against gravity. Along with eye "righting" reflex, upright posture differentiates us from monkeys. Further, the bony vertebrae protect our spinal column, which is most vulnerable at the neck. The spine has series of 45° spring-loading areas: neck, thoracic, lumbar. Our necks need to balance the weight of head. Having a "military neck" wrecks ligaments at back of neck and smashes anterior cervical discs.

Here are the diagnostic criterion for Chiari syndrome, a congenital spinal stenosis:

1. headache/neck pain
2. dizziness/vertigo
3. vague pains throughout body
4. impaired balance
5. foggy thinking
6. urinary incontinence
7. IBS
8. voice changes

Maybe FM is *not* a rheumatologic or infectious problem. Maybe it's spinal stenosis, but not necessarily Chiari syndrome. Kingston made a good case for why chronic pain patients often have bad necks. Modern life sets us up for upper spinal injury. Consider that acceleration as slow as 5 mph can cause whiplash.

The suboccipital muscles are part muscle (stretchy) and part ligament ➤

(not stretchy). They lock the head in extension in situations causing rapid forward movement of the head. Righting reflexes cause the forward moved head to lift chin and push butt back, especially in women, who carry their weight low. In men, weight is abdominal, pulling weight forward, causing neck to compensate forward, actually opening cervical spaces. Men are less prone to neck problems. Intermittent abutment of the spinal cord causes massive autonomic arousal. In FM this situation is chronic. It feels to the FM patient as if the tiger is constantly in the room. Forward head posture affects CSF flow and leads to not only local but also central pain. The good news is, this can be corrected, but you may have to spend 3 weeks or so in Utah.

Next I attended the exercise/nutrition module. Kim Jones presented new research showing that physical inactivity and poor muscle strength are linked to all-cause mortality. She discussed growth hormone (GH), a small peptide with a 20 minute half-life, secreted by pituitary in pulses throughout day. FM patients don't make enough because it's mostly secreted during stage 3 and 4 sleep. Unfortunately, administering GH is very expensive and did not help FM patients much.

Insulin-like growth factor (IGF-1) holds more promise. It is also a small peptide but with a much longer (21-hour) half-life. Serum levels reflect pulsatile secretion of GH over the previous 48 hours.

FM patients have low IGF-1. Replacement (with intramuscular injections) works to bring up levels, and folks feel better. However, there are potential side effects such as weight gain and fluid retention.

Other option is exercise. Yay! That sounds better. At peak aerobic capacity, GH is maximally stimulated. The drug pyridostigmine (Mestinon) restores growth hormone to normal levels in exercising FM patients. However, good results were really only seen in patients taking the medicine *and* exercising. Eccentric movement seems best: maximize big muscles. Big steps going uphill; baby steps going down. Seek warm water options. Water adds natural resistance, thus mimics strength training. Jones did give an exercise caveat. Many FM patients are hypermobile and at risk of overstretching using weights, especially during water aerobics.

She closed with some general advice for exercise and FM:

1. Find a program that you *can* do.
2. Seeing others like you being successful can help.
3. Observe and track functional improvements. Keep a journal to chart progress. Functional improvement comes before symptom (pain) improvement.
4. Speak kindly to yourself.
5. Start low, go slow... but get there.

She shared this resource: the Fibromyalgia Information Foundation website, which offers videos (http://myalgia.com/VIDEOS/Video_Introduction.htm)

Dr. Kathleen Holton, nutrition researcher with the NIH, presented accessible information about the power of vegetables (loads of minerals) and good fats. She emphasized that dietary choices absolutely can affect neurotransmitter function. In general, high-carb diets reduce GH and high-protein diets promote GH. She states, and I agree, that nutrition is the single most important factor in optimizing your health.

Positive choices include produce and "clean" meat high in vitamins, minerals, protein, essential fatty acids, and fiber. Negative food choices include fast food and processed edibles that contain additives, pesticides, herbicides, trans fats, heavy metals, and other chemicals.

Holton introduced the idea of health-robbing excitotoxins. These are food additives such as glutamate, carrageenan, aspartate, and L-cysteine, which add shelf-life and addictive potential. Carrageenan is used to induce pain in lab rats. Glutamate is a nonessential, negatively charged amino acid found in nature. The bound form in meat digests slowly and in a balanced way, so it is OK. The free form is mostly found in soy products (soy sauce naturally contains high amounts) – and spikes blood levels of glutamate quickly after ingestion. Chronic pain patients, or any patients with neurodegenerative diseases such as ALS or Parkinson's, should avoid soy sauce. Glutamate is also a neurotransmitter, the most ubiquitous one in the body, and a major player in pain transmission. Disordered glutaminergic neurotransmission has been implicated in FM. FM patients have higher brain and CFS levels of glutamate. Doritos have 11 excitotoxins.

Seizures and migraines are caused by excess glutamate. The important nutrients vitamin C (500 mg daily), vitamin E (400 IU daily, found in nuts, seeds, olives), vitamin D (4000 IU daily but check serum levels because this might not be enough) and omega-3 fatty acids (salmon, sardines), and zinc (mostly from meat) were discussed briefly. More time was spent on magnesium. Fifty percent of the FM population is deficient. Stress lowers magnesium levels. Magnesium deficiency causes neuromuscular excitability, high blood pressure, dizziness, seizures, and tachycardia. The best food sources of magnesium are buckwheat flour, bulgur, semisweet chocolate, halibut, spinach, and white and black beans.

In summary, the optimal diet contains only real food, and is naturally low in additives and trans fats and high in nutrients and fiber.

I then jumped over to learn a bit more about the TP-locating ultrasound technique pioneered by Bauermeister. He uses a "shock wave" device – similar to lithotripsy – to reorganize the dysfunctional "neurotransmitter soup" that defines the milieu of a TP. The therapeutic effects of shock waves have been studied extensively. They change the neurobiology of the tissue. TPs create the ongoing nociceptive input from the periphery that creates the centrally appreciated pain. Breaking up TPs can provide immediate and often enduring relief. Other effective modalities include acupuncture and dry needling.

Not wanting to miss some of the self-care tips presented by the energetic Mary Biancalana, I spent the last hour of the conference using hand-held self-massage tools and lying on the floor watching short videos. A perfect closing!

Let us take what we have learned out into the world to help reduce suffering.

www.DrEmilyKane.com
www.AKANP.org
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Pathways to Healing

by Elaine Zablocki

AIHM Spearheads Efforts Toward Sustainable Health Care

The Academy of Integrative Health & Medicine (AIHM) emerged in 2014 when two well-established organizations united to better serve and magnify broad efforts to transform the way that we think about health and health care. AIHM is a unique interprofessional entity, supporting team-based approaches to care.

One of AIHM's central goals is to move toward a more sustainable health system through education, community, and training. The organization displays a chart, called the Wellness Route Map, which encapsulates its vision for our potential future:

moving
- from sickness to health and well-being
- from institution-led service to health and social care as part of a community
- from procedure-focused treatment to chronic illness management focused on a return to health
- from waste and overuse of resources to a balanced use of resources

The WELLNESS ROUTE MAP

Moving to a more sustainable health system and a new way of thinking

Health care as an institution-led service	Health and social care as part of a community
Curative and fixing medical care	Early intervention and preventative care
Procedure-focused treatment	Chronic illness management focused on a return to health
Sickness	Health and wellbeing
Isolated and segregated	Integrated and in partnership
Buildings	Healing environments
Decision-making based on today's finances	An integrated value of the future that accounts for the impacts of society and nature
Single indicators and out-of-date measurements	Meaningful scorecard information and in real time
Sustainability as an add-on	Integration in culture, practice and training
Waste and overuse of resources	A balanced use of resources where waste becomes a resource
Nobody's business	Caring community

Source: Adapted from England's National Health Service (NHS) Route Map for Sustainable Health [10]

The organization is multifaceted, with focus areas that include education, membership support, an interprofessional fellowship, and advocacy. The academy educates and trains clinicians in integrative health and medicine to assure exemplary health care. The annual conference has emerged as a central event, while the interprofessional fellowship, under the direction of Tieraona Low Dog, MD, launched this February with a full class.

"The people who are most excited about this organization are often those who come to a conference and say 'I've been looking for this group my whole life,'" said AIHM chair Daniel Friedland, MD. "We're becoming the virtual home for integrative health practitioners."

Established by health-care practitioners and health seekers connected by a shared holistic philosophy, AIHM could prove to be a "communication channel" to propel integrative medicine forward. It is working toward meaningful policy changes through a partnership with the Integrative Health Policy Consortium (IHPC). "The advocacy work will change the landscape so that integrative clinicians can better serve the patient," Friedland said. "While education is key to advancing the skills and practices of integrative health practitioners, it's through advocacy, policy, and legislation that qualified integrative health-care practitioners will be fully empowered to work together transforming the delivery of health care."

Historic Collaboration, Shared Vision for the Future

In 2014, two respected integrative medicine organizations merged to form AIHM. One was the American Holistic Medical Association (AHMA), founded in 1978 as a professional membership organization for MDs and DOs. The second was the American Board of Integrative Holistic Medicine (ABHM), created by a group

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of AHMA members in 1996 to certify physicians in integrative holistic medicine.

Mimi Guarneri, MD, FACC, AIHM president, was an active participant in the transition towards the new academy. "The only way we will transform the health-care system is through community, new ways of thinking and working collaboratively," she said.

Tieraona Low Dog, MD

In 2013 both organizations began preparing their members for the planned merger. Up to that point, about 3000 MDs and DOs had passed the ABIHM exam and were ABIHM diplomates. Going forward, Diplomates will maintain their certification through AIHM. Meanwhile, a new board called the American Board of Integrative Medicine (ABOIM) began offering certification exams in comprehensive integrative medicine for MD and DO physicians. ABOIM, overseen by the American Board of Physician Specialties (ABPS), sets a new standard by requiring a 1000-hour fellowship in integrative medicine for MD and DO physicians.

The final ABIHM exam was offered in 2014. The next year, the organization transformed its premier education event, the "People, Planet, Purpose" conference, to serve the interprofessional AIHM vision. Tabatha Parker, ND, AIHM director of education, expanded the faculty to 76 experts and invited luminaries such as Dean Ornish, MD; Jean Watson, RN, PhD; and Deepak Chopra, MD, as speakers. "The vision of the AIHM Conference was to transcend our silos and come together in collective purpose toward a new model of health care, with collaboration at the center," she said.

First-Ever Interprofessional Fellowship Program

Last year, the AIHM also launched the first truly Interprofessional Fellowship program under the direction of Low Dog. In this program, medical and osteopathic physicians, pharmacists, licensed acupuncturists, masters-prepared nurses, psychologists, and many other professionals train side by side academically and in clinical settings. "The AIHM Interprofessional Fellowship Program will provide a much-needed framework for a bold, paradigm-shifting approach to clinical practice and outcomes research," said Guarneri. "It will give rise to next-generation, interprofessional collaborations, and activate fundamental, systemic change. Note that the fellowship qualifies MDs and DOs for the ABOIM exam."

The Interprofessional Fellowship is a two-year, graduate-level training program for integrative clinicians. It combines a virtual classroom of media-rich training, discussion groups, and an interactive Web-based curriculum with in-person residential retreats and clinical immersion experiences. The executive-delivery model allows clinicians to live and work in their current location.

"We must consider the social conditions that perpetuate disease, and the undeniable connection between the health of our planet and ourselves," Low Dog said. "Through the fellowship program we will nurture clinicians who are trained to work together in order to use safe, lower-cost interventions for prevention and, when appropriate, treatment of disease."

To support the fellowship program, AIHM has partnered with the Oregon Collaborative for Integrative Medicine (OCIM), a nonprofit organization that includes the National College of Natural Medicine, Oregon College of Oriental Medicine, Oregon Health & Science University, Pacific University, and the University of Western States. OCIM has been committed to integrative education, research, and patient care for more than 25 years. "Our first class began early in February, and we're already accepting applications for the next class, which will start in August, 2016." Guarneri said.

Daniel Friedland, MD

A New, United Voice on the National Scene

Over the past decade, integrative medicine has expanded nationally and been recognized by prestigious medical centers. Leading academic hospitals including the Mayo Clinic, Yale, and Duke now boast top-notch integrative medicine centers, and many accredited MD programs incorporate integrative medicine into their course of study.

Section 2706 of the Affordable Care Act mandates "Non-Discrimination in Healthcare," saying that any health plan or health insurance issuer offering health insurance coverage "shall not discriminate with respect to participation under the plan or coverage against any health-care provider who is acting within the scope of that provider's license or certification under applicable state law." However, making that section of the law a reality requires constant public pressure on the state and local level.

In the past, while organizations representing specific providers have advocated for appropriate insurance coverage under the law, there hasn't been a strong unified public voice representing all of those who are committed to integrative medicine.

In 1983, I served on the administrative staff of the Oregon Senate Health and Human Services Committee. I recall that when a bill came up that affected several different health-care professions, and they all agreed on an appropriate action, legislators were eager to respond to their needs. On the other hand, when the professions did not agree, those bills were likely to languish in committee, and die at the end of the legislative session.

Now AIHM will be able to help unite those who support a transformed, patient-centered, wellness-focused health-care system. AIHM is a 501(c)3 organization, which means that it can carry out educational and lobbying activities within certain limits. It is working together with the Integrative Health Policy Consortium (IHPC), a 501(c)4 organization which will be able to take a broader political role.

"While non-discrimination is now the law, it is not widely enforced," Friedland said. "At our last AIHM conference we found many people attending had never heard of Section 2706, even though many of them would benefit from it. We need to educate our members and the general public about these issues. Section 2706 provides all with a choice in selecting qualified health practitioners and disciplines. Over time, IHPC is engaging in a strategy to reach decision makers who can make non-discrimination a reality."

In addition, AIHM encourages gatherings in local areas. "We've been working to form local chapters because so many things are best done at the local level," Friedland said. "In each town, practitioners will have the option to get together on a regular basis, to network with others as well as find opportunities to work together in common cause."

AIHM also partners with a wide variety of organizations through its Association Leadership Council, which offers a networking platform, shared communications, and many ways to participate in a robust dialogue on advocacy in health and medicine. Current members of the Council include academic institutions, professional associations, the American Academy of Environmental Medicine, the Institute for a Sustainable Future, Integrative Medicine for the Underserved, the National Consortium for Credentialing Health & Wellness Coaches, and many more.

All these new forums for communication and partnership lead to a hopeful future for integrative medicine. "We now have an opportunity to work for a shared vision that will empower people to be involved in their own health-care decisions, that will promote and restore their health," Low Dog said. "We will recognize, respect and actively engage the wide range of health professions that can play a role in improving lives."

Pathways to Healing

A basis of deep respect for the healing professions underlies the academy's fellowship program, which fosters collaborative training and a team-based approach to healing. "In this new era of interprofessional collaboration, the paradigm is shifting," Friedland said. "Our focus will be on health creation to promote optimal wellness and well-being, in both the presence and absence of disease."

Resources

AIHM Annual Conference: People, Planet, Purpose
www.aihm.org
The next AIHM annual conference, "People, Planet, Purpose" will be held at the Paradise Point Resort and Spa in San Diego. It runs from October 30 to November 3, with preconference workshops scheduled on October 29. The event features many sessions on self-care for health-care practitioners, plus a luncheon focused on the Fellowship program. AIHM is partnering with the University of California, San Diego, for the conference, and registration opened in April. In addition, there will be a postconference workshop on consciousness, featuring Deepak Chopra, MD, as keynoter. The postconference workshop is a collaborative effort with Shamini Jain, PhD, and the Consciousness and Healing Initiative (CHI).

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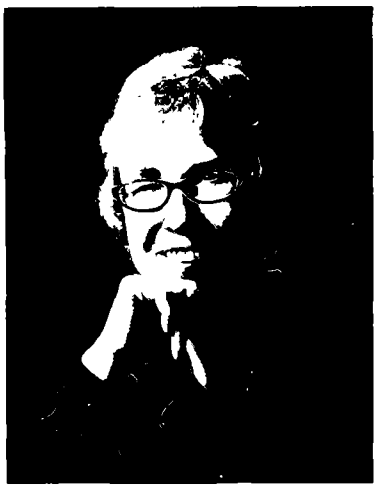
Article
Riley DS et al. The Academy of Integrative Health and Medicine and the evolution of integrative medicine practice, education, and fellowships. *Integr Med*. February 2016.38–40. http://www.imjournal.com/index.cfm/fuseaction/Content.Main/id/81/FeaturedArticle

Elaine Zablocki has been a freelance health-care journalist for more than 20 years. She was the editor of *Alternative Medicine Business News* and *CHRF News Files*. She writes regularly for many health-care publications. ◆



Shorts

briefed by Jule Klotter
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Ginger Extract and Kidneys

In animal studies, ginger has protected kidneys against injury from numerous insults, including ischemia/reperfusion, alcohol, streptozotocin, and carbon tetrachloride. Ginger has analgesic, anti-inflammatory, and antioxidant properties. Hypothesizing that ginger root extract might also protect against metabolic syndrome-associated kidney damage, Ming Yang and colleagues conducted a controlled experiment with rats. In earlier animal studies, Yang et al. had found that ginger improved fructose consumption-induced fatty liver and adipose tissue insulin resistance. Renal injury is another dysfunction observed in animals with metabolic syndrome. Chronic kidney disease has also been associated with metabolic syndrome in humans in the 2004 NHANES III study (National Health and Nutrition Examination Survey) and a 2005 California-based study led by M. Kurella (*J Am Soc Nephrol.* 2005;16:2134–2140).

Yang et al. divided 24 rats into four groups: drinking water control, 10% fructose drinking solution control, fructose drinking solution + ginger 20 mg/kg (by gavage), and fructose drinking solution + ginger 50 mg/kg (by gavage). Blood samples were taken after 4 weeks to measure total cholesterol, triglycerides, glucose, and insulin. A week later, the animals were killed, and kidney and epididymal fat tissues taken.

Slides of the tissue samples showed that 5-week fructose consumption produced changes in kidneys that included tubular damage in the cortex and outer stripe of the medullas and excessive interstitial collagen deposits. At this point, alterations in kidney function, as indicated by BUN and plasma creatinine, were minimal. "Supplementing with a ginger extract (50 mg/kg) attenuated the proximal tubular damage and interstitial fibrosis in the kidneys and these effects were accompanied by improvements in hyperinsulinemia and hypertriglyceridemia," Yang et al. report. The lower dose of ginger had no effect. The researchers say that ginger appears to suppress the kidney's overexpression of macrophage-associated pro-inflammatory cytokines, induced by the fructose solution.

Yang M, Liu C, Jiang J, et al. Ginger extract diminishes chronic fructose consumption-induced kidney injury through suppression of renal overexpression of proinflammatory cytokines in rats. *BMC Complement Altern Med.* 2014,14:174

Magnesium and Cardiovascular Health

"In a sample of Mexican-mestizo subjects, low serum magnesium was independently associated to higher prevalence not only of hypertension and [type 2 diabetes], but also to coronary artery calcification, which is a marker of atherosclerosis and a predictor of cardiovascular morbidity and mortality," according to a 2016 study in *Nutrition Journal.* Magnesium takes part in numerous biochemical processes including ATP transfer reactions. This mineral is necessary for cardiovascular health as it modulates vasomotor tone, blood pressure, and peripheral blood flow. In addition, animal studies show that magnesium deficiency produces endothelial dysfunction and systemic inflammation.

The 2016 study is a cross-sectional analysis of 1276 Mexican-mestizo participants, aged 30 to 75 years, who were control subjects in the Genetics of Atherosclerotic Disease (GEA) study. These participants had no personal history of cardiovascular disease and no family history of premature heart disease. All GEA participants completed questionnaires about family history, diet, physical activity, medications, smoking, alcohol intake, and demographics. Other measures included blood pressure, weight, BMI, and blood levels of magnesium and CV-related factors (e.g., cholesterol, triglycerides, plasma glucose, insulin, apolipoproteins A and B, creatinine, uric acid, aspartate aminotransferase [AST], alanine aminotransferase [ALT], and C-reactive protein). After adjusting for confounders, participants with the highest serum magnesium levels (fourth quartile) had 48% lower odds of hypertension ($p = 0.028$), 69% lower odds of type 2 diabetes ($p = 0.003$), and 42% lower odds of a positive coronary artery calcification ($p = 0.016$) compared with those in the lowest quartile.

The authors state that the cross-sectional design "does not ... establish causal or temporal relationships between serum magnesium and coronary artery calcification," and the association between magnesium deficiency and arterial calcification may not hold true for people with a different ethnicity. Still, this study provides another bit of evidence for something that many practitioners have already observed: magnesium is necessary for cardiovascular health.

Posadas-Sánchez R, Rosadas-Romero C, Cardoso-Saldaña G, et al. Serum magnesium is inversely associated with coronary artery calcification in the Genetics of atherosclerotic Disease (GEA) study. *Nutr J* 2016;15:22

Statins and Heart Disease

Cholesterol-lowering statin drugs, which are supposed to reduce the risk of heart disease, actually contribute to heart failure and atherosclerosis, according to a 2015 Japanese pharmacological review. Skeletal muscle weakness and pain are recognized adverse effects, but the heart is a muscle too. In their paper, Harumi Okuyama, PhD, and colleagues explain that statins impair muscle function, including heart and blood vessel muscles, by inhibiting ATP production, accelerating arterial calcification, and decreasing antioxidant protection.

Statins inhibit CoQ10 and "heme A" biosynthesis, compounds required for ATP generation and mitochondrial maintenance and repair. ATP energy fuels cellular metabolism and is vital for normal heart function. Okuyama and colleagues say that the limitation on ATP caused by statins "could be a major cause for heart muscle and coronary artery damage." In addition to being necessary for ATP generation, CoQ10 in its reduced form (ubiquinol) helps protect mitochondrial DNA from oxidative damage. Consequently, statin use decreases mitochondrial DNA levels and the concentration of mitochondria in muscle.

In addition, statins promote arterial calcification by inhibiting the conversion of vitamin K1 to vitamin K2. Vitamin K2, an enzyme cofactor, is needed to convert Gla protein into a form that binds calcium, protecting blood vessels from calcification. Statin users have more calcium-containing coronary plaques than nonusers in clinical trials.

Statins also inhibit the biosynthesis of selenium-containing proteins, such as glutathione peroxidase, an enzyme that detoxifies peroxides as part of the body's cellular antioxidant defense. Glutathione peroxidase activity is inversely associated with coronary heart disease events. Patients with high quartile of red blood cell glutathione peroxidase activity were the ones most likely to have event-free survival during a 5-plus year follow-up, according to a 2003 *New England Journal of Medicine* study led by S. Blankenberg. Selenoproteins also take part in glucose metabolism, which may explain the increased incidence of diabetes among statin users.

Although statins have been recommended for people with familial hypercholesterol, Okuyama and colleagues indicate that these patients are more vulnerable to decreased ATP generation and cell damage that contribute to heart disease. People with familial hypercholesterolemia have impaired LDL-receptor function, which restricts transport of nutrients needed for ATP generation and cellular repair. German pathologist Walter Hartenbach found evidence that arterial cellular damage, not cholesterol accumulation and fatty plaques, is the initial pathology in these patients. Statins' inhibition of CoQ10 and heme A biosynthesis further impairs cellular energy supplies.

Medical literature contains several reports of deterioration in cardiovascular function within months of beginning statin treatment, according to Okuyama and colleagues. Some patients developed diastole impairment after a few months on the drugs, an early sign of congestive heart failure. (Diastole is ATP dependent.) Others developed a significant increase in brain natriuretic peptide (a well-known marker for congestive heart failure) and CoQ10 after 3 months of atorvastatin treatment. In most cases, symptoms are reversed with CoQ10 supplementation and by eliminating the statins. Long-term statin treatment, however, can lead to "overt and often permanent congestive heart failure." Okuyama and colleagues report 130 cases of statin cardiomyopathy within 4 years at a solo cardiology practice. These patients developed heart function impairment after commencing statin therapy.

In an interview with Kirk Hamilton, Okuyama said, "I can propose no safe and effective means to protect from the side effects of statins. Instead, I recommend those taking statins to start discussing with their doctors that they replace their statins with safer omega-3 fatty acids." He also urged health professionals to be more critical of practice guidelines that are based on flawed, industry-run studies and study abstracts that do not accurately reflect text content.

Blankenberg S, Rupprecht HJ, Bickel C, et al Glutathione peroxidase 1 activity and cardiovascular events in patients with coronary artery diseases *N Engl J Med.* 2003;349(17) 1605–1613

Hamilton K, Okuyama H Atherosclerosis and heart failure stimulated by statins [interview)] December 2015. Available at www prescription2000 com

Okuyama H, Langsjoen PH, Hamazaki T, et al Statins stimulate atherosclerosis and heart failure. pharmacological mechanisms. *Exper Rev Clin Pharmacol* March 2015,8(2) 189–199

Vaccines and Renal Function

In 2009, board-certified nephrologist Suzanne Humphries encountered a 56-year-old patient who developed kidney failure within 2 weeks after receiving the H1N1 vaccine. The man, whose kidneys had functioned normally before the vaccine, told her, "'I was fine until I had that flu shot. ...'" After 3 weeks of dialysis, he regained 70% of his original kidney function.

Instead of assuming that the vaccine had no part in the patient's sudden downturn, Humphries began asking other patients when they had last been vaccinated. As she relates in the YouTube video "Vaccines-Honesty vs. Policy," Humphries came across several people, in ages ranging from 32 to 76 years, with normal kidney function who suddenly developed severe kidney damage that required dialysis within days or weeks after receiving H1N1, seasonal flu, and/or pneumonia vaccines. "On the other hand no patients were dialyzed, in my eleven years of service at this hospital, simply after a case of influenza," she writes in a referenced 2011 article. "We can see patients develop renal failure during flu-like illnesses – but almost exclusively only if they are prescribed and take large doses of NSAID pain medicine (e.g., ibuprophen), Angiotensin-Converting Enzyme Inhibitors (blood pressure drugs), Angiotensin Receptor Blockers, and/or they were severely volume depleted (dehydrated)."

Nothing in Humphries's medical background or training caused her to question the safety of vaccines for her patients. Like most doctors, she "accepted vaccines as safe and effective ... except perhaps in a very small minority of people – maybe one in a million." She realized that the kidney failure that she had observed could be unrelated to vaccination. Still, the incidence was high enough for her to begin researching medical literature. Although she did not find conclusive data, Humphries did find plenty of smoking guns in the literature that made her skeptical of the hospital policy to give a flu vaccine upon admission. "Vaccines are designed to create a state of inflammation, and raise LDL and CRP levels," she writes. "Why then would we give a vaccine to a patient who already has an inflammatory kidney or heart event?" Moreover, vaccines have several components known to be toxic to the kidneys.

Aluminum compounds, found in many vaccines including the pneumococcal conjugate vaccine, "hyperstimulate" the immune response to vaccine antigens. Aluminum is toxic to kidney

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patients on dialysis, which is why treatment water is screened for aluminum contamination. This metal causes granuloma formation, characteristic of some kidney diseases. Humphries writes, "... there is no certainty that aluminum in vaccines is not the cause of many occult or idiopathic kidney problems."

Mercury, found in the preservative thimerosal, is in multidose influenza vaccines. Each adult dose of Fluzone, manufactured by Sanofi Pasteur, contains 25 mcg of mercury, according to the FDA. Mercury accumulates in organs, particularly the brain and kidneys. It is known to contribute to hypertension, proteinuria, renal tubular necrosis, renal failure, and many other dysfunctions.

Phenol, used to inactivate vaccine bacteria and viruses, damages the kidneys, liver, and central nervous system. The EPA limit for phenol in lakes and streams is 21 ppm. Adult pneumonia vaccines contain 2500 ppm, according to Humphries.

In addition to toxic chemicals, vaccines contain viruses from animal organs used during manufacturing. Some of these viruses are known to cause cancer and other diseases in humans. The simian virus 40 (SV40), for example, is a polyoma virus found in the monkey kidneys used to make polio and smallpox vaccines. SV40 has been associated with two kidney diseases: focal and segmental glomerulosclerosis (FSGS) and tubular necrosis. "Vaccines are tested for occult viruses, and if they are not found are considered 'specific-pathogen free,'" Humphries writes. "But vaccines can only be tested for viruses that are known, and for which a test has been developed."

In addition to finding information about vaccine contents, Humphries found case reports linking kidney damage and vaccines in the medical literature. A 2013 article, for example, presents two case reports of antineutrophil cytoplasmic antibody-associated vasculitis (AAV) with renal involvement that arose 2 to 4 weeks after receiving flu vaccination. The authors reported finding six other cases of AAV that arose after flu vaccination in the medical literature. "A causal role of vaccines in AAV cannot be confirmed with these case reports," the authors write. "The temporality suggests that the influenza vaccine may be a triggering factor for induction of vasculitis in predisposed individuals."

More data are needed – which means that clinicians, researchers, and health agencies need to be open-minded enough to consider the possibility that vaccines might compromise kidney function. Despite her own observations and her search in medical literature, Humphries was unable to convince hospital administrators to set aside their standing order for flu vaccination upon hospital admission and delay vaccination until discharge day.

Humphries writes: " ... at the very least for kidney patients, vaccination recommendations and assumptions have outpaced their science base. It therefore rests on the shoulders of health care providers who wish to give the best possible care, to individualize treatment for those patients for whom data is absent, incomplete or questionable. Physicians are free to individualize medical care and that includes vaccination, but in order to do so they must independently research the very real risks involved in assembly-line vaccination."

Duggal T, Segal P, Shah M, el al. Antineutrophil cytoplasmic antibody vasculitis associated with influenza vaccination *Am J Nephrol* August 2013,38:174–178

Humphries S Vaccination and renal patients a critical examination of assumed safety and effectiveness [online article]. International Medical Council on Vaccination October 4, 2011 Available at www.vaccinationcouncil org

Vitamin K2 and Arterial Stiffness

Vitamin K2 is a necessary cofactor for preventing calcification in soft tissue including arterial vessels. This vitamin, composed of several compounds called menaquinones, is transported by low-density lipoproteins to vessel walls, where it activates matrix Gla-protein (MGP), "the strongest inhibitor of soft tissue calcification presently known," according to Dutch biochemist Cees Vermeer. Vermeer and colleagues have found that the circulating inactive form of MGP (dp-ucMGP) is a clinically useful marker for evaluating vascular vitamin K2 status. Higher levels of dp-ucMGP (indicating less available vitamin K2) are associated with arterial calcification and stiffness and increased risk of cardiovascular-related death. Moreover, people who eat more menaquinone-rich foods have a lower risk of arterial calcification and coronary heart disease mortality, according to observational studies. Menaquinones are found in the Japanese food natto (fermented soybeans), fermented cheese, meat, and egg yolk.

While testing a menaquinone-7 (M-7) supplement for its effect on bone strength, Vermeer and colleagues noticed that it improved arterial stiffness in healthy postmenopausal women. Arterial stiffness is an independent predictor of CV disease risk. The 3-year, double-blind randomized clinical trial involved 244 healthy postmenopausal women between 55 and 65 years of age. Participants were randomly assigned to take a placebo capsule (n = 124) or a proprietary product containing 180 µg MK-7 (n = 120). Circulating blood markers, weight, height, and vascular characteristics were measured yearly. The researchers used echo-tracking to assess vascular characteristics of the common carotid artery and mechanotransducers applied to the skin to measure arm (crPWV) and carotid-femoral (cfPWV) pulse wave velocity.

After 3 years, arterial stiffness had decreased in the MK-7 group and slightly increased in the control (−0.67 ± 2.78 vs. +0.15 ± 2.51, respectively; p = 0.018). Women with more arterial stiffness at baseline showed the most response. The researchers observed no adverse effects from M-7 treatment in this population.

Because the number of participants was calculated to give results for a different primary outcome, the Dutch researchers are performing a confirmatory study involving men and women with high circulating dp-ucMGP levels, indicating an increased risk for arterial stiffness. While decreased arterial stiffness is a positive, reducing stiffness doesn't necessarily increase lifespan; the effect of M-7 supplementation on cardiovascular events and life expectancy needs to be tested as well.

Hamilton K, Vermeer C Cardiovascular disease, arterial calcification and vitamin K2 September 2015 www prescription2000 com

Knapen MHJ, Braam LAJL, Drummen NE, et al Menaquinone-7 supplementation improves arterial stiffness in healthy postmenopausal women double-blind randomized clinical trial *Thromb Haemostas* February 19, 2015,113(5)

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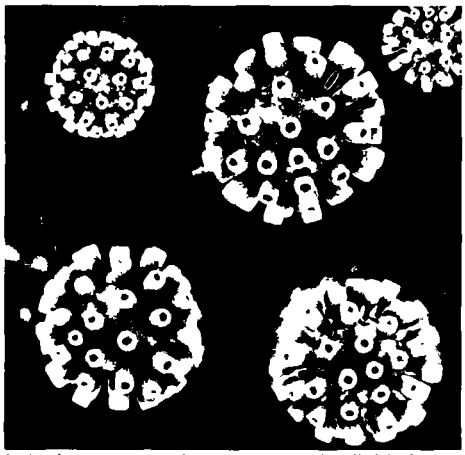
The All-Natural Alternative for Liver Health and Hepatitis C

Recently, the FDA approved new cures for hepatitis C which have a success rate of 80-90% in as few as 12 weeks of treatment. It sure sounds like good news, but these drugs are so costly, some insurance companies will only cover them for the sickest patients, and the VA admits it can't afford the drugs for their patients. With an estimated 130-170 million individuals chronically infected worldwide, hepatitis C is a major public health problem. So, how do you offer hope to your hepatitis C and cirrhosis patients who can't afford the high cost of medication or a transplant?

The good news is that research focusing on safe and affordable natural products with activity against the hepatitis C virus has revealed the antiviral activity of the lactoferrin protein which binds and neutralizes the circulating virion. Lactoferrin for the management of viral infections is hardly a new concept, but it's only part of the story. For true healing to occur, a patient's leaky gut must be healed FIRST with bovine colostrum. It is imperative to halt the massive crossover of toxins into the bloodstream, and colostrum assists by three primary mechanisms. First, immunoglobulins and antibodies destroy gut-based pathogens. Second, proline-rich polypeptides modulate the immune system to fight off viral infections and quell inflammation. Third and most importantly, colostrum's growth factors close the leaky gut so that none of the pathogens or the toxins produced by the pathogen die-off can enter the bloodstream. Only after the liver is relieved of its overwhelming burden of detoxifying the body, does it have a chance to regenerate itself. At this point, the growth factors repair RNA and DNA, stimulate stem cell production, and influence stem cell differentiation.



Bovine colostrum contains high concentrations of lactoferrin, immune and growth factors which give the liver its best opportunity to heal itself once. Colostrum is not a cure for the scourge of hepatitis, but it can help the body manage the infection, thereby avoiding a costly or hard-to-find transplant. Absolutely no other substance on earth can provide these healing benefits. That's why we call it "nature's healing miracle."

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Viralox contains Lactopeptide, a proprietary concentration of PRPs and lactoferrin peptides, which has been clinically proven to eliminate viral infections. The added benefit is that Viralox helps (1) produce immunity to viruses and activate memory cells to shorten response time, if a future viral attack occurs, and (2) assists the immune system to adapt to viral mutations.

For more information, visit ColostrumTherapy.com (for professionals) or CenterforNutritionalResearch.org (for consumers).

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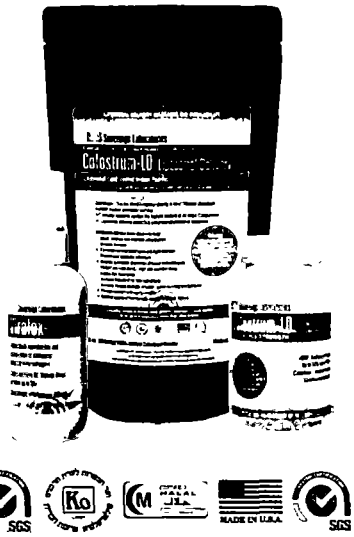

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by Ingrid Kohlstadt MD, MPH
www.INGRIDients.com

New Research Questions Proton Pump Inhibitors' Use

Are the stomach medications called proton pump inhibitors right for you? New findings throw a curveball worth discussing with your doctor

Statistics is common ground for baseball and medicine, as both seek to play the averages. Baseball catcher Yogi Berra (1925–2015) may have put it best, "It's tough to make predictions, especially about the future."

Benjamin Lazarus, MBBS, of Johns Hopkins University and his all-star coauthors rose to Berra's challenge. Their *JAMA Internal Medicine* article "Proton Pump Inhibitors and Chronic Kidney Disease" links long-term use of a common stomach medicine to kidney disease. While additional studies will help in understanding the connection, Lazarus's team found something that can help doctors and their patients "play the averages" about whether to take proton pump inhibitors (PPIs).

How serious is the risk of this medicine to the kidneys? Says Lynda Frassetto, MD, nephrologist and professor of medicine at UCSF for additional perspective, "When I was a medical doctor in training in the 1970s, it was tragically common that people died from bleeding ulcers in the emergency room. That hardly happens anymore because of proton pump inhibitors." So how can we predict when the risks outweigh the potentially life-saving benefits? Frassetto explains "There's no straightforward answer." There are however, four ways that the Lazarus study helps us optimize health outcomes.

PPIs are linked to kidney damage that is difficult to detect early in the process. The Lazarus study reminds clinicians to look more closely for subtle early warning signs. Early diagnosis is a physician's equivalent of a baseball player's great catch ending a play that might otherwise have finished in a grand slam for the opposing team. PPIs are theorized to damage the kidneys by causing repeated episodes of an inflammatory allergic reaction called interstitial nephritis. Interstitial nephritis is diagnosed based on a needle biopsy of the kidney. Since biopsy is not a routine procedure, first a clinician would need to suspect that there is a kidney problem. Suspecting interstitial nephritis is difficult because it lacks clear symptoms for a patient to report to their doctor, and routine kidney blood tests can be in the normal range. Blood tests are more likely to indicate a problem when compared to prior labs. Based on the Lazarus study, practitioners may want to zoom in on even normal range kidney function tests in their patients taking PPIs, especially if the patients are also taking aspirin

and antibiotics, other medicines associated with interstitial nephritis.

The Lazarus study reassures us that the overall chances of developing kidney disease from PPIs are fairly small. Sizing up the risk is especially important for patients with multiple medical conditions. When it comes to medication side effects, the people who have the most risk of side effects often derive the most benefit. Dr. Frassetto maintains that this is the case here. People with preexisting kidney disease from high blood pressure and diabetes are more likely to develop bleeding stomach ulcers, against which PPIs protect.

The Lazarus study gives prescribing doctors and over-the-counter users yet another reason to read the package insert. Most people taking PPIs (up to 70% in this study) aren't taking them for the right reasons and often incorrectly.[1] But why would people disregard the FDA's best prediction? Perhaps they think it's too restrictive. This study wouldn't support that argument and neither would a concurrently published article in *Science* with unexpected relevance.[2] It's an autopsy report on the world's oldest patient, Ötzi the Iceman, preserved in Alpine ice for 5300 years. Ötzi was infected with the bacterium associated with stomach ulcers, and PPIs would have been indicated were he a patient today. Yet his stomach showed no signs of ulceration. If he had been taking a PPI, he wouldn't have had enough stomach acid to digest the large portion of ibex meat also found in his stomach. If Ötzi didn't need PPIs, maybe we don't either, at least not for reasons off the list.

"The [Lazarus] study reminds us to periodically reevaluate the need for a medication, even one a patient has been taking for years," explains Dr. Frassetto. It estimates that 1 in 4 longtime PPI users could stop therapy and remain symptom free, especially if they take Yogi Berra's famous advice, "When you come to a fork in the road, take it." In other words, if you can improve your health by changing what you put on your fork – take the fork instead of the medicine! The recently released US dietary guidelines similarly advise Americans to pay attention to "home plate."[3]

The most compelling reason to quit unnecessary PPIs may be that across all mammals, waning stomach acid is a sign of old age. While science has assumed that it's old age which causes stomach acid production to decline, it could be the other way around, too. New understanding of the microbiome adds plausible mechanisms by which *inadequate* stomach acid could contribute to aging. If that's the case, PPIs are indeed a curveball, but it's possible to be a home-run hitter – especially if you *ask your doctor the right questions*.

Notes

1. Gunaratnam NT, Jessup TP, Inadomi J, Lascewski DP. Sub-optimal proton pump inhibitor dosing is prevalent in patients with poorly controlled gastro-oesophageal reflux disease. *Aliment Pharmacol Ther.* 2006,23(10):1473–1477. http://www.medscape.com/viewarticle/531605_4.
2. Gibbons A. The Iceman had a tummy bug *Science.* Jan. 7, 2006 Available at http://www.sciencemag.org/news/2016/01/iceman-had-tummy-bug
3. U.S. Department of Health and Human Services and U.S. Department of Agriculture *2015 – 2020 Dietary Guidelines for Americans.* 8th ed. December 2015. Available at http://health.gov/dietaryguidelines/2015/guidelines.

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Literature Review & Commentary

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

B Vitamins Prevent Thrombotic Episodes at High Altitudes

Twelve thousand newly inducted Indian soldiers who were scheduled to be stationed at a height greater than 3500 m above sea level were randomly assigned to receive, in double-blind fashion, daily folic acid (5 mg), vitamin B12 (1,000 µg), and vitamin B6 (3 mg) or placebo. After 1 year, the mean plasma homocysteine concentration was significantly lower in the vitamin group than in the placebo group (11.0 vs. 15.1 µmol/L; $p < 0.001$). After 2 years, the number of thrombotic episodes was significantly lower by 71% in the vitamin group than in the placebo group (5 vs. 17).

Comment: Prolonged stay at high altitude and hyperhomocysteinemia are each associated with an increased risk of thrombosis. Folic acid, vitamin B6, and vitamin B12 have been shown to lower homocysteine levels. The results of the present study indicate that supplementation with these vitamins can reduce homocysteine levels and prevent thrombotic episodes in soldiers stationed at high altitudes for prolonged periods of time.

Kotwal J et al Effectiveness of homocysteine lowering vitamins in prevention of thrombotic tendency at high altitude area. A randomized field trial. *Thromb Res*. 2015,136.758–762

Does Eating Sugar Contribute to Heart Failure?

The association between consumption of sweetened beverages and risk of heart failure was examined in a population-based prospective cohort study of 42,400 Swedish men (aged 45–79 years). During a mean follow-up period of 11.7 years, a total of 4113 heart failure events were identified. After adjustment for other risk factors, there was a significant positive association between consumption of sweetened beverages and risk of heart failure (p for trend < 0.001). Men who consumed 2 or more servings of sweetened beverages per day had a significant 23% higher risk of developing heart failure, compared with men who did not consume sweetened beverages.

Comment: Observational studies cannot prove causation. However, there are a number of plausible mechanisms by which excessive sugar consumption could promote the development of heart failure. For example, eating too many sweets may lead to insulin resistance, which is a risk factor for heart failure. In addition, consumption of empty calories reduces overall intake of vitamins, minerals, and accessory food factors, many of which play a role in healthy cardiac function. Moreover, sugar consumption may promote or exacerbate periodontal disease, which is another risk factor for heart disease (possibly mediated by chronic inflammation). High sugar intake can also increase blood pressure, which places additional stress on the heart and increases the risk of developing heart failure.

Rahman I et al The relationship between sweetened beverage consumption and risk of heart failure in men. *Heart* 2015,101·1961–1965

Carnitine, Trimethylamine-N-Oxide (TMAO), and Cardiovascular Disease

Plasma levels of trimethylamine-N-oxide (TMAO) were measured in 339 patients undergoing coronary angiography for suspected coronary artery disease. Plasma concentrations of TMAO were higher in patients with diabetes than in those without diabetes, and increased significantly with decreasing renal function ($p < 0.001$). Plasma levels of TMAO were not associated with a history of myocardial infarction or with the presence of angiographically documented coronary heart disease. In addition, during an 8-year follow-up period, there was no association between baseline TMAO levels and risk of suffering a cardiovascular event, either in the unadjusted analysis or after adjustment for baseline HbA1c levels and renal function.

Comment: In April, 2013, a story was widely disseminated in the news media claiming that L-carnitine, a nutritional supplement that has been shown to be effective for preventing and treating cardiovascular disease, might actually cause heart disease. That conclusion was based mainly on the observation that carnitine can be L-converted by intestinal bacteria to the purportedly heart-damaging compound TMAO. The results of the present study do not support the concept that TMAO is cardiotoxic. L-carnitine has been shown in clinical trials to improve angina, intermittent claudication, and congestive heart failure. The bulk of the evidence suggests that the beneficial effects of L-carnitine outweigh any potential deleterious effect of its breakdown product TMAO.

Mueller DM et al Plasma levels of trimethylamine-N-oxide are confounded by impaired kidney function and poor metabolic control *Atherosclerosis* 2015;243 638–644.

continued on page 34 ➤

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Gaby's Literature Review

➤ *continued from page 32*

Acetyl-L-Carnitine for Hepatic Encephalopathy

One hundred twenty-one patients with overt hepatic encephalopathy (61 with HE1 [mild grade] and 60 with HE2 [moderate grade]) were randomly assigned to receive, in double-blind fashion, 2 g of acetyl-L-carnitine (ALC) or placebo twice a day for 90 days. In the HE1 group, compared with placebo, ALC significantly improved mental fatigue ($p < 0.05$), fatigue severity ($p < 0.001$), the 7-day Physical Activity Recall questionnaire score ($p < 0.001$), and Short Physical Performance Battery ($p < 0.001$). In the HE2 group, compared with placebo, ALC significantly improved fatigue severity ($p < 0.001$) and the 6-minute walk test ($p < 0.05$). The mean serum ammonia concentration decreased to a significantly greater extent in both active-treatment groups than in the respective placebo groups ($p < 0.001$).

Comment: Patients with hepatic encephalopathy frequently experience fatigue, possibly due to hyperammonemia. ALC may have a neuroprotective effect and, as a source of carnitine, may improve mitochondrial energy production and improve ammonia metabolism. In the present study, ALC decreased the severity of both mental and physical fatigue, increased physical activity, and decreased serum ammonia concentrations in patients with both mild and moderate hepatic encephalopathy.

Malaguarnera M, Vacante M, Giordano M, et al Oral acetyl-L-carnitine therapy reduces fatigue in overt hepatic encephalopathy: a randomized, double-blind, placebo-controlled study *Am J Clin Nutr.* 2011;93:799–808

Testing Vitamin D Levels in Patients with Cirrhosis

Of 82 patients with cirrhosis, 54 (66%) had a low serum albumin level and 28 (34%) had a normal albumin level. Compared with patients with normal albumin levels, those with low albumin levels had lower levels of vitamin D-binding protein, total 25-hydroxyvitamin D (25[OH]D), and free 25(OH)D. The expected relationship between total or free 25(OH)D and parathyroid hormone levels was observed in patients with normal albumin levels but not in those with low albumin levels.

Comment: In previous columns in the *Townsend Letter*, I have questioned the reliability of serum 25(OH)D as an indicator of vitamin D status. The results of the present study suggest that neither total 25(OH)D nor free 25(OH)D is an accurate indicator of bioactive vitamin D status in patients with cirrhosis and low albumin levels.

Lai JC et al. Total 25(OH) vitamin D, free 25(OH) vitamin D and markers of bone turnover in cirrhotics with and without synthetic dysfunction. *Liver Int* 2015;35:2294–2300

Selenium deficiency in patients with cirrhosis

Eighty-two patients with cirrhosis (Child-Pugh classes A, B, and C; mild, moderate, and severe, respectively) were randomly assigned to receive 200 or 400 mcg/day of selenium as selenate, 200 µg/day of selenium as selenomethionine, or placebo for 4 weeks. In class B patients, both doses of selenate, but not selenomethionine, increased glutathione peroxidase activity more than did placebo.

Comment: In previous research, circulating selenium levels were low in patients with cirrhosis, but the activity of the selenium-dependent enzyme glutathione peroxidase was elevated in these patients. The reduction in selenium levels appeared to be due largely to a decrease in the amount of selenomethionine incorporated into albumin (a form of selenium that is not biologically active). Investigators initially had thought that the high glutathione peroxidase activity in patients with cirrhosis argued against these patients' being selenium deficient. However, the finding from the present study, that selenium supplementation increased glutathione peroxidase activity in patients with cirrhosis, appears to indicate that these patients had a mild functional selenium deficiency. Selenium (200 µg/day) in the form of selenate increased glutathione peroxidase activity, but the same dose of selenium in the form of selenomethionine had no effect on glutathione peroxidase activity. The authors of this report suggested that cirrhosis results in impaired hepatic metabolism of selenomethionine to selenide (one of the biologically active forms of selenium). Thus, for patients with cirrhosis who require selenium supplementation, a form other than selenomethionine may be preferable.

Burk RF, Hill KE, Motley AK, et al Selenium deficiency occurs in some patients with moderate-to-severe cirrhosis and can be corrected by administration of selenate but not selenomethionine: a randomized controlled trial *Am J Clin Nutr.* 2015;102 1126–1133

Silymarin Prevents Drug-Induced Liver Injury

Fifty-five Thai patients with tuberculosis were randomly assigned to receive, in double-blind fashion, 140 mg of silymarin 3 times per day or placebo, in addition to a standard antituberculosis treatment regimen of isoniazid (5 mg/kg/day), rifampicin (10 mg/kg/day), pyrazinamide (25 mg/kg/day), and ethambutol (15 mg/kg/day). The incidence of drug-induced liver injury during the first 4 weeks (defined according to symptoms and elevation of liver enzymes) was significantly lower in the silymarin group than in the placebo group (3.7% vs. 32.1%; $p = 0.012$).

Comment: Silymarin is a flavonoid complex derived from milk thistle (*Silybum marianum*). Silymarin has antioxidant and hepatoprotective effects, and has been used to treat various liver diseases. The results of the present study indicate that silymarin can prevent drug-induced liver injury in patients being treated for tuberculosis. For every 100 patients treated with silymarin, 28 cases of drug-induced liver injury would be prevented.

Luangchosiri C et al A double-blinded randomized controlled trial of silymarin for the prevention of antituberculosis drug-induced liver injury *BMC Complement Altern Med.* 2015;15:334.

Vitamin E for Periodontal Disease

Thirty-eight patients with chronic periodontitis who were receiving standard dental care (scaling and root planing) were randomly assigned to receive or not to receive 300 IU of vitamin E every other day for 3 months. Compared with no vitamin E, vitamin E supplementation significantly improved median scores on various indicators of periodontal health, including plaque index, gingival index, bleeding on probing, and clinical attachment level.

Comment: In this study, vitamin E supplementation, when used as an adjunct to scaling and root planing, improved chronic periodontitis. Vitamin E probably worked by decreasing inflammation and promoting tissue healing. Other nutritional supplements that have been shown to improve gingivitis or periodontal disease include coenzyme Q10, vitamin C with flavonoids, and mouth rinses with folic acid (5 ml of a 0.1% solution, swished for 5 minutes, twice a day for 60 days).

Singh N et al. Vitamin E supplementation, superoxide dismutase status, and outcome of scaling and root planing in patients with chronic periodontitis a randomized clinical trial *J Periodontol.* 2014;85:242–249. ◆

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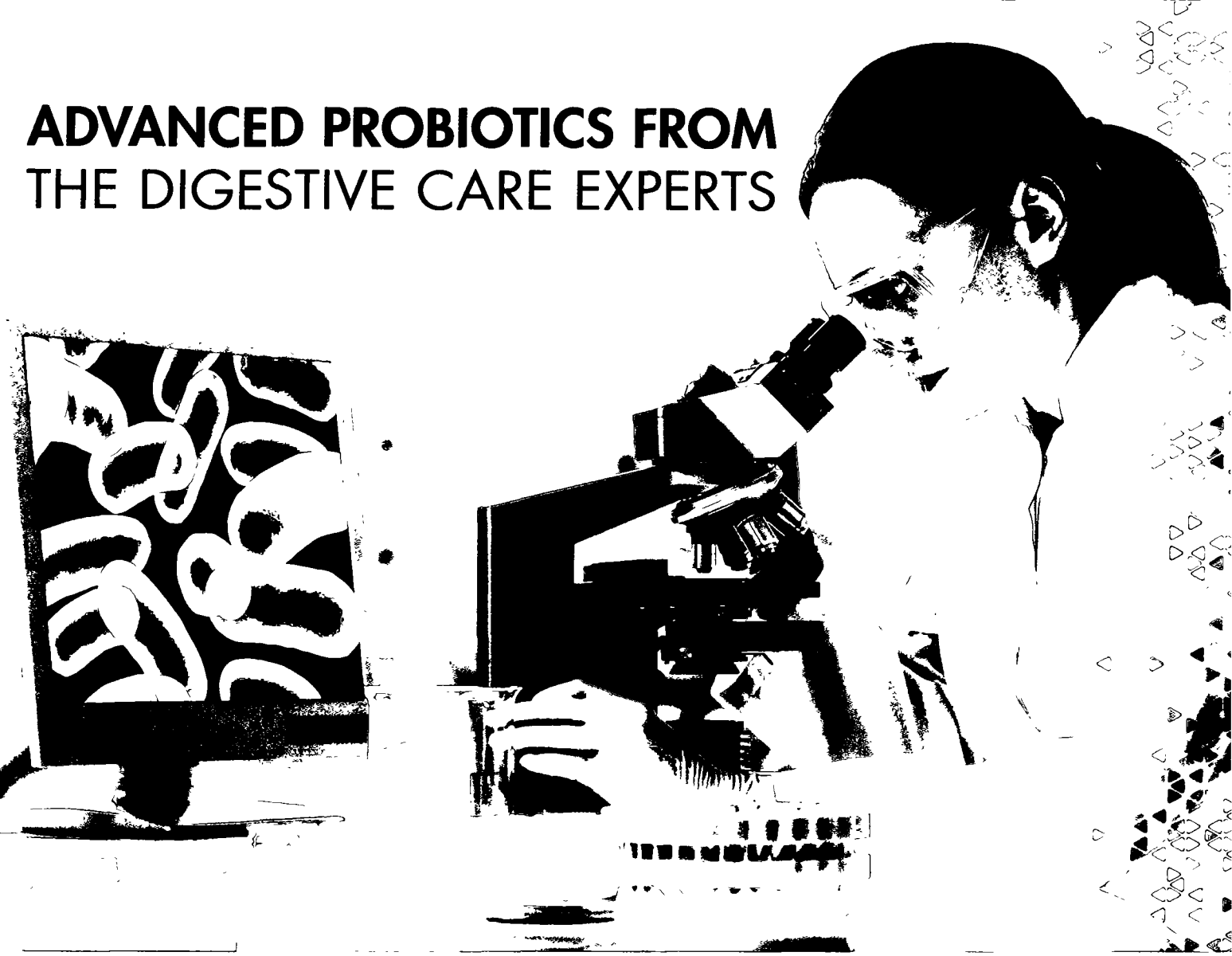

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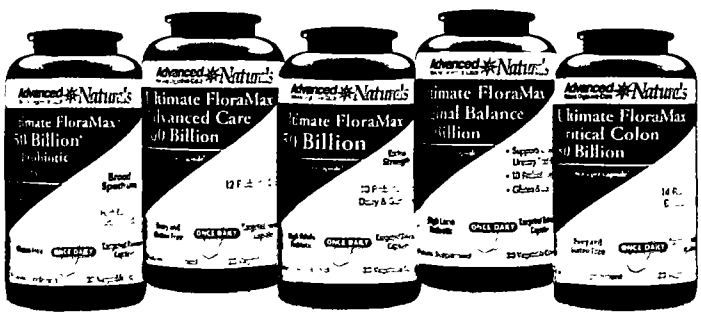

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AN-7425

Monsanto's Sealed Documents Reveal the Truth behind Roundup's Toxicological Dangers

by Richard Gale and Gary Null

Progressive Radio Network

The year 2015 wasn't kind to Monsanto. That March, the World Health Organization declared that the company's flagship product, its herbicide glyphosate or Roundup, is a probable human carcinogen. Increasingly, national health ministries are taking a hard second look at glyphosate's health and environmental dangers and efforts are underway to ban the herbicide.[1] To protect their citizens, last year the Netherlands, Bermuda, and Sri Lanka either banned or imposed strict limits on Roundup. Last June, France banned its use in gardens. Brazil, Germany, and Argentina are considering legislative bans. And in September, California's Environmental Protection Agency launched plans to label Roundup as a carcinogen.[2]

Glyphosate is the most widely used herbicide in the world today. Over 130 countries currently permit extensive use of the chemical. The US is the largest consumer, using approximately 20% of the world's Roundup.[3] The latest reliable figures from the US Geological Survey record that 280 million pounds of Roundup were used in 2012, nearly a pound for every American.[4] In 2013, gross profit of $371 million on crop chemicals including Roundup climbed 73% due to a 37% increase in sales. That same year Monsanto's net income rose 22% to $1.48 billion.[5]

Over the years, a large body of independent research has accumulated and now collectively provides a sound scientific rationale to confirm that glyphosate is far more toxic and poses more serious health risks to animals and humans than Monsanto and the US government admit. Among the many diseases and health conditions that nonindustry studies identified as associated with glyphosate are Alzheimer's, Parkinson's, and autism, since Roundup has been shown to instigate aluminum accumulation in the brain. The herbicide has been responsible for reproductive problems such as infertility, miscarriages, and neural tube and birth defects. It is a causal agent for a variety of cancers: brain, breast, prostate, lung, and non-Hodgkin lymphoma. Other disorders include chronic kidney and liver diseases, diabetes, heart disease, hypothyroidism, and leaky gut syndrome. In addition to lung cancer, glyphosate may be responsible for today's growing epidemics of chronic respiratory illnesses among farm workers and their families.[6] However, these findings derive from outside the Big Agriculture industry. Private industries routinely defend themselves by positing their own research to refute independent reports. Consequently, for several decades it has been a he-said/she-said stalemate. Monsanto is content with this. It can conduct business as usual, Roundup sales increase, and the debates and media wars continue without government interference. Then who is protecting the public?

Government officials and health regulators more often than not simply ignore these studies even if published in peer-reviewed journals. The bulk of the studies are independently funded. Most have been performed in foreign nations and therefore American bias dismisses them outright. Furthermore, Monsanto and other large chemical agricultural companies are quick to counter and discredit adverse scientific findings. The company has the financial means to retain large international PR firms, such as Burson-Marsteller and Fleishman Hillard, consultation firms and think tanks, as well as large armies of hired trolls and academic spokespersons to mobilize damage control upon notice and protect the integrity of Monsanto's products and public image. It funds and orchestrates self-serving research at universities and research laboratories to increase an arsenal of junk science. And of course it has Hillary Clinton and Bill Gates as its celebrity cheerleaders.

The EPA continues to align itself with Monsanto's safety claims and limits glyphosate's risks to kidney, reproductive, and carcinogenic damage; and the warning only applies for very long-term exposure to high levels of the toxin. Anything under that is considered harmless. The EPA continues to approve small amounts of glyphosate as safe in

continued on page 38 ➤

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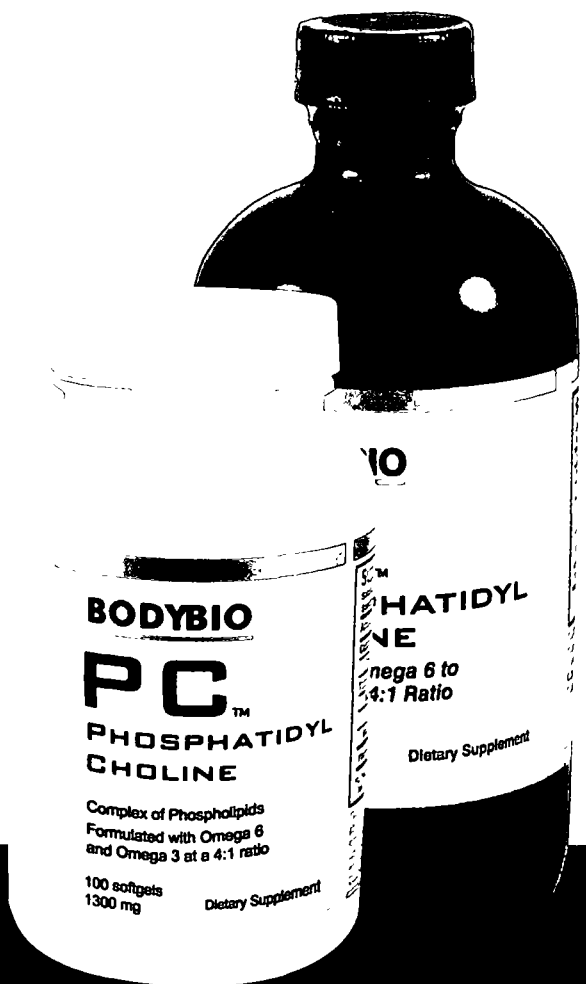

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Truth behind Roundup's Toxicological Dangers

➤ *continued from page 36*

drinking water to children. Its safety level is 0.7 ug/L. This was determined back in 1994, and after 20 years of further research into glyphosate's biomolecular activities and health risks, the level has remained the same.[7,8] A review of existing data sponsored by Moms Across America found that out of 21 drinking water samples analyzed, 13 had glyphosate levels between 0.08 and 0.3 ug/L, well below the EPA's limit, but significantly above the European Union's limit of 0.1 ug/L.[9]

While the company manages to successfully dodge scientific research outside its purview, the tables would certainly turn if it could be proved in a court of law that Monsanto has known for decades that glyphosate is one of the most toxic substances ever launched on the public, adversely affecting almost every tissue and cell in a mammal's body.

Imagine for a minute that evidence emerged to implicate Monsanto on a massive cover-up and manipulation of scientific data from hundreds of research trials. If it were Monsanto's data indicting itself about glyphosate's toxicity, and if it can be shown the company falsified, masked, or fudged its data to win regulatory approval, it may likely be the largest corporate scandal in history. The question: could Monsanto be charged with crimes of omission and more deservingly crimes against humanity?

This scenario may not be fantasy or the wishful thinking of GMO opponents. The case has a precedent and has been played out in the courts before. In November 1998, the US government won a judgment against the four largest US tobacco companies: Philip Morris, RJ Reynolds, Brown & Williamson, and Lorillard. The case came to trial after a former vice president of research and development at Brown & Williamson, Jeffrey Wigand, turned whistleblower and revealed that his company concealed the tobacco's health risks and was making concerted efforts to addict people to smoking. High-ranking executives were found to have approved the inclusion of known addictive and carcinogenic chemicals, such as coumarin, in its cigarettes to increase smoking, sales, and profits.

Before the trial there had never been a lawsuit lost by a tobacco company because no one could prove with absolute medical certainty that smoking had ever caused lung cancer or emphysema. During congressional hearings, all seven CEOs representing the four tobacco giants lied under oath, stating that they had no knowledge about an association between nicotine and brain addiction. Their rationale was that they believed that their research data and marketing strategies were protected under propriety secrecy claims and therefore they could avoid conviction. Although FDA scientists possessed all the necessary information that could condemn Big Tobacco's false claims, the industry relied upon proprietary rules in order to hide behind legal protection. The FDA was silenced and powerless to make the industry's information public. Consequently, it is estimated that millions of people died from a risk that could have been prevented or at least reduced substantially. Instead, the FDA honored the tobacco industry above all human life.

The guilty verdict, which resulted in the Tobacco Master Settlement Agreement against the tobacco companies, enforced a minimum $206 billion settlement over a 25-year period. While the majority of payments were to settle 46 states' Medicaid lawsuits to recover smoking-related health costs, the settlement unfortunately exempted the industry from private tort claims. Many critics of the agreement state that the settlement was too merciful. No tobacco executive went to prison, and evidence indicates the industry emerged stronger and consolidated the companies into an ever more powerful cartel.[10]

What busted the tobacco companies was not the scientific evidence piling up outside the industry. Rather it was its crimes of omission about cigarettes' health risks within the industry. The industry's own research prosecuted itself. And this is demanded today in order to bring down Monsanto's chemical regime and to protect populations and children throughout the world.

Perhaps we might want to consider the atmosphere that Monsanto faced after it first developed glyphosate in 1973 and prepare for EPA approval for the remainder of the decade.

During the latter half of the 1970s, Monsanto's leading products were under federal inquiry and public assault regarding safety. Dioxin had been banned. Safety concerns arose over its sweetener saccharin, and cyclamate was removed from the market. The company's attempts to get its new artificial sweetener aspartame approved confronted obstacles during FDA scientific review. Independent research had shown that aspartame caused brain tumors in mammals. And its best-selling herbicide at the time, Lasso, was showing signs of carcinogenicity. Today Lasso is a restricted-use pesticide due to its oncogenicity. With sales falling and future growth under threat, Monsanto faced a desperate need to launch a novel flagship product. Monsanto found itself banking its future on its new herbicide glyphosate. As we recently discovered, enormous amounts of research, analysis, and hundreds of trials were conducted to learn as much as possible about the compound's bioactivity in mammals and its potential health risks. All of this research data, studies, and reports were subsequently sealed as trade secrets upon submission to the EPA. For over 30 years, it has sat in the EPA vaults.

Monsanto has yet to be caught and charged for falsifying scientific data on glyphosate. However, on earlier occasions, two laboratories that Monsanto outsourced research to were caught and indicted. In 1978, the EPA busted Industrial Biotest Laboratories for rigging laboratory results; the company's executives were found

continued on page 41 ➤

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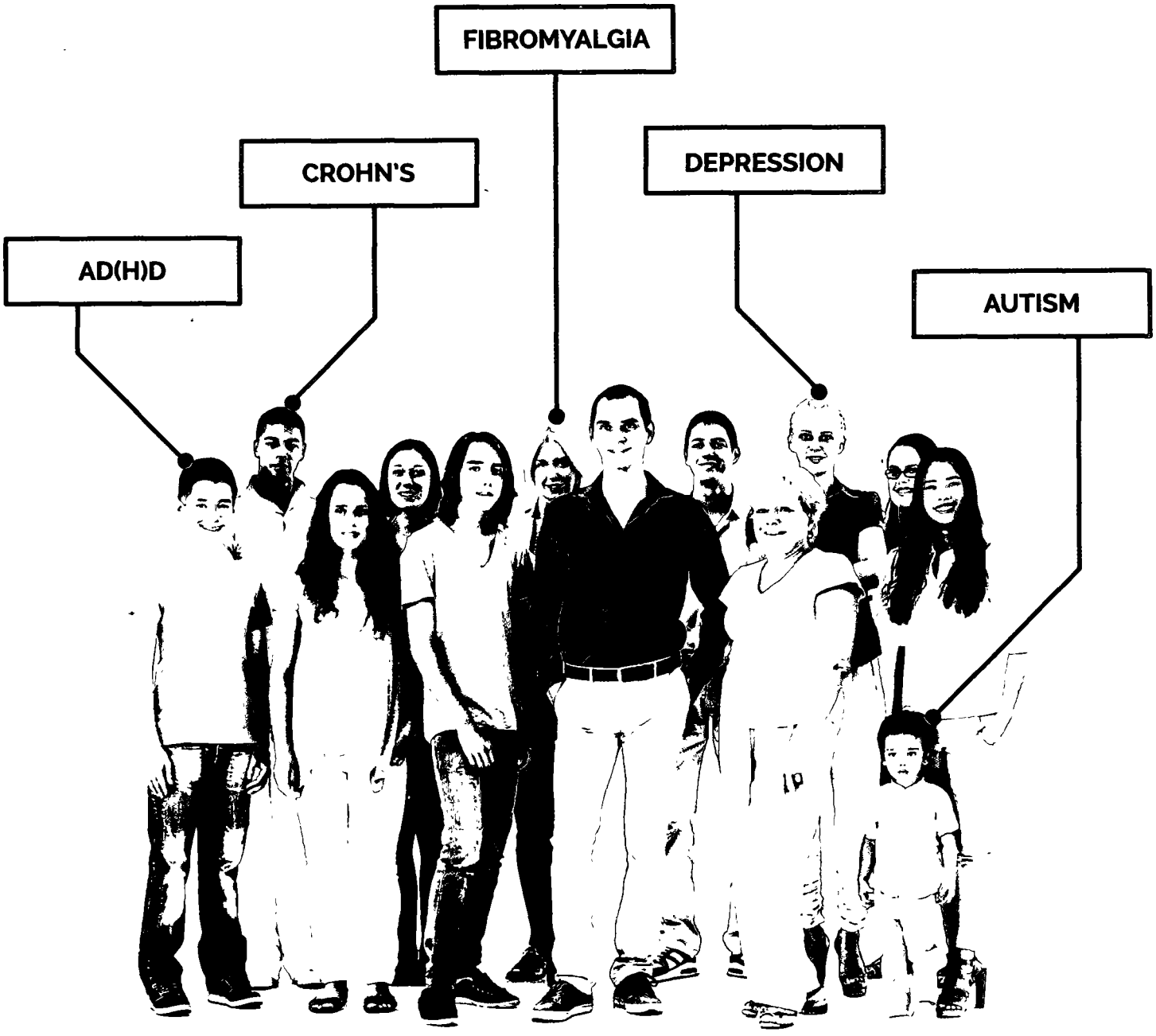

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Truth behind Roundup's Toxicological Dangers

➤ *continued from page 38*

guilty for submitting fabricated data supporting glyphosate positively to the government. In 1991, another firm, Craven Labs, was found guilty on similar charges with 20 felony counts.[11]

To this day, Monsanto continues to assert that Roundup is environmentally friendly. We are told that it biodegrades rapidly and therefore poses no long-term risks after repeated usage. We are told that the herbicide is ideal for weed control. Throughout the US, it is liberally sprayed on our public parks, school playgrounds, sporting fields, and lawns and gardens. We are told that it doesn't bioaccumulate in the body's cells and tissues and is excreted rapidly. We are also told that glyphosate toxicity is dose specific. Only exceedingly high levels of the pesticide pose any serious health risks.[12]

How factual are these claims? Or are they mere propaganda to obscure scientific truths far more deceptive and sinister? To answer that, we would have to know for certain whether Monsanto conducted long-term studies on glyphosate that revealed devastating toxic effects on mammal health. We would need evidence that its own data clearly negate its scientific declarations, and that the company intentionally, and with forethought, either distorted or concealed data from federal regulatory officials and the public.

There is now an enormous cache of evidence on both scientific and legal grounds that Monsanto in fact conducted numerous studies in the 1970s and 1980s on glyphosate's toxicity and health risks and intentionally sealed this research from independent and public review and scrutiny. As with Big Tobacco's proprietary claims that prevented the FDA from publicly warning Americans about the dangers of smoking, the EPA has sat on Monsanto's own deleterious data for decades.

Anthony Samsel is an independent research scientist working internationally in the interest of public health and the environment. He is a member of the Union of Concerned Scientists, and a former scientist and consultant at Arthur D. Little, one of the world's leading management consulting firms. Now retired, Samsel has devoted much of his independent research on Roundup's toxicological characteristics and bioactivity. Unable to gain access to research reports and data that Monsanto submitted to the EPA through FOIAs, he turned to his senator's office, which assisted in the procurement of studies and reports he sought. Months later he received a hoard of scientific documents, over 15,000 pages' worth, covering Monsanto's complete glyphosate research.

He and coinvestigator Dr. Stephanie Seneff of MIT have been reviewing Monsanto's data. Their conclusion is that Monsanto's claims about glyphosate's safety are patently false. The company has known for almost four decades that glyphosate is responsible for a large variety of cancers and organ failures. Clearly it was for this reason that Monsanto demanded that the data and reports be sealed and hidden from public scrutiny as proprietary trade secrets.

During an exclusive interview on the Progressive Radio Network on September 4, 2015, Samsel stated that Monsanto used an industry trick to dismiss evidence about glyphosate's risks in its own research. "Monsanto misrepresented the data," says Samsel, "and deliberately covered up data to bring the product [glyphosate] to market."[13]

To minimize and cancel out its adverse findings, Samsel explained, Monsanto had relied upon earlier historical animal control data, toxicological research with lab animals afflicted with cancer and organ failures, and completely unrelated to glyphosate. In some cases, the control animals displayed kidney, liver, and pancreatic diseases. Many of Monsanto's own studies required the inclusion of extraneous studies in order to cancel out damaging results. This is not an uncommon industry habit, particularly in toxicological science. It enables corporations to mask undesirable outcomes and make claims that observable illnesses and disease are spontaneous occurrences without known causal factors. Frequently, Monsanto would have to rely on three external control studies to negate the adverse effects of a single one of its own. Samsel found other incidences in Monsanto's data where 5, 7, and in one case 11 unrelated studies were necessary to diminish the severity of its own findings. In effect, glyphosate received licensure based upon a platform of junk tobacco science. By ignoring causal relationships behind the onset of multiple cancers and other life-threatening diseases throughout many of its research trials, Monsanto engaged in a radical scientific denialism that has since raked in tens of billions of dollars.

But the cache of Monsanto documents, after Samsel's and Seneff's review, reveals much more that we should be worried about.

In addition, Monsanto's studies included doses from low to high range. Samsel observed that low glyphosate doses were equally if not more toxic than higher doses. The company later discontinued low-dose trials, relying only on higher levels because it is customarily assumed to have greater toxicological risks. Samsel's observation has recently been confirmed by a study published in the August issue of the *Environmental Health Journal* by scientists at King's College London and the University of Caen in France. The 2-year study found that glyphosate administered at an ultralow dose of 0.1 ppb (the EU's safety limit) in drinking water altered over 4000 gene clusters in the livers and kidneys of rats. These alterations, the study reports, "were consistent with fibrosis, necrosis, phospholipidosis, mitochondria membrane dysfunction and ischemia."[14] Consequently, low doses of Roundup are far more toxic than US EPA limits.

During its years investigating glyphosate's bioactivity, Monsanto

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conducted hundreds of trials on mice, rats, beagle dogs, rabbits, and other life. Among the many cancers and diseases that Monsanto's own research found associated with glyphosate are:

- adenoma cancer in the pituitary gland
- glioma tumors in the brain
- reticular cell sarcomas in the heart
- malignant tumors in the lungs
- salivary mandibular reticular cell carcinoma
- metastatic sarcomas of the lymph gland
- prostate carcinoma
- cancer of the bladder
- thyroid carcinoma
- adrenal reticulum cell sarcomas
- cortical adenomas
- basal cell squamous skin tumors

In female mammals, there were cancers of the lung, liver, thymus, stomach, bladder, adrenal glands, ovaries, colon, uterus, parathyroid, and mammary glands.

Samsel and Seneff also noticed that Monsanto had conducted many long-term studies, as long as 2 years, on mice and rats. When Gilles-Eric Séralini and his French team reproduced and extended the length of Monsanto's 3-month GM maize-fed rat study for the life of the animals, they observed that profuse cancer and tumor development started after the 4th month of the study. Monsanto continues to stand by its 3-month study as sufficient proof of GM maize's safety. Yet the thoroughness and variety of Monsanto's research operations should give strong reason to suspect that Monsanto has likewise conducted long-term studies and knows all too well the deleterious effects of its pesticides, herbicides, and genetically modified crops.

One of Monsanto's claims is that glyphosate doesn't bioaccumulate in tissues, rapidly biodegrades, and is excreted from the body readily. Contrary to this claim, Monsanto carried out meticulous studies to determine levels of accumulation and the organs, tissues, and cells that glyphosate reaches. Glyphosate was radiolabeled with carbon-14 and given in 10 mg doses to seven groups of animals, male and female. After only 24 hours, the toxic chemical was found in the lungs and all body fluids: lymph, blood, urine, and cerebrospinal fluid. Glyphosate also accumulated in the bone by 30 ppm and in the bone marrow by 4 ppm. Monsanto's studies were comprehensive. It found an accumulation of the chemical in red cells, thyroid, uterus, colon, testes and ovaries, shoulder muscle, nasal mucosa, heart, lung, small intestine, abdominal muscle, and eyes.

Samsel and Seneff noted that the bioaccumulation in the pancreas was not reported. Why would such meticulous efforts be made to measure radiolabeled carbon-14 laced glyphosate levels in all the other organs, tissues, and bodily fluids and then ignore the pancreas? The scientists believe that this was deliberate.

Samsel notes that glyphosate does a "particular number on the lungs." According to a 2014 report by the National Cancer Institute, lung cancer rates have been declining. The decline is largely due to the national decrease in smoking. However, other lung cancers such as adenocarcinomas are on the rise. The NCI cannot account for this anomaly.[15] Yet is the institute not considering that Americans are increasingly being exposed to glyphosate in their food, water, and environment?

During the PRN interview, Seneff stated that the pancreas may be driving glyphosate to gather in the lungs. The pancreas is responsible for the release of the enzyme trypsin, which in turn infiltrates the lungs. A study published by Brazil's Universidade Federal de Santa Maria in the medical journal *Ciência Rural* measured glyphosate's reactivity with digestive enzymes, including trypsin. Trypsin activity was found to increase in parallel to higher glyphosate concentrations.[16] Seneff suggests that this may be contributing to the increase of glyphosate in the lungs, leading to the dramatic rise in COPD and asthma conditions, as well as lung cancers.

The occurrence of cataracts is rising rapidly, particularly in Midwestern states such as North Dakota, South Dakota, Nebraska, Iowa, Kansas, and Missouri. According to Prevent Blindness America's statistics, 17% of adults over 40 years have cataract problems. The NIH projects that the rate will reach nearly 40% by 2030.[17] Monsanto's study showing glyphosate activity in the eye may be contributing to this epidemic. Seneff stated that the eye's exposure to sunlight reacts with glyphosate residue, thereby potentially making the chemical more toxic. Farmers often apply glyphosate on crops when it is warm and moist and when there is plenty of sunlight in order for the chemical to activate more effectively. These are similar conditions

to our eyes during the day.

Monsanto's research was not limited solely to the Roundup compound. It also performed extensive research on glyphosate's individual metabolites, the intermediate molecules that result after Roundup's breakdown through metabolic reactions. Many of these metabolites are every bit as toxic as glyphosate. All the glyphosate metabolites in solutions fed to rats were measured before and after feeding. One of Samsel's more disturbing discoveries was that levels of the metabolite N-nitrosoglyphosate (NNG) were found in higher concentrations in the rats' feces and urine excretions than the original amount in the feeding solutions. NNG is a known carcinogen and endocrine disruptor. Samsel postulates that our own bodies' natural nitrous acid reacts immediately with glyphosate, without requiring a catalyst, to produce NNG. Both the EPA and the World Health Organization acknowledge that NNG is present in glyphosate during the manufacturing process. The agencies therefore have established safety limits for NNG. However, for any endocrine disruptor, there is no realistic safety limit because such chemical disruptors destroy cells on a molecule to molecule basis.

Nitrous acid naturally occurs in the colon, urinary tract, and skin tissue. According to the CDC, skin cancer is the most common form of cancer in the US, and affects more men than women. The Skin Cancer Foundation estimates that "each year there are more new cases of skin cancer than the combined incidence of cancers of the breast, prostate, lung and colon."[18,19] Basal cell and squamous cell carcinomas are the two most common forms, both which have been associated by Monsanto with glyphosate exposure, particularly in males. When glyphosate reacts in the skin along with nitrous acid, NNG contributes to skin melanomas. Other chemicals are added to Monsanto's Roundup to increase its effectiveness such as the surfactant POEA (polyethoxylated tallow amine), which also increases its toxicity.

We don't pay enough attention to these other ingredients, Samsel states, because the EPA permits Monsanto to add anything that it wants to enhance Roundup's potency while identifying these substances innocuously as "inert." When Monsanto convinces the public that glyphosate breaks down quickly, we are not told that the compound's metabolic byproducts are equally toxic.

Therefore, Anthony Samsel's unprecedented discovery and review of Monsanto's actual scientific and toxicological data of Roundup has provided us with information that warrants a thoughtful pause. Samsel and Seneff cover the subject in more detail in a new peer-reviewed paper titled "Glyphosate Pathways to Modern Diseases IV: Cancer and Related Pathologies."[20]

During recent years dozens of states are submitting bills to label GMO foods. These food crops are heavily laced with glyphosate residue. Not only GM crops, but even non-GM produce are sprayed with Roundup. According to the Organic Consumers Association, non-organic and non-GM foods such as wheat, barley, oats, flax, peas, lentils, beans, and sugar cane are also being sold to farmers "as a desiccant, to dry out all their crops so they could harvest them faster."[21] Monsanto, Dupont, Syngenta, Grocery Manufacturers of America, and other agro-chemical companies are aggressively combating labeling efforts. The Big Ag lobby is today pushing for a national bill to prevent GMO labeling that would supersede individual state's rights. We can only wonder what the voting outcome in California, Colorado, Washington, and Oregon may have been had Monsanto's own research been made available to the media and public. Is it therefore not time for full Congressional hearings to learn the truth and make the disclosure of Monsanto's Roundup research public for all?

Notes

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Kidney Skin Detox

by Dr. Jenna C. Henderson

Patients with chronic kidney disease are looking for a way to boost kidney function, and those with late-stage kidney disease hope to stave off the need for dialysis or a transplant. Even healthy individuals who wish to improve their kidneys look to herbal diuretics sold as detox products, to temporarily boost kidney output. Although various interventions can help improve the efficiency of the kidneys, one of the best and often overlooked strategies to help the kidneys is pushing detoxification through the skin.

If the kidneys work at all, the kidneys work hard. Damage to the kidneys is often not apparent until the patient is in an advanced state of disease. With approximately 1 million nephrons each, the kidneys can compensate for damage to the parenchymal tissue. The remaining functioning nephrons simply work harder to keep up with the demands of the body. This state of hyperfiltration can go on for years with no overt signs of kidney trouble. It is only when the kidneys reach a breaking point, where they cannot work any harder, that the creatinine starts to rise and the body becomes uremic. Patients often attribute a sudden shift in their lab work to causes from the recent past, but generally it is the day-to-day stress on the kidneys that occurs over the course of years that sets the stage for compromised function.

The uremic products most often considered are creatinine, BUN, and uric acid. However, currently 4054 metabolic waste products have been identified in urine. The Canadian government has sponsored the Human Urine Metabolome Database, which is yielding new insights into the chemical composition of urine as well as what urine compounds are associated with specific disease states.[1]

These uremic waste products also come through the skin. Skin lesions are often the first sign of systemic disease with renal involvement, such as amyloidosis and porphyria.[2] Patients who suffer severe burns over large portions of the body often experience kidney failure. The waste products that were once eliminated through the skin now must be processed through the kidneys. This extra burden has the potential to overwhelm the kidneys. But it also shows the reciprocal relationship between the skin and the kidneys, and how these detox systems complement each other.[3]

If one encounters homeless people, one of the first qualities noticed is that these individuals often smell like urine. This is not necessarily the result of accidents or a weak bladder; a person who does not have access to daily showers cannot remove the uremic wastes that come through the skin every day. We also see the relationship of the skin to the kidneys with the phenomenon of uremic frost, a powdery discharge on the skin, which is typically seen when the BUN levels are around 200.[4]

This is in line with traditional medicines that emphasized skin detoxification. Many in Traditional Chinese Medicine refer to the skin as the third kidney. Pioneers in naturopathic medicine also knew the value of skin detoxification, with recommendations for extended baths and showers. Baths could be as long as 5 hours, at which time the bath water would be noted to be especially foul, making it difficult for the patient to continue. Showers could be as long as 8 hours, an outrageous proposition to many concerned with modern droughts.[5]

Modern research is yielding new insights into the value of skin detoxification for kidney patients. One German study evaluated the benefit of sweating for Stage 4 chronic kidney disease patients. Patients sweated into towels, and the towels were then chemically analyzed for content of uremic waste. Not only were uremic waste products found, but the researchers noted that the more often the patients experienced these sweating sessions, the more uremia came out in each session. The body learns to push this pathway through repeated stimulation.[6] Another study found upregulation of urea transporters in the skin and sweat glands of uremic patients compared with normal subjects.[7] In fact, urea concentrations may be up to 50 times greater in the sweat of uremic subjects when compared with serum concentrations.[8]

Some in mainstream nephrology have even suggested that skin detox can help bridge the gap if dialysis patients miss a session. Anuric patients on long-term dialysis have issues of fluid buildup between dialysis sessions. This necessitates fluid restriction, one of the most difficult aspects of life on dialysis. Although the fluid volume of sweat is small, the high salt concentration of sweat does much to help fluid balance. By utilizing the skin to eliminate water and salt, these patients may be able ease up on fluid restriction, which goes

a long way to improving quality of life.[9]

On an ongoing basis, skin detoxification can be an adjunct therapy for those in renal failure. Some uremic waste products are easily eliminated with dialysis, such as BUN, and adequacy of dialysis can be measured with URR (urea reduction rate) by comparing the concentration of BUN before and after a session. But this is only one of thousands of uremic waste products. Other uremic wastes, particularly those of low molecular weight such as aluminum, can be hard to remove with dialysis, as these waste products may not be caught on the filter of the dialysis machine. [10]

Over time as uremic waste products build up in the body, many patients experience "uremic bronzing," a yellow-orange tone that occurs as wastes are deposited in the skin. Xerosis and pruritus are also noted with late-stage kidney disease.[11] Pruritus is often the consequence of buildup of serum phosphate.[12] In practice, the author works with many late-stage chronic kidney disease patients and dialysis patients on skin detox. Often in a short period of time, the uremic bronzing resolves and the symptomatic pruritus improves.

Patients and practitioners often have questions on what is the best way to go about skin detoxification for kidney health. The extended bath or shower is often a difficult proposition. Busy patients worried about loss of time with a 3- to 4-hour dialysis session are not likely to agree to spending several hours in the bathtub each week. Of all of the recommendations that the author gives in protocols to kidney patients, skin detoxification unfortunately is usually the last piece they implement. However, once patients start with this, they do notice that they feel better, and continuing is self-reinforcing. For those already on dialysis, a 30-minute session on nondialysis days is associated with improvements across a wide range of clinical parameters.[13]

Another added benefit to sweating therapy is an improvement in potassium balance.[14] As those in kidney failure cannot pass potassium out in the urine, serum potassium levels may rise to dangerous levels. The cardiac effects of hyperkalemia is the most immediate threat that dialysis patients face. The necessity of a low-potassium diet, however, eliminates a wide range of fruits and vegetables. Many end-stage renal disease patients believe that they have no choice but to eat processed foods of low nutritional value in order to control potassium. By improving potassium balance, these patients may be able to adopt more healthful eating habits.

While dry-brushing is convenient, and moving lymph is a good idea, there is far less transfer through air as through water. Some form of hydrotherapy is usually more effective. Traditional saunas and steam rooms are effective, but often too extreme for kidney patients. The sudden expansion of blood vessels with a very high temperature may lead to orthostatic hypotension with patients on hypertension medications.[15] Footpads or ionic foot baths do not seem to give a substantial results, possibly due to not including enough surface area for significant skin detox.[16]

Infrared (IR) sauna, when available, is often a good option for kidney patients. These units typically use a lower temperature than traditional saunas and have a deeper penetration into the skin. A wide variety of IR saunas are available. Patients who invest in a home unit have the option of doing a 15-minute sauna daily. Frequency of sessions may be even more important than duration, as uremic wastes are generated 24/7. Some portable home IR saunas are more energy efficient than others, which can be a consideration over time. Also units with the heating element throughout are preferred over those that have discrete panels and only detoxify the area of skin directly in front of the panel. Some units also heat almost instantly, a big advantage over those that can take an hour to warm up. These convenience factors are a big consideration if one is to make IR sauna a part of the everyday routine.

The cardiovascular benefits of IR sauna should also be considered. The cause of mortality for most renal patients is not renal failure but secondary heart disease. Thermal therapy, which includes water immersion, traditional sauna, and IR sauna, was found to improve several parameters of cardiac health, including endothelial function, hemodynamics, cardiac geometry, neurohormonal markers, and quality of life.[17]

If IR sauna is not an option, detox baths may be the next best option. One cup of Epsom salt and 2 cups of apple cider vinegar in a standard bathtub can help create a draw in the bath water to pull out uremic toxins. (Bentonite clay is also useful, but one must consider that it can be hard on plumbing and difficult to drain.) The Epsom salt/apple cider vinegar combination has proved clinically useful, and the feedback from uremic patients has noted a significant improvement with uremic bronzing. Twenty minutes in the tub a few times a week is often all it takes. Patients would do well to scrub the skin and aim to maximize the surface area in the tub, submerging the upper body as much as possible. Some patients are concerned with the smell of apple cider vinegar staying with them after the detox bath. This is usually not a problem, but a quick shower after the bath will take care of any issue.

Another type of bath that can be helpful for kidney support is the salt bath. This uses two 1 lb. boxes of regular table salt. It makes the water especially salty, like seawater, and creates an osmotic gradient that can be helpful for skin detoxification. The salt bath is especially warming. Usually after a hot bath, a person feels chilled stepping out into the cooler air. A hot salt bath is deeply warming and closes the pores of the skin so that the heat stays with the person. TCM associates kidney chi with body heat, and many with kidney failure have a chronically low body temperature.[18,19] For these patients, regular salt baths are especially helpful with cold and damp weather conditions.

Detox baths and salt baths can be used for patients at all stages of kidney disease. With diabetics, it is advisable to caution them to check the temperature

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of the water and make sure that it is not above 104 °F. Posttransplant patients should only have a warm bath and not a hot bath, as the high temperature acts like a fever, stimulating the immune response.[20] Those with a transplanted kidney should also avoid IR sauna, as this is also too immune stimulating.

The benefits of skin detox happen over time with repeated sessions. Evidence from hair analysis indicates that it may take several months to clear aluminum and lead. Arsenic may clear even more slowly.[21] Patients often report feeling better shortly after beginning a skin detox protocol, but they should be aware that this can be a long-term process.

In conclusion, skin detoxification is an especially useful approach for kidney patients or anyone interested in maintaining good kidney health. Rather than look to diuretics, which push the kidneys to work harder, skin detoxification helps reduce the stress on the kidneys. By reducing the workload, therapeutic baths and saunas offer support for chronically overworked kidneys.

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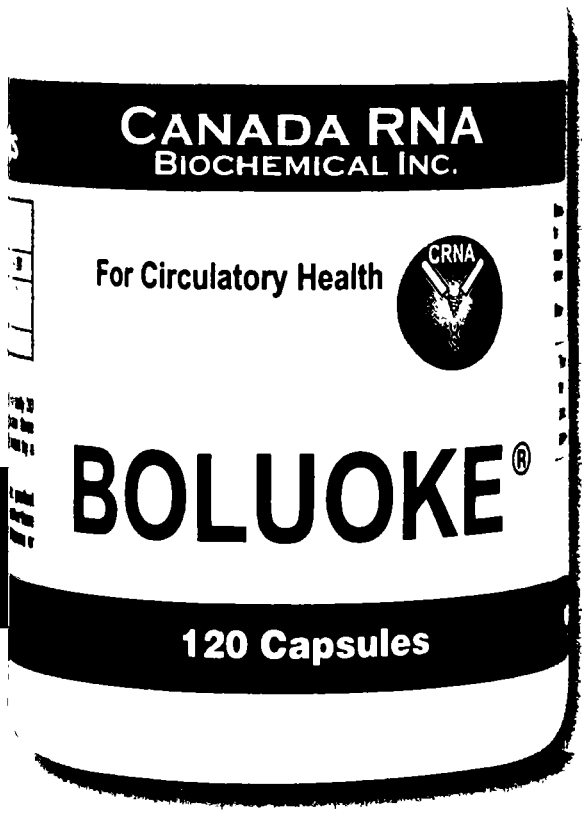

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Straight Talk about Heart Failure

by Kasra Pournadeali, ND

Q: Dr. P, I was told that I have heart failure; what are the ramifications?

A: Simply put, heart failure is when the heart (a pump) is unable to meet the demands of the body. It means that tissues no longer get the oxygen needed, and back pressure results, producing edema in the lungs, liver, kidneys, digestive system, and other areas. In addition to the body's failing to properly circulate blood and oxygen, heart failure also impairs immune function.[1,2] Finally, with heart failure, the body's detoxification processes are compromised, with altered perfusion to the kidneys and liver – two important organs of detoxification.[3–6]

Heart failure can be categorized as *systolic*, *diastolic*, or both. Systolic heart failure is when the heart cannot contract with adequate force to eject blood, while diastolic heart failure is when the heart muscle has impaired relaxation, preventing adequate blood from entering the heart prior to ejection. It is important to note that heart failure has different levels of severity designated by New York Heart Association (NYHA) Functional Classes (I–IV). Class I is when the person has no physical limitations. Class II means that a person is symptomatic on extra exertion. Class III is symptomatic on mild exertion, while Class IV is having symptoms at rest. A person's Functional Class determines the level of intervention needed.[7]

Q: What is the etiology of heart failure?

A: Heart failure has a variety of causes. Untreated hypertension, heart attacks, coronary disease, and valve disease are examples. Cardiomyopathy, a condition due to nutritional deficiencies, toxic exposures, hormonal problems, and sometimes unknown causes, can also cause heart failure. Finally, infections, muscular disease, and infiltrative conditions such as amyloidosis can in rare cases cause heart failure.

Q: I have heart failure. Will my heart ever recover?

A: This depends on the severity of disease, but also whom you ask. I recall one of my patients, Wes, 68, who had diabetes, hypertension, and renal failure. Wes came looking for alternatives for the blood pressure drugs that he was taking: metoprolol, lisinopril, and hydrochlorothiazide. Despite the drugs, his blood pressure was poorly managed, with his systolic pressure still in the 180s. He had dyspnea on exertion, and while lying down (orthopnea). He had cyanosis in his fingernails and mouth, and edema in his abdomen and legs – all signs and symptoms consistent with heart failure. Based on his history and an exam, Wes's Functional Class was between III and IV. For the short term, he needed extraction of the excess fluid; and for both the short and long term, natural approaches to improve his cardiac function.

After securing a blood sample, which later confirmed renal failure and NYHA Class III heart failure respectively, and performing an ECG (negative for MI,) we initiated short and long term plans. First, I encouraged Wes to stay on metoprolol and lisinopril for his high blood pressure, but changed the timing to between meals to improve bioavailability. I switched his thiazide diuretic to spironolactone (to help with fluid overload) and added digoxin (to improve cardiac contractility) and herbs and nutrients including hawthorn, CoQ10, L-carnitine, taurine, a multivitamin, and magnesium. Within 24 hours, Wes's shortness of breath resolved, his leg and abdominal edema improved, and his fingernail and mouth color returned to a healthy pink. Over the following 6 weeks, his blood pressure normalized, as did his blood tests. Then, over the remainder of the year, subsequent to improving his diet, walking daily, and staying on his natural medicines, Wes was able to get off his drugs, and he never again had a recurrence of heart failure symptoms. So when you ask if your heart can ever recover, although in medicine we are taught that the answer is no, in many cases (as with Wes), the answer is a resounding *yes*!

Q: What are the treatments for heart failure?

A: There are a wide range of treatment options, depending on the severity of disease. Generally, the goal is to reduce pressure caused by volume overload, decrease the risk/occurrence of life-threatening arrhythmias, and improve cardiac output. Of course, we want to find the cause and address it if possible; for example, stopping alcohol in the case of alcohol-induced cardiomyopathy.

Conventional approaches to treat heart failure include beta blockers to prevent/manage arrhythmias, diuretics to reduce volume overload and edema, ACE inhibitors and ARBs to decrease blood pressure, and potentially decrease the unfavorable enlargement of heart chambers, and digoxin for inotropic (improving contractile) effects. These drugs are excellent in addressing symptoms, and bringing a person out of life-threatening Class IV. They can be used orally or intravenously with other drugs, or with mechanical assists, if the situation warrants hospitalization or if a person becomes "hemodynamically unstable." Finally, transplantation is required if one's heart is damaged beyond a point when the condition cannot be managed by other means.[8]

Natural approaches for heart failure are numerous – some supported by the literature, some not. They can have similar effects to drugs in reducing blood pressure and occurrence of arrhythmias, and improving the heart's contractile force.[9–11] However, many are unique in comparison with drugs in that they can be "nutritive" to the heart. For example: nutrients such as CoQ10, magnesium, and L-carnitine serve as necessary components of energy production at the cell level. By improving the energy production of heart cells, one can improve the output of the heart itself.[12] Other approaches such as consuming an antioxidant-rich diet, taking antioxidants, and addressing heavy metal toxicity and chronic alcohol consumption are also important components of a comprehensive treatment plan. These interventions can reduce oxidative stress, and thereby affect "aging" often cited as the "cause" of diastolic heart failure. Finally, the importance of lifestyle modifications, including restricting sodium, tobacco cessation, and regular exercise, cannot be overstated.

Q: What are the benefits of the drugs, and what are the caveats?

A: Drugs are essential in addressing urgencies, wherein it is important to bring things under control quickly. They can reduce fluid rapidly and the occurrence of bad rhythms that put a person at risk of sudden death. There are caveats, however. For example, diuretics that reduce volume overload in people with heart failure can also cause loss of important nutrients such as potassium, magnesium, calcium, and B vitamins – critical for healthy heart chemistry.[13] So, although drugs are indispensable at times, it is essential to include nutritional approaches to mitigate the negative effects of drug therapy when it is necessary.

Q: Now that I have heart failure I am on several drugs. Must I continue them, and if so, how long?

A: The universal answer is, it depends! As in Wes's case, many who have heart failure and are also on a solid natural medicine plan, can discontinue (or reduce the dose of) medications as heart function improves. This considered, the last thing we want to do is throw someone who is stable and asymptomatic into Class IV (or worse) by quitting a conventional plan that was working. When someone is a candidate for drug tapering, I typically reduce the drugs over the course of several months, sometimes longer, and with concomitant use of multiple nutritional, herbal, and lifestyle supports. The monitoring of diagnostic tests, symptoms, and physical exams are also important to allow the medication withdrawal to be conducted safely and effectively. In cases wherein a person who is on drugs can't safely get off, natural approaches can still improve quality of life, and mitigate the unfavorable side effects of drugs.

Q: What tests should I be getting to monitor my condition?

A: Two diagnostic tests are critical for monitoring heart function: A BNP (B-type natriuretic peptide) and an echocardiogram (a heart ultrasound).[14]

First, the BNP is a blood test, the level of which rises as the heart fails. It serves as a useful confirmation of Functional Class, and can differentiate between (some) lung diseases and heart failure. BNP can also give an indication of the efficacy of a treatment. I routinely use BNP to assess the value of treatments in my patients with heart failure, particularly during the initial year. A normal BNP value is <100 pg/ml, but it is often elevated during initial phases of treatment. Once a person is stable, BNP should be followed every 6 or 12 months, depending on other risk factors or concomitant disease.

Second, an echocardiogram is one of the most valuable tests for assessment of heart structure and function. It provides information on valves, chamber size, wall thickness, contractility, relaxation, flow, pressures, volume ejected, and overall cardiac output. It is unique in that it can assess both systolic and diastolic failure. For the purposes of an initial assessment, I review all aspects of the echocardiogram, and for monitoring, I follow ejection fraction (EF; useful to assess and follow systolic dysfunction). And I follow the E/A and E/E ratios that allow "grading" of any diastolic dysfunction. A normal EF is 60% or higher although some references cite normal as low as 40 (higher indicates better contractile function). Diastolic dysfunction is categorized as Grade I (mild) generally asymptomatic, to Grades III and IV (severe) with symptoms of heart failure.

Q: What are the questions that I need to ask my doctor at every visit?

A: Good communication with your doctor is perhaps the single most important factor to insure that you get what you need, with heart failure or any condition. Several things are important to ask:

1. Medications, nutrients, and herbal medicines: Should any be adjusted or discontinued; or should any new agents be started, and why?
2. Lifestyle: Should diet, activity, or other practices that relate to your condition be modified?
3. Monitoring: When should your next BNP occur? What is the actual level, and is it stable, improving or deteriorating? When should you have your next echocardiogram? What

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was your ejection fraction? And, if you have diastolic dysfunction, what grade? Are these parameters stable, improving, or deteriorating?

4. New discoveries or possibilities for treatment: Can hormones or other agents be of value? Are there any new tests that should be considered that would alter my treatment course?

Q: What do I need to watch for if I have heart failure?

A: As with any heart condition, if you have shortness of breath at rest, chest pain, tightness, arm or jaw pain, a sustained rapid heart rate at rest, sustained dizziness, or a sense of doom, you should call 911. If you have known heart failure and are gaining weight; noticing a change to your breathing, urination, or appetite; your lips, mouth, or fingernails start to turn purple or blue; or your ankles, feet, or legs start to swell, it's time to call your doctor's office and communicate it.

Q: I've done some Internet research on natural approaches. What are your "go to" treatments in patients with heart failure?

A: First and foremost, it is critical to try and eliminate "causes." Alcohol, despite its growing popularity as "heart healthy," is *cardiotoxic*.[15] A standard American (inflammatory) diet high in sodium and sugar, inactivity, obesity, heavy metal toxicity, high blood pressure, hormonal imbalances, and smoking (of any kind) are all potential contributors that should be addressed.

Although every person gets an individualized plan, I typically consider the following lifestyle and natural approaches for my patients with systolic heart failure:

1. high-antioxidant plant-food rich diet, minimizing sodium and sucrose
2. CoQ10: 60–300 mg daily
3. L-carnitine: 1500–2000 mg daily
4. taurine: 1000–1500 mg daily
5. magnesium: 120–400 mg daily
6. hawthorn: (standardized extract of *Crataegus oxyacantha*) 2000–3000 mg daily
7. B complex (B50): 1 cap daily
8. multimineral +/– potassium (if hypokalemic and not on potassium-sparing medications)

Dr. Kasra Pournadeali is one of the country's authorities in naturopathic cardiology. He has been a provider for over 25 years, and practices at the Northwest Center for Optimal Health in Marysville, Washington. You can hear his talk show *Sound Living Thursdays* at 4 p.m. PT on Independent Public Radio at kser.org. Find out more about Dr. Pournadeali online at ncoh.net or facebook.com/naturalmedicinedoctors.

If the patient has diastolic dysfunction or coronary disease, I'll consider addition of:

1. turmeric: 1000 mg daily of a standardized extract
2. digestive enzymes daily with meals
3. vitamin C 500-1000 mg daily with bioflavonoids
4. fish oil with approximately 1000 mg EPA daily.

Please bear in mind that the preceding list should not be considered a recipe for everyone with heart failure. Hawthorn can cause stomach upset. CoQ10 may interact with blood pressure medications. Multiminerals can produce hyperkalemia, while B vitamins can aggravate palpitations and anxiety. Therefore, it is prudent to consult with a knowledgeable physician to identify the "right" recipe for each person.

Q: What is the take-home message about heart failure and alternative approaches?

A: Regardless of NYHA class, those of us with heart failure can benefit from natural approaches. Heart failure not only causes physical limitations, but also can cause detoxification and immune dysfunction. It is important to make use of drug therapies when necessary, but also use nutritional and herbal approaches to mitigate the side effects of those very drugs. I've observed improvements in my patients with heart failure when using many nondrug therapies such as CoQ10, magnesium, L-carnitine, B-vitamins, and others. That said, the right recipe for each person varies, so it is prudent to make use of alternative therapies and medications under professional guidance.

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A Cardiac Patient Is Sliding into Heart Failure As Opportunities to Turn Things Around Are Missed: How She Found Her Eventual Road to Recovery

by Laurie Dennison Busby, BEd

Dilated cardiomyopathy (DCM), atrial fibrillation (A-fib), and orthostatic intolerance (OI) appear to run in our family. However, we didn't realize that there might be a genetic predisposition as Mom started sliding into heart failure, and we started a search for answers.

1999

Mom seemed to be in pretty good shape for her age, 61, other than a history of frequent respiratory infections. In May, an X-ray taken for suspected pneumonia showed her heart to be within normal limits. She was starting to develop hypertension, so in June she was started on a calcium channel blocker.

2000

Exactly one year later, despite another X-ray showing her heart to be within normal limits (WNL), our family doctor heard a murmur and referred her to a cardiologist. An echocardiogram (echo) showed moderate left ventricle (LV) enlargement and a left ventricular ejection fraction (LVEF) of 30% to 35%. (The LVEF measures the percent of blood being pumped out of the left ventricle. 55% to 70% is considered normal.) A month later, a cardiac catheterization (cath) showed moderate to severe left ventricle dysfunction. Her vessels were "pristine."

2001

A month before last year's cardiac cath, hydralazine had been added to her medications, and now her calcium channel blocker was switched to atenolol, a beta blocker selective for beta-1 adrenergic receptors, which primarily affects pulse. Afterward, her pulse was good, 68 to 78, but her blood pressure was still mild to moderately high. Although we could not find the echo referred to, the cardiologist's notes stated that an echo still showed LV dysfunction. In October, a calcium channel blocker was again added back into her regimen along with the other two medications.

2002

On the three medicines, an echo showed a LVEF of 60%, which was good, but she had mild dilation of the left atrium (LA) and moderate concentric hypertrophy of the left ventricle.

During that spring and into the summer, she started developing new symptoms, particularly weakness in her arms. She described barely being able to pour milk for her cereal.

In May, they tested her erythrocyte sedimentation rate (ESR; a.k.a. sed rate), and it was 32. To me, what she described sounded like the symptoms of an autoimmune disease, but given the fact that she fell outside the normal age of onset for many of them, I wanted them to look at the possibility it was being triggered by one of her medications, but Mom didn't feel comfortable telling her doctors what to do.

Despite a positive antinuclear antibody (ANA) and elevated sed rate (58) and rheumatoid factor (RF) in June and an ANA of 1:640 in August, it wasn't until November, when her sed rate was still 27 despite prednisone, that they decided it was most likely a reaction to one of her medications, probably hydralazine, and had her immediately stop the hydralazine and atenolol and continue on a calcium channel blocker. About this same time, they started down titrating the prednisone, although it would take almost a year on prednisone before the positive ANA was resolved.

2003

One morning 3 months later, she was sitting on a lounge chair with her feet up, and she just passed out. A hospital EKG found sinus tachycardia, diffuse nonspecific ST and T wave changes, and a nonspecific intraventricular conduction delay. An echo showed a LVEF of 50% to 55% and mentioned only mild thickening of the mitral valve leaflet. Her carotid arteries were OK. Creatine kinase was 24, troponin was

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less than 3, and a test for diabetes was negative, which meant that the episode wasn't caused by a heart attack or a hyperglycemia-triggered arrhythmia.

When I later looked through Mom's medical records, they showed that after stopping the beta blocker, her pulse at her pulmonologist's office had jumped from 78 (October 2002) to 117 (November 2002) and 114 (January 2003).

2004

It had been over a year since the loss of consciousness episode, and the pulmonologist's records continued to show that her pulse was elevated: 110 (January 2004) and 121 (April 2004). No one seemed to notice, and by the end of the year, she was in trouble. In November, an X-ray showed mild to moderate heart enlargement. In December, another X-ray showed, in addition to the enlargement, "Some slight central pulmonary vascular congestion is noted on the current examination. The findings suggest borderline congestive heart failure."

An echo done the next day showed LV enlargement and a LVEF of 25%. The cardiologist wrote to Mom's primary doctor, "She [Mom] has a markedly dilated, very poorly contractile ventricle, with overall severe left ventricular dysfunction."

Rather than look back through Mom's medical records to see if there might have been a pattern, if any of her medications might have contributed to that positive echo done in February 2003, which showed a LVEF of 50% to 55%, the cardiologist questioned its validity, writing: "In retrospect I wonder if this was actually accurate."

Two days later our family doctor, seeking a second opinion on treatment options, had Mom in to see another cardiologist, who ran another echo, which basically had the same findings including a LVEF of 20% to 25%. He had nothing new to offer.

2005

After Mom saw a third cardiologist with no improvement in her echo, our family doctor strongly suggested to me that we take her to Mayo or someplace similar.

In trying to find the right doctor and educate myself as well, I immediately started reading the medical studies on DCM and started putting together Mom's medical records. I wanted to chart her records for the cardiologist, knowing that our time with him would be limited.

Reading the studies along with Mom's medical records was like putting together the pieces of a puzzle. The hydralazine reaction had been a huge clue in that the risk of a reaction was associated with multiple factors which included female gender, according to some studies; slower activity of the enzyme N-acetyltransferase 2 (NAT2), that breaks down hydralazine; and carrying human leukocyte antigen

(HLA)-DR4.[1,2] HLA-DR4 had also been associated with an increased risk of developing the other diseases that ran in our personal and/or family medical history: DCM, Hashimoto's thyroiditis, and Hürthle cell thyroid tumors.[3–6] I asked our doctor if Mom and I could be tested for HLA-DR4, and we were both positive.

DCM had multiple potential causes, but one team had found a strong association between HLA-DR4 positive DCM and having beta-1 adrenoceptor autoantibodies, "72% of the HLA-DR4 dilated cardiomyopathy patients had anti-beta-receptor antibodies compared to 22% HLA-DR4-negative patients; conversely, 67% of the antibody-positive patients were typed as HLA-DR4 compared to only 10% of the antibody-negative patients."[3] It was thought that beta-1 adrenoceptor stimulating autoantibodies could lead to tachycardia and DCM and eventually to decreased beta-1 adrenoceptor expression or sensitivity and heart failure.[7–9] It was also thought beta blockers could reverse some of the abnormalities.[7,8]

Her medicines had been changed multiple times, but when I charted the results of the echoes and the medicines that she was receiving in the 6 months prior to each echo, a pattern seemed to emerge. She seemed better on the beta blocker, which she was not currently taking, and worse on the calcium channel blocker.

120 studies and 2 inches of medical records later, including the tachycardia that went unnoticed, I was convinced that Mom was on the wrong medicine and needed to be on a beta blocker. Despite her worsening echo results including LVEF, Mom's B-type natriuretic peptide (BNP) was not that far out of range 106 (range 0–100), which gave me hope that her condition might be reversible.

Mom's response? "I believe you. You were right about my reaction to my medicine, but I can't tell my Ivy league-educated cardiologist, 'My daughter thinks I am on the wrong medicine.'" Luckily, my mom's immunologist noticed that Mom was taking a calcium channel blocker and told Mom that, while she hesitated mentioning it, she thought that Mom was on the wrong medicine; she thought calcium channel blockers weren't suppose to be given in DCM. That gave Mom the push that she needed to go to our family doctor and argue for changing her medicine to atenolol, which he did.

We felt comfortable making this switch in her medicine knowing that in a month we had an appointment for Mom to see a cardiologist* at Baylor Heart Hospital in Houston, Texas. His name kept showing up on some of the most forward-thinking studies at the time.[10,11] They were about things that we were interested in.[11,12] While in Houston, they did a another cardiac cath and additional blood tests to make sure that nothing had been missed, asked to be sent her previous echoes, and reiterated that we had her on the right medicine and that calcium channel blockers were contraindicated in DCM.[13]

Within a year on the beta blocker and hydrochlorothiazide (HCTZ), Mom's LVEF improved, from an estimated low of 20% to 25%, to 45%; and the size of her heart responded favorably as well. Almost a decade later, she is still alive and in good health for her age, 76.

Looking back, I think that things could have been done differently. Her medications weren't reevaluated when new symptoms arose, the beta blocker wasn't down-titrated slowly as the *PDR* advises, her changes in pulse rate went unnoticed, symptoms were treated instead of diseases, and the echo done February 2003 (after Mom had been on all three medicines) appeared to be disregarded, written off as a mistake.

One of the things that doctors are less likely to be familiar with, which could have been useful, is the HLA tests. Testing for HLA-DR4 in female patients with DCM may help predict which patients may have a problem with hydralazine.[1–3] In one study, up to 73% of hydralazine-induced systemic lupus erythematosus (SLE) patients were HLA-DR4 positive, and, "If the slow acetylators treated with Hydralazine were analysed as one group, it was observed that all women with DR4 developed Hydralazine-induced SLE."[1] This test might spare other patients from going through what Mom did.

Cardiac Recovery

I first learned to read medical studies prior to Mom's getting sick when, after my own health problems, my aunt, a nurse anesthetist, handed me some studies and a huge medical dictionary, and said, "In the very least, you need to learn enough to make informed decisions. They're having you try things that appear to be making you worse." We had accomplished what she had hoped for and learned to make informed decisions.

*Ironically, the cardiologist from Houston has since became head of cardiology at the teaching hospital in the city where my mom lives. It is the same teaching hospital where my aunt got her nursing degree.

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An Integrative Medical Approach To Reversing Cardiovascular Disease: Practicing Beyond the Standard of Care

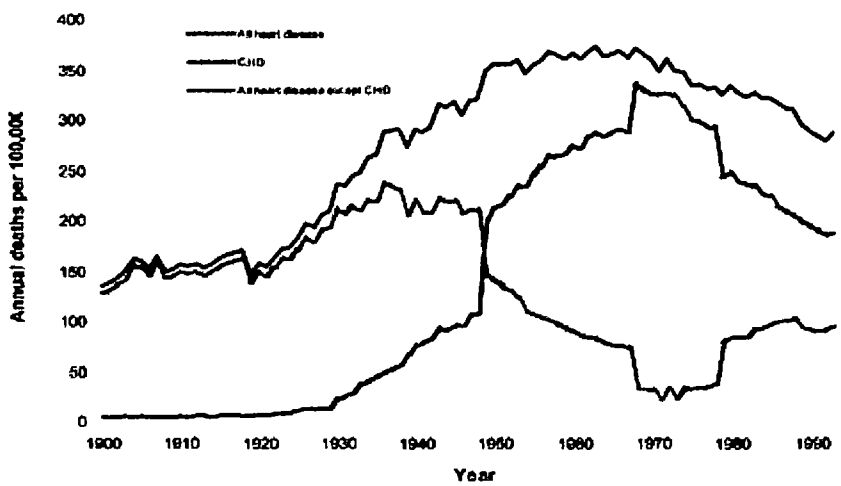
by Gary Huber, DO, AOBEM, and Brittany Bankemper, PharmD

Coronary heart disease (CHD) kills more than 370,000 people annually in the US.[1] The standard of care for reducing this risk is to monitor a traditional lipid panel and fasting blood sugar, despite clear evidence that these two tests are inefficient. It has been demonstrated that the majority of CHD occurs in patients with normal lipid panels. The 2013 ACC/AHA (American College of Cardiology/American Heart Association) guidelines on management of cholesterol and atherosclerotic disease ignored all evidence that more in-depth testing such as LDL (low-density lipoprotein) particle number, particle size, measurements of oxidized LDL, CRP (C-reactive protein), or other easily obtainable markers hold any value despite ample evidence to the contrary.[2–4]

The use of fasting glucose as a measure of efficient glucose management by the body is still standard, despite evidence that it fails to detect up to 40% of active type 2 diabetics or patients with active insulin resistance.[5] Given that CHD is our No. 1 killer in this country, I want to propose an approach that goes beyond our current standard to expand into the integrative model of overall health. I have already discussed primary lab options in previous articles and want to direct discussion here to treatment options and approaches.[6,7]

The US represents just 5% of the world population, yet we consume 50% of all the drugs made globally. If drugs truly made us healthy, then obviously we would have to be the healthiest people on the planet; but clearly this is not the case. We rank 30th in life expectancy globally and hold the world record for rates of diabetes, cardiovascular disease, and obesity. Following the 2013 ACC/AHA guidelines to offer statins to an ever-widening audience and employing polypharmacy may help modify the disease progression, but it doesn't allow us to truly reverse the course of the disease. To accomplish this, we need to attack the cause. The modern integrative care physician or practitioner has an arsenal of tools available that have been shown to be far more effective at targeting the cause of the inflammation that drives CHD.

Figure 1a. Unadjusted CHD, all heart disease except CHD, and all heart disease mortality between 1900-1993.



Adapted from: US National Vital Statistics, years 1900-1993. Available online
Available online: http://www.cdc.gov/nchs/products/pubs/pubd/hus/hus.htm

A Brief Exploration of the History of Heart Disease

Exploring numbers from the US Centers for Disease Control (CDC), we can track the history of coronary heart disease to its origin in the 1930s.[8] The occurrence of heart disease from 1900 to 1930 was nearly all structural disease,

valvular issues, aneurysms, and so on. CHD was rare. In 1930, we see the first stir of CHD as processed foods became more available to the American diet. Notice the dramatic increase in CHD in 1950. What happened that year? The introduction of manufactured hydrogenated oils to the American diet. Margarine was born, and processed foods multiplied dramatically. We stopped eating food and began to eat synthetic foodlike substrates. This overlaps the advent of surgical techniques and Dr. DeBakey's solutions for structural heart disease, and soon we see death from structural heart disease plummet as CHD rises.

President Eisenhower's myocardial infarction (MI) while in office in 1955 introduced America to a new vernacular.[9,10] For the first time in history, our nation was asking about the cause and condition of "heart attacks." The AMA was overrun with demands by the public for an explanation and how to avoid this new disease. It had no answer, and in frustration turned to Ancel Keys, a nutritionist and scientist of the day who had loudly proclaimed the "lipid hypothesis" as an explanation for heart disease. His theories were incorrect but gave birth to what lives today as the belief that fat causes heart disease.

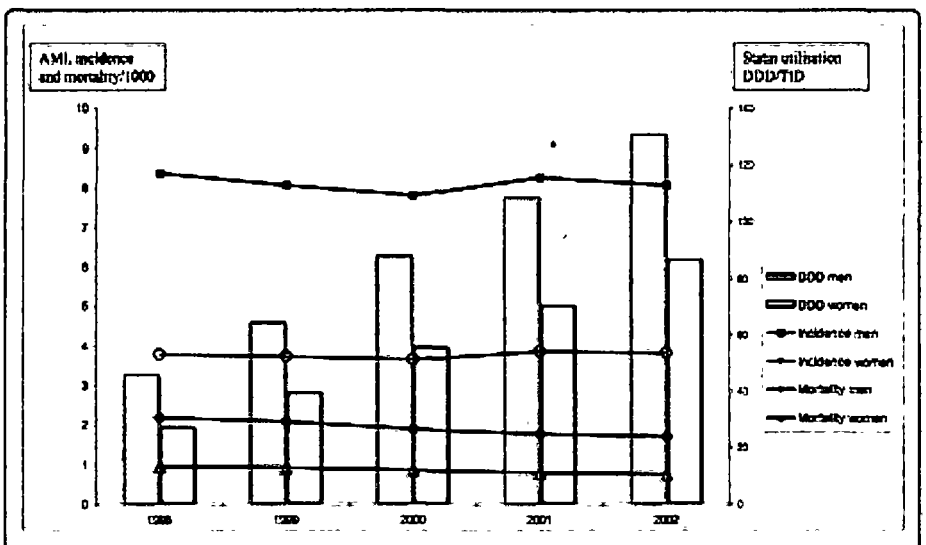
Eisenhower took the advice of his physician, and removed eggs and all forms of fat from his diet and increased his use of margarine and grains. His cholesterol continued to rise and he went on to have several more MIs before he died in 1969. But as we look at Eisenhower's disease history, it is peppered with sources of inflammation, including Crohn's, arthritis, and melanoma.[10] It was his high-carb inflammatory diet, inflammatory bowel disease, and stressful life that brought his ultimate demise.

Statin drugs were born in the late 1970s, and since then we have relied heavily on this growing group of drugs to corral what we thought was the cause of heart disease. By the 1990s, research had clearly shown that fat and cholesterol were not the cause of heart disease, but conveying that message to the public and to doctors is on ongoing challenge. Statins are efficacious agents in lowering the LDL, but given that this is not the cause of heart disease, the use of this approach as a sole methodology will lead to less than ideal results. The 2013 guidelines of the ACC/AHA, with 33% of members working for statin manufacturers, are not free of bias and recommended the use of a "Risk Calculator" to be employed in determining who needed statin therapy. They admitted that they had no studies to show that use of this calculator was valid, as it had not been tested in human trials.[2] The Risk Calculator would dramatically increase the number of individuals who now qualify for statin use.

What is needed to return to CHD risk rates of the 1920s is not more statin use but a return to healthful lifestyle and diet. As Hippocrates once said, "Let food be thy medicine." The 2013 ACC/AHA board failed to offer any meaningful guidance here. This board offered lip service to diet and lifestyle, saying that these modalities should be used as "first-line" therapy but then fell short, as they did not offer any guidance for the application of exercise and their only dietary insight was to employ the DASH diet. The DASH diet recommends the consumption of 6 to 8 pieces of bread daily. This recommendation needs to be questioned, as the intake of a highly allergenic, high-glycemic wheat products such as bread will most assuredly drive the very inflammatory process that in fact causes atherosclerotic disease.[11,12]

Before we leave the topic of statin drugs, let's explore a few current controversies. Despite all of the grand statements made in defense of statins, the truth is that we need to treat 1000 people in order to stop a mere 20 to 30 heart attacks. This benefit comes at a cost both financial and physical, as statin use causes well-known side effects, leading a full 40% of all statin users to stop therapy due to complications. If we were to compile all of the well-known studies, including JUPITER, CORONA, LIPID, WOSCOPS, PROSPER, MEGA, GISSI-HF, GISSI PREV, ALLHAT, 4S, ASCOT-LLA, HPS, and AFCAPS/TEXCAPS, we would have a total of 90,056 patients. One of the concerns expressed by many is that all of these studies are funded by the very pharmaceutical companies that produce the statin drugs being tested, so there is inherent bias.

The largest statin study ever done was not funded by a statin manufacturer and needs to be included in our assessment if we are to arrive at an educated position. The Nilsson study was conducted in 2011 by a governmental agency seeking to assess the benefit of statins on reducing cardiovascular events and deaths.[13] Researchers studied 4 million people over 5 years and tracked use of statin therapy and reported that they saw no evidence that statins reduced cardiovascular events or risk. This study doesn't have a pharmaceutical-funded bias and dwarfs the other studies in sheer numbers.



Change of cut off level of Cardiac troponin T, troponin I or creatine kinase (CK-MB) for AMI.

Figure 1 Incidence and mortality of acute myocardial infarction (AMI) and statin utilisation in the Swedish population, 40-70 years old, 1998-2002. Utilisation of statins expressed in Defined Daily Doses per 1000 inhabitants and day (DDD/TID).

The use of statins tripled over the 5-year period, yet the number of myocardial infarctions and deaths from myocardial infarctions did not change significantly. In fact, in subgroup analysis, we saw that the occurrence rates of vascular events in men aged 50 to 59 increased 19.5% despite a 310% increase in statin use. This warrants an explanation in light of our current fascination with statin therapy.

One explanation may be the rise in diabetic disease under the influence of statins. Statins cause diabetes, and this has been shown in multiple studies.[14–16] The Women's Health Initiative, after stratifying for other risk factors, determined that the occurrence rate of diabetes directly due to the use of statins was 36 new diabetic cases out of 1000 people treated.[14] Other studies such as PROSPER have confirmed this effect.[17] We know that 80% of deaths in diabetic patients are due to vascular disease such as CHD and cerebral vascular accidents. Does the diabetic insult caused by statin use offset their benefit, leaving us the results seen in the Nilsson study?

Studies show that CRP is twice as sensitive as LDL in predicating MI.[18] CRP is more than just a marker of inflammation; it is an agent of harm, as it reduces functionality of the insulin receptor itself. Lowering CRP is critical to reversing the vascular risk and its progression. Statins may offer a modest impact here, but other tools such as hormonal balance, nutrition, nutraceuticals, and lifestyle changes offer a greater impact and certainly with less adverse risk.[19–22]

Exploring the Cause

The field of epigenetics has been a remarkable teacher and changed the complexion of medicine. At least 90% of chronic disease is driven by environmental exposure and not the genome.[23] If we are to keep pace with the science, we need to embrace the idea that the quality of our food, water, and environment dictates disease process. Inflammation comes at us from all directions, including gut problems, poor sleep, stress, excess weight, hormones, dental factors, and all other sources that drive cytokine signaling. Food is the No. 1 element to drive all of these issues. High-glycemic, chemical-laden food drives oxidation and food allergy. A body exposed to stress and poor sleep will spike cortisol and trend toward selection of higher-glycemic foods and greater caloric intake. Stress of any kind drives weight gain, and both will combine to create rolling inflammation.

Atherosclerosis begins as a disease of the subendothelium and the vessel wall in direct response to the foods and inflammatory milieu that we create.[24] Long before the first plaque appears, we can detect the inflammation lying below the endothelial surface and address it. Cardiovascular disease is the result of uncontrolled inflammation.[25] Inflammatory responses occur within the wall:

- Expression of adhesion molecules by endothelial cells.
- Attachment of leukocytes to the arterial wall.
- Vascular cell adhesion molecule-1 (VCAM-1) binds monocytes and T lymphocytes, preceding the appearance of macrophages.
- Oxidized lipids and cytokines IL-1 and TNF-alpha induce VCAM-1 expression via nuclear factor-kappa B.
- The presence of nitric oxide limits VCAM-1, but glucose and insulin presence retards nitric oxide production.
- Inflammation and oxidative stress drives production of monocyte chemoattractant protein-1 (MCP-1), recruiting monocytes and facilitating their penetration past the endothelium into the intima.
- Monocytes mature into macrophages and engulf lipoproteins and become foam cells.
- The atheroma is born and the atherosclerotic process is fed by daily habits.

Processed foods are by nature inflammatory foods due to their commonly low fiber content and added sugar. Processed grains may not taste sweet, but their ability to break down quickly into simple sugars drives hyperglycemia, which in turn generates insulin rise. As insulin rises, triglycerides are stored and not used as cellular fuel, leading to abundance and hypertriglyceridemia. The presence of sugar promotes yeast growth and oxidative stress in the gut, and the lack of soluble fiber hinders maintenance of proper flora, leading to gut disturbance. This collusion of events favors autoimmune vascular dysfunction and inflammation.[26]

The healthful antioxidant content of a whole-foods diet blunts endothelial dysfunction. Phytonutrients such as carotenoids, flavonoids, and polyphenols from a vegetable-based diet block vascular inflammation. Healthful fats such as omega 3 fatty acids and monounsaturated fats affect the caveolae of the endothelial cell wall to induce an anti-inflammatory signal.

The caveolae are invaginations in the wall of the endothelial cells and play a major role in cell signaling. Caveolin-1 is a natural protein found within the caveolae and influences cell signaling events, and can facilitate the development of atherosclerosis if stimulated by the inflammatory signaling network. Caveolin-1 is necessary to stimulate the intracellular TNF-α-induced NF-κB-dependent induction of cyclooxygenase-2 and prostaglandin E2.[27] Caveolin-1 is known to contribute to endothelial dysfunction through its ability to reduce nitric oxide levels and increase ROS. Strategies to lower the level of caveolin-1 result in the opposite impact, an anti-inflammatory signal. If caveolin-1 is reduced, we see reduced levels of proatherogenic VCAM-1. Here are some of the mechanisms shown to help down regulate caveolin-1:

- Reducing TNF-alpha and lipopolysaccharides (LPS) levels inhibits caevolin-1 activity.
- Sulforaphane activates Nrf2 thus attenuating LPS induced endothelial activation.[28]
- Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) displace caveolin-1 from caveolae in endothelial cells, causing increased (nitric oxide (NO) production and reduced ICAM-1 expression.[29]

- By contrast, omega-6 fatty acids increase caveolin-1 expression.
- Green tea polyphenols, specifically EGCG, were able to reduce caveolin-1 levels.[30]

Caveolin-1 if provoked by inflammation promotes endothelial lipid accumulation in the subendothelial space and enhanced monocyte/macrophage recruitment.

In 2002 Dr. Mark Houston pointed out the three distinct responses of the blood vessel as a result of inflammatory exposures:

1. oxidative stress – as a result of a reduced oxidative defense
2. inflammatory response as outlined above
3. autoimmune – involvement of CD4 T-helper cells and CD8 cytotoxic cells

These three vascular responses that lead to atherosclerotic disease are commonly ignited by the simple choices that we make in the course of daily events. To defuse this bomb, we need to invest our collective energies in educating our patients about the impact of their choices. Integrative clinicians distinguish themselves by offering action, not lip service, to this important agenda.

Integrative Care and Solutions

"It is more important to know what type of person has a disease than what disease a person has," said Hippocrates. If we are to change the mindset and thus the habits of our patients, we need to understand them and their hurdles and then educate them appropriately. So let's venture into the terrain of the integrative physician. Let's explore the potential that we all have to truly reverse cardiovascular disease and exceed the standard of care.

Lifestyle

A comprehensive lifestyle change has dramatic impact on all aspects of the inflammatory process. Exercise, optimal nutrition with fruits and vegetables, moderate alcohol consumption, and smoking cessation reduce the risk of MI by 80%.[31] The Lifestyle Heart Trial included a plant-based diet, exercise, and stress management and showed a 5% regression of coronary plaque compared with the control group, who demonstrated a 8% progression in plaque size in just 1 year.[32]

Gut Health and Food Allergies

The gut represents the heart and soul of the immune system, as Peyer's patches line the intestines and respond to the millions of antigens that pass through us each day. Therefore, the gut microbiota are central in determining the pathogenesis of inflammatory induced obesity, CHD, atherosclerosis, and type 2 diabetes.[33] Gut microbiota play a key role in an individual's potential risk for autoimmune disease, cardiovascular inflammation, and other chronic diseases.[34] Microbial diversity and number are important in disease prevention and resiliency to maintain function. Lower diversity is observed in obesity, inflammatory bowel disease, meat-based dietary patterns, diabetes, and CHD. Higher diversity in vegetarian-based dietary patterns with high dietary fiber, nondigestible carbohydrates, resistant starches, SCFA prebiotics, and probiotics have a lower incidence of diabetes and CHD.[35]

Nutrition

Studies consistently show that altering lifestyle and diet is more powerful than simple drug therapy. In the Becker trial at the Mayo Clinic, a Mediterranean-style diet that removes high-glycemic carbs in conjunction with exercise, basic omega-3 fatty acid supplementation, low-dose red yeast rice, and education outperformed simvastatin (40 mg) on all fronts.[36] Significant elevation in valuable HDL (high-density lipoprotein) was seen in the lifestyle group but not with statin use. Studies by Ornish and others have demonstrated reduction in plaque size with diet and lifestyle that was unobtainable through drug use.[32,33]

We have seen that oxidized LDL is one of the best lab predictors for CHD. This simple test is inexpensive and greater than 400% more predictive than total LDL measures.[37] Addressing the cause of oxidized LDL is key to reversing CHD. There are many toxins in our environment capable of unbalancing our redox potential, but the greatest threat is the constant dietary threat from processed foods. It is estimated that Americans consume more than 150 pounds of sugar and that a full 20% of our caloric intake is from wheat. Today's wheat contains a unique amylopectin A that is produced via hybridization.[11] Its branching pattern and ease of breakdown create a sharp rise in blood glucose and thus insulin that generates significant inflammation and oxidative stress.

The content of antioxidants in your diet has the ability to reduce CHD risk. In a study quantifying the antioxidant content of individual diets, those with the highest-quality foods and antioxidant content had a 20% lower risk for cardiovascular disease.[38]

Glutamate is an amino acid commonly found in our food supply, but in nature it is bound to protein and found in small amounts. When food manufacturers use a concentrated form known as monosodium glutamate (MSG), this is not natural or healthful and creates toxicity. Glutamate causes a loss in human cerebral endothelial barrier integrity through activation of NMDA receptor.[39] Glutamate increases lipid peroxidation and thus increases oxidized LDL. Through its interaction in the vascular beds and the endothelium, it increases reactive oxygen species, reducing antioxidant protection such as superoxide dismutase and glutathione.[40] This inflammatory food additive thus increases risk for CHD and alters neurologic balance between sympathetic and parasympathetic balance, driving hypertension and atherosclerosis.

The greatest source of antioxidants in the diet is from plant-based foods such as vegetables. Each serving of fruit has roughly 100 more calories from sugar than vegetables, so even abuse of healthful fruit can be problematic. The soluble fiber in vegetables feeds the gut flora, binds toxins, lowers both blood glucose and cholesterol levels, and is critical for proper elimination.[35] Plant-based diets continue to demonstrate protection from heart disease in multiple studies, and yet physicians

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continue to struggle with this simple recommendation and follow-through. How is it possible that we use our powers of persuasion to convince patients to undergo colonoscopies, painful injections, digital exams, or all types of medical procedures yet struggle mightily to persuade them to eat a healthful diet?

Asking a patient to give up inflammatory foods is paramount to success. Many physicians feel ill equipped for this discussion, as food and nutrition were not taught in medical school and are not a part of our general operating procedure. There are many tools to aid success here. Work with a local dietitian, recommend reading material, offer classes and educational options in your office, but most importantly hold your patient accountable for follow-through. They will succeed if you carefully monitor and insist.

Exercise

The benefits of exercise include the following[41]:

- Intense exercise can raise our anaerobic threshold, increase basal metabolic rate, and reduce fat stores, thus cytokine production.
- Exercise strengthens cardiovascular and respiratory systems, and cardiac output, and lowers resting heart rate.
- It stimulates osteoblast activity, increasing bone density and preventing osteoporosis.
- Exercise with intensity induces sweat, which reduces toxic burden from cells and can improve cell to cell signaling and endocrine function.
- Eases depression and helps manage pain and stress.
- Normalizes cortisol release through support of proper parasympathetic tone.
- Prevent and manage diabetes through optimization of insulin receptor function.
- Enhances better sleep patterns. Sleep loss is directly correlated with blood glucose and cortisol rise.
- Cognitive improvement: Exercise increases oxygen delivery to brain tissue, allowing us to have greater mental stamina, more creativity of thought, and greater problem-solving ability.
- It also stimulates the production of an important brain protein called brain-derived neurotrophic factor that helps in repair and function of neurons.

Naci reviewed 16 meta-analyses on the effectiveness of exercise on mortality outcomes across 4 conditions: secondary prevention of coronary heart disease, rehabilitation of stroke, treatment of heart failure, and prevention of diabetes. In CHD, the odds of mortality were reduced with use of statins, β blockers, angiotensin-converting enzyme inhibitors, and antiplatelets compared with control, whereas exercise interventions had a similar reduction but with wider confidence intervals.[42] The authors stated: "When compared head to head in network meta-analyses, all interventions were not different beyond chance: there were no statistically detectable differences among any of the exercise and drug interventions in terms of their effects on mortality outcomes. ... When compared head to head in network meta-analyses, exercise interventions were more effective than anticoagulants and antiplatelets." Our prescriptions need to occur beyond the prescription pad to include proper physical training.

In a well publicized trial in the *New England Journal of Medicine* from 2002, lifestyle including exercise was far superior to metformin in its ability to prevent prediabetics from advancing to diabetes.[43] Lifestyle intervention reduced the incidence by 58% while metformin use only reduced it 31%.

Armed with this knowledge, we have a responsibility to get our patients moving. There is a huge variety of exercise options, and the knowledge base to implement different approaches can be daunting. Rely on experts to dispense this information, but not random "personal trainers." Forge a relationship with trainers in your area and discuss your specific needs for your patient population. Develop a network of trusted options and track progress as your patients engage.

A simple text that I find very helpful for patients of all abilities is *The New Rules of Lifting Supercharged: Ten All-New Muscle-Building Programs for Men and Women*, by Lou Schuler and Alwyn Cosgrove. Search the Internet for tools that work in your practice; learn to rely on websites of your choosing that offer sound advice that is in alignment with your preferences.

Cortisol

Cortisol reflects one of the most destructive forces in our physiology when it is not kept in balance. The nature of modern life is wrought with overcommitments on our time and resources, leaving us exposed to high risk for HPA axis dysfunction and the unhealthful rise in cortisol. If we truly want to expose the cause of heart disease, it is critical to assess and modulate the action of cortisol. Many of us cheat our sleep, exercise, and diet, all in the name of, "I don't have time!" The Caerphilly study looked at the simple ratio of cortisol to testosterone and how it related to CHD. The answer was clear to see that as cortisol rose higher, leading to suppression of testosterone, this shift in ratio easily predicted those at increasing risk for a vascular event, specifically CHD.[44]

Sustained elevation in cortisol will have the following negative impact:

- Blood glucose regulation leading to insulin resistance and diabetes
- Poor conversion of levothyroxine into its active liothyronine form
- Drop in testosterone and dihydrotestosterone
- Reduced levels of adiponectin further driving insulin resistance
- Elevation in IL1, IL-6, and TNF-alpha, thus CRP
- Loss of muscle and bone mass
- Gut disturbance, dysbiosis, and immune dysregulation

Meditation and Heart Rate Variability Training Reduce Risk

Heart rate variability is a normal beat to beat variation that reflects the health and balance of the sympathetic:parasympathetic nervous system. Physiologic stress adversely

affects this, leading to direct increased risk for hypertension and heart disease. The use of heart rate variability training (emWave) has been shown to be extremely powerful in restoring balance. In a study comparing its use with drug therapy, the group using this relaxation technique experienced a significantly greater drop in systolic blood pressure.[45]

In a study employing meditation, subjects were asked to meditate daily for just 13 minutes, and cortisol was tracked over a 3-month time frame. There was a consistent reduction in overall cortisol expression of 28% over time.[46] This reduction in cortisol is critical to proper sleep and weight management, both factors for the reduction of CHD. Chronic stress leads to feeling of fatigue, drop in energy, and increased irritability and hostility, and these emotions have been linked to the development of insulin resistance.[47]

Hormones

The hormones estradiol and testosterone have dozens of roles to play in our normal physiology. Both affect blood sugar and cholesterol metabolism. Abnormally low levels of testosterone or estradiol will increase risk for diabetes, vascular inflammation, and CHD.[48–54] Restoring low testosterone to normal levels aids in the reversal of type 2 diabetes and metabolic syndrome. CHD occurrence in menopausal women drops 40% to 50% with the use of bioidentical estrogen.

Administration of testosterone to men with high CRP and low testosterone will in fact reduce CRP. There is a consistent inverse relationship between testosterone levels and CRP.[55] Low testosterone states are predictive of diabetes, and normalization of testosterone levels is therapeutic in the reversal of diabetes as it affects the mitochondrial restoration of ATP production.[56–62]

Sleep and Sleep Apnea

Sleep is key for recovery from daily oxidative stresses that are normal wear and tear. Poor sleep quality that lacks slow wave sleep or a short sleep cycle is directly linked to predictable rise in ghrelin, a drop in leptin, and a rising BMI.[63] The average night's sleep in Americans has shrunk from an average of 8 to 9 hours back in 1970 to an average of 6 hours as of 2004.

After just 2 nights of fragmented sleep, insulin sensitivity is reduced and craving patterns for high-glycemic foods rise dramatically.[64] General calorie intake rises and exercise is reduced following fragmented sleep. This combination will obviously lead to weight gain, and all the elements of inflammatory chemistry are in place to drive CHD.[65]

Obstructive sleep apnea (OSA) is associated with considerable morbidity and mortality and is directly linked to CHD, hypertension, and diabetes.[66] OSA results in fatigue, loss of quality of life, weight gain, and obesity. First-line therapy includes CPAP (continuous positive airway pressure), but compliance is poor. The reality is that treatment of obesity and weight gain through diet and lifestyle will greatly affect both risk for OSA and severity of OSA. Using a simple Epworth score to identify those at risk is a great start. Be suspicious of any patient who reports snoring. Have a low threshold for ordering sleep studies and assessment for CPAP. If CPAP is unacceptable to the patient, then refer them to a local dentist familiar with the construction and use of dental appliances to help position the jaw and tongue in a more anterior position out of the airway. If unfamiliar with these approaches, then contact the American Academy of Dental Sleep Medicine (AADSM) for a clinician in your area. Be very cautious to never use sedation in an effort to improve sleep if the patient has risk for apnea.

Conclusion

Coronary artery disease involves a complex web of factors and physiology, but when we step back and assess the common pathways, it's easy to see that we have left the lifestyle of the 1920s. We don't eat food anymore; we consume foodlike substrates that come from factories, not fields. The things that do come from fields are often genetically manipulated and dangerous. Instead of talking on the back porch, we text, tweet, e-mail, Instagram, and Facebook all day every day. Look around you – no one is looking back because everyone's noses are buried in screens in their hands.

We don't exercise our bodies, we don't walk, and we don't stretch. We sit in soft seats and expand. We have lost our way. We are anxious and overcommitted and we surely don't sleep anymore.

The human condition needs a few simple things to thrive. Clean food and water. Good sleep. A little exercise or simple movement. A normal cortisol level reflective of a calm existence where stress is "managed" or at least balanced with meditation and exercise. If we are to claim victory as true "health"-care providers, then we must find a way to drive healthful lifestyle into our patients. We must become the leaders in educating our communities in healthful lifestyle choices. We have fabulous resources at our disposal, as the Internet is bursting with tools that are user friendly.

We need to offer options to our patients that can weave into the fabric of their current lives but, more importantly, help them see the damage that they are creating if their lives are destructive. To simply offer drug therapy as the totality of our solution is akin to fastening a seatbelt on our patients as they race at 100 mph toward a brick wall. It may reduce the damage, but it's not going to stop the crash. We need instead to step inside the vehicle and apply the brake.

As physicians, we have tremendous influence on what our patients think, believe, and do. We need to expand our powers of persuasion to include lifestyle.

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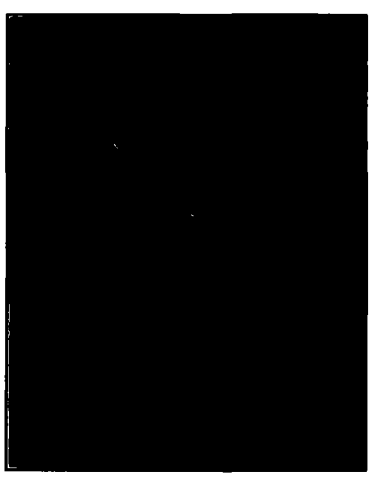

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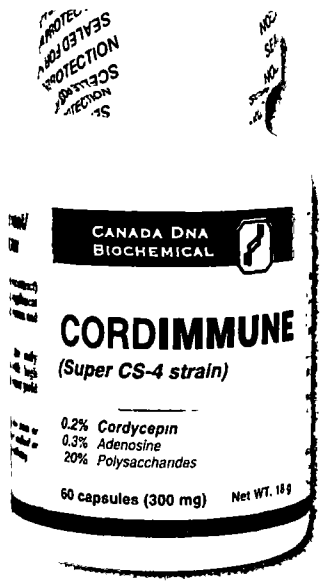

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Sugar Toxicity: A Silent Epidemic

A View from the Trenches of Daily Primary Integrative Medical Praxis

by David A. Edwards, MD, HMD; Jean Malik, MD, APH; Edna Espig, CNA, CHA; Renoir Morillo, BSN, CHA; Erika Bryant, EECP Tech; and Jesusa Ludahl

Sugar is the generalized name for sweet, short-chained soluble carbohydrates. Carbohydrates are composed of carbon, hydrogen, and oxygen (basically carbon + water). The term *sugar* refers loosely to a number of different types of carbohydrates, including monosaccharides (glucose, fructose), disaccharides (sucrose, lactose), oligosaccharides, and polysaccharides (common components of glycoproteins and glycolipids). The most biologically important and well-known monosaccharide is glucose. Glucose is the main source of energy fueling aerobic metabolism – a fundamental necessity of living mammalian cells. The most common disaccharide is sucrose (glucose + fructose) or common table sugar. Biopolymers (oligo- and polysaccharides) of sugar are common structural forms of carbohydrates in nature. Plants produce sugar and sugar biopolymers through the process of photosynthesis. These biopolymers are converted into structural polysaccharides, such as cellulose and pectin found in plant cell walls. They also may serve as a form of energy storage, such as starch or inulin. In addition, DNA and RNA are polymers of the monosaccharides deoxyribose and ribose respectively and constitute the basis of genetic blueprint and memory for almost all forms of life. The importance of sugar for life in its various functional and structural forms cannot be overstated. However, like oxygen, which is both essential for most life forms and also extremely toxic to life (physiologic function versus toxic free-radical damage), sugar also has a dark side for living tissue.

Studies in animals and humans have suggested that chronic consumption of added sugar contributes to metabolic and cardiovascular dysfunction. There is also growing evidence that added fructose is more damaging than refined glucose in terms of cardiovascular risk. Cardiac performance has been shown to be impaired by switching from a low-carbohydrate diet including fiber to a high-carbohydrate diet. Switching from saturated fatty acids to carbohydrates with high glycemic index values shows a statistically significant increase in the risk of myocardial infarction. Other studies have shown that the risk of developing coronary heart disease is decreased by adopting a diet high in polyunsaturated fatty acids and low in sugar, but a low-fat, high-carbohydrate diet showed no reduction. This suggests that consuming a diet with high glycemic load ("high glycemic" = causes a rapid rise in blood sugar) is strongly associated with the development of coronary artery disease. The consumption of added sugars has been positively associated with multiple measures known to increase cardiovascular disease risk in adolescents as well as adults. Multiple studies suggest that the impact of refined carbohydrates or high glycemic load carbohydrates is more significant than the impact of saturated fatty acids on cardiovascular disease. In addition, a connection between Alzheimer's disease and fructose has been suggested, but remains the subject of debate. Finally, the possible addictive effects of refined sugar simply adds to the scientific concern regarding the toxic effects of sugar in the development of cardiovascular disease.

Glycocalyx

One of the lesser-known structural/functional physiologic aspects of sugar is the glycocalyx. The glycocalyx is a polysaccharide sugar polymer coating that surrounds all cell membranes. This "sugar" coating consists of several carbohydrate moieties of structural membrane glycolipids and glycoproteins which serve as a backbone for support and cell–cell communication. Pischinger's matrix theory of rapid cell to cell communication is centered on the functional aspects of the glycocalyx (Pischinger A. *Matrix and Matrix Regulation Basis for a Holistic Theory in Medicine*. Brussels: Haug International; 1991). This carbohydrate ("sugar") portion of plasma membranes contributes to cell–cell recognition and communication, and intracellular adhesion. The slime on the outside of a fish is a common example of a glycocalyx. It is essentially a functional "biofilm." The term *glycocalyx* was initially applied to the polysaccharide matrix coating epithelial cells, but its functions have

been discovered to go well beyond that. The glycocalyx plays a major role in regulation of endothelial vascular tissue, including the modulation of red cell volume in capillaries. It is located on the apical surface of vascular endothelial cells which line the lumen of all blood vessels and may be up to 11 um thick. It is present throughout a diverse range of microvascular beds (capillaries) and macrovessels (arteries and veins). The glycocalyx also consists of a wide range of enzymes (eNOS, ACE, SOD3, etc.) and proteins (growth factors, chemokines, antithrombin, etc.) that regulate and protect the endothelium. They serve to reinforce the glycocalyx barrier against vascular and other diseases. Another function of the glycocalyx within the vascular endothelium is to shield the vascular walls from direct exposure to blood flow while serving as a vascular permeability barrier. Its protective functions are universal throughout the vascular system. In microvascular tissue the glycocalyx inhibits coagulation and leukocyte adhesion. It also affects the filtration of interstitial fluid from capillaries into the interstitial space. Research has shown that the glycocalyx is composed of a negatively charged network of proteoglycans, glycoproteins, and glycolipids.

The glycocalyx plays a crucial role in cardiovascular system health. Initial dysfunction of the glycocalyx can be caused by hyperglycemia or oxidized LDL cholesterol. In the microvessels, dysfunction of the glycocalyx leads to internal fluid imbalance and potentially edema. In arterial vascular tissue, glycocalyx disruption causes inflammation and atherothrombosis. Fluid shear stress is also a potential problem if the glycocalyx is disrupted for any reason. This type of frictional stress is caused by the movement of viscous fluid (i.e., blood) along the lumen boundary, damaging the delicate glycocalyx. Minimal ischemic damage to the glycocalyx increases capillary hematocrit. Endothelial (glycocalyx) dysfunction can be tested by a variety of methods. Of all the current tests employed in a research setting, flow mediated dilatation (postocclusive reactive hyperemia; PORH) is the most widely used noninvasive test for assessing endothelial dysfunction. This technique measures endothelial function by inducing reactive hyperemia via temporary arterial occlusion and measuring the resultant relative increase in blood vessel (capillary) diameter via ultrasound or plethysmography. A reduction of small arteriole/capillary compliance is a marker for endothelial (glycocalyx) dysfunction that is associated with both functional and structural changes in the microcirculation and is predictive of subsequent morbid events. These changes can be distinguished from large artery (macrocirculation) stiffness and obstruction by the use of pulse volume recording (PVR).

Endothelium

The endothelium is a thin layer of squamous endothelial cells that line the inner surface of blood and lymphatic vessels, forming an interface between circulating blood or lymph fluid in the lumen and the vessel wall. Endothelial cells in direct contact with blood are called vascular endothelial cells, whereas those in direct contact with lymph fluid are known as lymphatic endothelial cells. Endothelium is mesodermal in embryonic origin. Vascular endothelial cells line the entire circulatory system, from the heart ("endocardium") to the smallest capillaries. These cells have unique functions in vascular biology. Both blood and lymphatic capillaries are composed of a single layer of cells called a monolayer. All endothelial cells are coated with glycocalyx biopolymers. Endothelial dysfunction is a hallmark for vascular disease, and is often regarded as a key early event in the development of cardiovascular disease. Impaired endothelial function has been related to hypertension and vascular thrombosis and is seen in patients with coronary artery disease, diabetes mellitus, and hypercholesterolemia. Endothelial dysfunction is a systemic pathological state of the inner lining of blood vessels and can be broadly defined as an imbalance between vasodilating and vasoconstricting forces acting on endothelial cells. Endothelial dysfunction has been shown to be of prognostic significance in independently predicting vascular events including stroke and myocardial infarction. Endothelial dysfunction can result from and contribute to several disease processes (hypertension, diabetes) and can also result from environmental factors such as smoking and exposure to air pollution. Thus, endothelial dysfunction is a major patho-physiological mechanism of vascular disease. Endothelial dysfunction is synonymous with glycocalyx dysfunction.

Macro- vs. Microcirculation

There are actually two "functionally interrelated" blood circulatory or vascular systems found in the human body: the macrocirculation and the microcirculation. The macrocirculation consists of the larger "conduit" arteries that conduct blood to the major organs. Included among these arteries are the aorta (chest and abdomen), carotid (neck), femoral (legs), coronary (heart) arteries, and others. These are the blood vessels commonly treated with surgery and angioplasty (balloon therapy/stenting). The *acute* treatment of these large conduit "macro" vessels is commonly the focus of cardiologists, vascular surgeons, the news media, websites, and television shows. These treatments are routinely used and "sold" by scientific (more properly called statistical) "evidenced-based" medical practitioners. These macrovessels are the arteries said to be chronically "plugged up" (arterial plaque buildup) from the common "statistical" risk factors promoted by "evidence-based" scientific medicine: cholesterol, "bad" genes, high blood pressure, smoking, and so on. Please note that no one who speaks from scientific authority has ever said that cholesterol or smoking actually "causes" plaque. No, that's not what has been said, but commonly that is what is *heard*. What is being "said" is these factors are statistically associated with plaque, but science still does not know what actually causes arterial plaque to form.

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Sugar Toxicity

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Arterial plaque occurs in localized, "specific" sites within macrovessels; but, oddly enough, the statistical risk factors, which occur throughout the entire vascular system, theoretically should affect all macroarteries in the same way. Despite this, one commonly sees plaque blocking 90% of one coronary heart artery and no evidence of any blockage in the heart artery right next to the blocked one in the same patient. Isn't just as much cholesterol passing through each artery? Why the difference in presence and/or size of plaque? No one, and certainly no one in "evidence-based" scientific medicine, knows. They simply "know" statistical risk factors that are associated (statistically) with the presence of plaque. Scientific "evidence-based" statistical treatment and/or prevention consists of advising lifestyle changes (weight reduction, exercise, stress control, etc.) or prescribing pharmaceutical drugs (statin drugs, ACE inhibitors, ARB blockers, beta blockers, aspirin, Plavix, etc.), angioplasty, or surgery. The typical advice in mild to moderate plaque buildup is to reduce or lower weight, lower cholesterol, lower blood pressure, reduce inflammation, and increase blood thinning – all strategies that have been "statistically" ("evidence-based") demonstrated to reduce the risk and severity of macrovascular disease. Interestingly, these statistically based approaches are not effective in all patients, simply a "statistically significant" number of patients. Therefore, many patients following the correct "evidence-based" scientific diet and lifestyle and using appropriate "evidence-based" medications or surgery will continue to demonstrate advancing plaque buildup over time. Advanced or high grade plaque buildup (80%–100%) is mechanically (surgery, angioplasty) repaired as if it is simply defective plumbing, but this mechanical therapy does not correct the actual *cause.* That's about it, "scientifically speaking," for macrocirculation treatment from a scientific, "evidence-based" perspective.

Microcirculation is turning out to be radically "different." Microcirculation is also referred to in scientific medical literature as the *capillary circulation*, *terminal circulation*, or *end-circulation*. These are the tiny blood vessels (capillaries and capillary networks) that actually supply oxygen and nutrients and remove carbon dioxide and other metabolic waste from the vital organs (i.e., heart, brain, kidney, liver, etc.). Incredibly, it now appears from a scientific perspective that microcirculatory disease is primarily related to the biological toxicity of sugar, not fat as in macrocirculatory theory. The "joke" of Mother Nature on modern medical science is that substances that are absolutely "essential" to life (oxygen, sugar) also turn out to be extremely toxic to life. Nature has placed a hidden "tax" on aerobic-based (oxygen-carbohydrate-sugar) metabolic energy efficiency. Thus, metabolically utilizing ("burning") oxygen and sugar for efficient production of energy comes at a potentially high metabolic price: free radical toxicity and protein glycation or glucotoxicity. By way of analogy, oxygen toxicity can be thought of in simple terms as being similar to "rusting" of molecules in the tissue or organ that these molecules make up (free-radical pathology). Sugar toxicity is being discovered to act by causing "glycation," or "caramelization" of essential structural and functional proteins, including the glycocalyx or endothelium. This process can be thought of in simple terms as causing protein "wrinkling." Another simple analogy would be that of melting caramel over an apple and the caramel-sugar "coating" then hardens or stiffens, thus slowly, but progressively "caramelizing" the microcirculatory endoskeleton of the affected vital organ (i.e., heart, brain, kidney, etc.). When this process involves living tissue it occurs with subtle but devastating physiological consequences over time. The "nonenzymatic" (meaning in the absence of the enzyme insulin) attaching of a sugar to a protein is currently thought to destroy (glycate or caramelize) proteins. Protein glycation is currently generally assumed to be nonreversible. This assumption is actually no longer scientifically correct.

The most widely scientifically recognized clinical condition involving abnormal tissue glycation leading to clinical microcirculatory disease is diabetes. This is the biochemical, structural, and regulatory basis of the commonly encountered condition of diabetic gangrene. Once a "black toe or foot" develops in diabetes, there is no bypass vascular operation, angioplasty, or drug that will help. There is only amputation of the dead tissue and usually problems with wound healing due to the subclinical microvascular disease in the remaining "viable" tissue. Diabetes is a condition that exists in the annals of "evidence-based" scientific medicine by definition and is, "by definition," irreversible. Diabetes is defined as a blood sugar that goes "too high ..." that exceeds the statistically derived "normal" height or peak of blood sugar seen in an "average" population. The definition includes establishing the "normal" and "abnormal" blood sugar levels during fasting, after eating, or during a laboratory glucose tolerance test. This definition of diabetes focuses on how high the blood sugar goes. It turns out that glycation from glucotoxicity also occurs from glucose (sugar) being in prolonged contact with tissue. Thus, the newly described "metabolic syndrome" (also called dysmetabolic syndrome, syndrome X, or insulin resistance), which also exists by definition (and is "by definition" reversible), involves the inability of potentially toxic sugar to exit or, in more technically correct scientific terminology, be "disposed of" from the blood into the cellular metabolism as quickly as possible. Thus, diabetes, by definition, is about how high blood sugar goes and metabolic syndrome, by definition, is also about how long sugar remains in the blood (impaired glucose disposal).

The pathological effect of microcirculatory protein glycation is a stiffening of the capillaries throughout the affected organ – actually a caramelization of the microvascular skeleton within the organ involved. This process involves both abnormal biochemistry (protein glycation) and

structural circulatory regulation changes (increased microvascular resistance). The gradual glycation of protein molecules ("endothelium") lining the small capillary microcirculation stiffens those microvessels so that they cannot pulsate with the heartbeat. In addition, glycation of the proteins on the red blood cell stiffens their external membranes, making it more difficult for the stiffened red cells to pass through the caramelized capillary beds one at a time. The resultant structural problem is the inability of the microcirculation to pulsate open with the kinetic (pumping) force of the heartbeat, coupled with the red blood cells' inability to bend, twist, and deform to slip through these stiffened capillaries one at a time. A capillary that is pulsed open during cardiac systole is 10 microns in diameter. During diastole, the capillary reduces to 5 microns in diameter. A red blood cell is 8 microns in diameter. Thus, the caramelized capillary cannot dilate effectively, and the older caramelized red cell has reduced flexibility. This situation results in small capillary "infarcts or strokes" in the affected microcirculatory vessel directly involving the affected organ or tissue (i.e., brain, heart, kidney, etc.).

Over time (years to decades) the collective effects of this process appears clinically. Interestingly, the clinical syndrome that appears depends on which organ(s) is (are) affected. Microcirculatory disease somewhat mimics macrocirculatory disease in that it may "skip" around, affecting different organs or areas of the body differently. Thus, if microcirculatory glycation occurs in the heart there will be a development not of a major clinical "heart attack" (myocardial infarction), but small areas of tissue damage (i.e., slight elevation of enzymes without ECG changes) or, more importantly, the gradual development of diastolic heart failure. This process does not involve the active process of the heart contracting but its inability to relax effectively (diastole) after contraction due to microvascular stiffening of capillaries within the involved heart muscle. Thus, the heart fails to fill effectively and clinical congestive heart failure (CHF; fluid backup into the lungs, legs, etc.) develops. CHF is the now the most common and least curable form or heart disease affecting the American population, with a large proportion being diastolic heart failure. Similarly, if capillary glycation involves primarily the kidney, high blood pressure will develop. Interestingly, diastolic dysfunction, diastolic heart failure, high blood pressure, and sugar toxicity ("metabolic syndrome") are now "epidemic" among Americans, old and young. If capillary glycation occurs mainly in the brain, a condition called leukoaraiosis or coalescing tiny (lacunar) strokes leading to scaring of the gray matter in the brain occurs, and memory loss/cognitive dysfunction and/or small strokes (lacunar infarcts) will develop. Leukoaraiosis is still being taught in scientific medical schools as "a result of aging" and is of "no medical consequence." This outdated thinking has been clearly and scientifically disproved. The presence of leukoaraiosis on an MRI or CT brain scan should be taken as direct clinical evidence of abnormal microvascular glycation (endothelial dysfunction). The connection between heart disease, hypertension, and Alzheimer's syndrome, suggesting a common underlying mechanism (microvascular disease), is now being formally recognized.

Interestingly, in addition to the toxic microcirculatory effects of glucose and subsequent endothelial glycation now being described in Alzheimer's-like senile dementia, scientific evidence also shows that the accumulation of abnormal proteins (β-amyloid and tau protein) in Alzheimer's disease also causes reduced microcirculation (vasoconstriction) in the brain. β-amyloid protein also reduces endothelium-dependent brain vasodilation. As if to add insult to injury, any temporary lack of oxygen in the brain can also lead to increased production of β-amyloid protein. Thus, it is apparent that microcirculatory compromise plays a very large role in the development of memory loss, cognitive dysfunction, and dementia syndromes, regardless of the actual "official name" of the clinical syndrome. In addition to and as further proof of this situation, the microscopic changes in brain tissue that are thought to be "specific" for Alzheimer's disease (β-amyloid, tau protein, neurofibrillary tangles) have also been described in patients with heart vascular disease and no evidence of dementia. The increase in body fat that is part of "metabolic syndrome" also contributes to the "bad" situation. Centralized body fat is actually a functioning endocrine organ. Body fat secretes certain pro-inflammatory cytokine hormones (tumor necrosis factor alpha and interleukin-6 , etc.). Thus, increased body fat leads to increased inflammation (a statistical risk factor for macrocirculation disease). Inflammation can be measured using the blood test C-reactive protein or CRP. Thus, many previously recognized "independent risk factors" can now be connected through the understanding of the biologically toxic properties of sugar related to malfunction of cellular insulin receptors.

Insulin Resistance/Metabolic Syndrome

The underlying metabolic basis of glucotoxicity is the inability of the enzyme insulin to activate insulin receptors on cell surfaces ("membranes") that allow the sugar to move quickly from the blood into the cellular metabolism, where it can be used for energy production (and the production of free radicals!). Thus insulin acts as a "key" that must fit into an insulin receptor or "lock" and open that lock so that potentially toxic sugar can be transported ("disposed of") quickly and efficiently from the blood into the cellular metabolism. When sugar is not disposed of quickly, several "bad" things begin to happen: (1) glycated microvessels and cellular red corpuscles "stiffen" and lose their ability to pulsate with the heart; (2) the undisposed-of sugar is immediately shunted into centralized body fat production. One of the clinical markers used to define *metabolic* syndrome is centralized body fat (a large waistline);

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(3) additional pathological events related to poor glucose disposal include excess sorbitol production leading to nerve damage (diabetic neuropathy) and cataracts. The "defining components" of metabolic syndrome that have been "suggested" or adopted by various scientific groups and societies are high blood pressure, high cholesterol, high triglycerides, high fasting insulin levels, and high fasting blood sugar. Interestingly, all the different criteria put forth by various scientific medical groups (the WHO, American College of Cardiology, American Association of Clinical Endocrinology, etc.) do not include any evidence of direct tissue sugar-protein glycation as criteria for diagnosis. Usually, the presence of three or more of these statistical risk factors "qualifies" as a diagnosis of "metabolic syndrome." In reality, by the time any individual actually "qualifies" for the formal diagnosis of metabolic syndrome, they are already manifesting significant and late-stage clinical evidence of severe microvascular glycation (i.e., high blood pressure, obesity, heart disease, dementia, etc.).

The main biochemistry involved in the pathology of glucotoxicity is known as the Maillard reaction. This common chemical reaction has been known for over 100 years. The main scientific focus of this reaction usually involves food spoilage and industrial applications. Other than in diabetes mellitus ("sugar diabetes"), there was really little medical scientific interest in the Maillard reaction in medical science or practice. However, with the recent and gradually increasing scientific realization that the cholesterol ("fat" toxicity) theory of cardiovascular disease is at best incomplete, or more likely simply wrong, more scientific interest and resources have been reevaluating the pathophysiological effects of the Maillard (sugar toxicity) reaction. There is also overwhelming scientific evidence rapidly accumulating that in vivo pathological Maillard reactions accumulate both from internal dysmetabolism of sugar and ingesting advanced glycation end products (AGEs) created by excessive heating of food that are toxic in living tissue. In addition to the Maillard reaction, the Amadori rearrangement and Schiff base reactions are also part of the complex biochemistry of sugar toxicity.

One major problem faced by clinicians interested in prevention of and early intervention in the manifestations of abnormal tissue glycation is that there is no single test in "evidenced-based" medicine that can "diagnose" metabolic syndrome. Abnormal glycation diseases can be diagnosed using several clinical and laboratory findings, but not by a single laboratory test. A simple blood test called the hemoglobin A1c or glycohemoglobin (HbA1c) test easily and cheaply provides critical clinical information about the ongoing degree of glycation in the body due to inadequate glucose disposal from blood. The "trick" in using this scientific (evidence-based) test as a "new and emerging risk factor for clinical vascular disease" (as it is now being discovered and described in scientific medical journals) is to understand that the laboratory statistical "norms" are not related to individual optimal values. A value for HbA1c above 4.6 should be considered "abnormal" (meaning evidence of accelerated cellular membrane glycation). In most commercial laboratories, diabetes is said to be present, by definition, if the value is 6.4 or higher. This is why most diabetics demonstrate severe vascular disease before scientific medicine diagnoses it. Membrane receptor resistance to the hormone Insulin is not acknowledged until late in the process (advanced tissue glycation) or a "high" HbA1c. Objectively testing using PORH for disturbed microcirculatory function and/or pulse volume recordings (PVR; microvascular disease of the vasa vasorum in macrovessels) can also demonstrate the effects of abnormal vascular glycation (loss of microvascular compliance).

As an aside regarding laboratory measurement of insulin or any other "hormone level," the clinical reality is that no hormone actually works in the blood (or urine, or saliva); hormones do their metabolic work by activating a hormone receptor (i.e., the "key in lock" analogy) located on a specific cell or nuclear membrane. The hormone receptor is usually located on the cell membrane (i.e., insulin receptor) or the nuclear membrane (i.e., thyroid receptor). Thus, in many individual ("not statistical") cases the "blood level" (and urine or saliva, for that matter) of a given hormone (i.e., thyroid, insulin, vitamin D, etc.) may be "statistically" normal or even "optimal" and yet the clinical symptoms of the particular hormone "deficiency" may clearly be present. This is a very common clinical phenomenon seen with insulin resistance syndrome. Blood simply acts as a transport medium to get the hormone from where it was made to where it will have its metabolic effect. As stated earlier, the insulin receptor is located on the cell membrane – and some

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cells have many more insulin receptors than others. This is the functional basis of IPT (insulin potentiation therapy) cancer chemotherapy: to use insulin to activate the insulin receptors on cancer cells. Cancer cells revert to a more primitive cellular metabolism referred to as anaerobic ("without oxygen") glycolysis (fermentation). Thus, cancer cells have significantly more insulin receptors on their cell surface than noncancer cells. Giving insulin to cause a drop in blood sugar, and at the low point of the blood sugar very small (15% to 20% of standard, recommended) doses of chemotherapy drugs to allow the cancer cell to preferentially take in the drugs as they are in their insulin activated sugar "feeding frenzy," creates a physiologic "Trojan horse" approach that significantly minimizes side effects and yet maximizes therapeutic benefit of chemotherapy to actually target the problem cancer cells, thus sparing drug toxicity to normal cells and tissue. The clinical results in cancer can be quite amazing when appropriately employing IPT.

Returning to the discussion of microvascular glycation related stiffening or lack of pulsatile ability of vascular tissue, pulsation of the microcirculation turns out to be critical for all major organ health. This is the simple reason that scientific medicine has not yet developed an effective implantable artificial heart. Pulsatile flow is something that is required in normal physiology. Any experimental animal that is put on a heart bypass pump that uses nonpulsatile or laminar flow dies within days of progressive, multiple organ (kidney, heart, brain) failure due to progressive microvascular dysfunction – called scientifically increased peripheral vascular resistance. Our best technological engineers can make pumps smaller than a dime that can operate in climates as alien as the Martian surface, but they have not yet mastered the essential, life-sustaining properties of biologically imperative pulsatile flow. The main physiologic cause of pathological microvascular stiffness is glucotoxicity. Clinical counterparts of this "laboratory" phenomenon of increased organ microcirculatory stiffness are commonly encountered, but just as commonly, the causal underlying mechanism (microvascular stiffening due to glycocalyx/endothelial caramelization) is usually not clinically recognized and thus crude, noncurative symptomatic drug or surgical therapy follows. One commonly missed clinical example of this phenomenon may be heart and peripheral arterial vascular stunning and hibernation. Integrative medicine employing chelation therapy has demonstrated clinical effectiveness in reversing stunning and hibernation, in both entire organs (heart microcirculation) and extremities (leg macrocirculation/vasa vasorum). The actual cause of the phenomenon of stunning and hibernation is "unknown" in evidence-based medicine, but glucotoxicity of the microcirculation in the corresponding capillary bed of the heart muscle or the vasa vasorum (or microcirculation) of the macrovessel arterial wall may be involved.

Another clinical "symptom pattern" manifestation of insulin resistance is polycystic ovary syndrome (PCOS). The currently accepted treatment for PCOS is either using synthetic hormone birth control pharmaceuticals (BCP) or the off-label use of the antidiabetic drug metformin. Interestingly, birth control helps PCOS symptomatically, although it is known to cause weight gain, high blood sugar, and, more importantly, increase vascular resistance. It appears that while improving the clinical picture, BCPs seem to be making the manifestations of endothelial dysfunction worse. The clinical and laboratory effects of metformin in PCOS were found to be clinically superior to BCPs. It is also possible that other chronic degenerative diseases may be related to underlying microvascular pathology. For example, osteoarthritis, which is really osteoarthrosis, since no true inflammation ("-itis") is involved, may be related to reduced microcirculation to the associated joint and cartilage tissue. This could explain why the simple clinical methods of heat, massage, and/or injecting ozone (prolozone therapy) into the affected joint and/or periarticular tissue results in reduction and elimination of pain by increasing microcirculation. Chronic unexplained pelvic pain in both sexes may be related to regional microvascular disease. Localized "trigger points" in muscles may also be due to localized microcirculatory disturbance. Much like the phenomenon of localized compromise of microcirculation in the brain (dementia), heart (diastolic heart failure), or kidney (hypertension) leads to different clinical patterns resulting from the same underlying pathology, perhaps other degenerative conditions will be found to be related to reduced microcirculation to an affected organ or anatomic/physiologic area.

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Due to space limitations we are not able to print the full text and references of "Sugar Toxicity: A Silent Epidemic." Please look on our website, www.townsendletter.com, under the contents for the May 2016 issue for the hyperlink to the unabridged article.

Head-On Collision Kills Millions Yearly

by John Parks Trowbridge, MD

America's highway design has improved markedly since the 1950s, when many of the long-haul routes were merely two-lane roads. Most of the rural/farm-to-market roads between smaller towns still are two-lane asphalt. We are a trusting sort, hurtling down the road at 60 or 70 miles per hour, listening to the radio, talking on the cell phone, or just enjoying the scenery.

At a closure rate of 140 mph, two 2000-pound vehicles will compress easily into tortured piles of metal and plastic should they collide head on. Certainly *you* wouldn't be so careless as to drift across the centerline into opposing traffic. After all, you value your life, and you expect to enjoy your family for years to come.

But ... what about the other guy? Is he cautious and considerate like you? Is she preoccupied because she just had a dispute with her husband or her boss? Is he a newly minted teen driver? Or perhaps a young adult is at the wheel, wanting to demonstrate his bravado to a new girlfriend? Worse, is she tipsy from just a little bit of alcohol – or a whole lot more – or stoned on marijuana or opiates? Something as simple as a phone call or text message being sent or received could evaporate the lives of two or more people, literally in the blink of an eye.

Some 30,000-plus Americans die in motor vehicle accidents each year. Head-on collisions that they certainly didn't expect account for only 2% of such tragedies – but they result in 10.1% of all fatal crashes. Each of these folks, innocent or not, have just taken a "five times" shortcut to their Final Judgment.

But the question remains – are *you* facing a more serious crash that virtually everyone is risking, some almost daily?

Clash of Values, Crashing Lives

Sadly, the clash of values in medical care can have consequences every bit as serious and with the finality of a head-on crash. We shake our heads, believing that the deadly motor vehicle accident was so avoidable, so unnecessary. But when friends and family suffer or die from modern conventional medical care (or surgery), we softly murmur to each other, forgivingly, "The doctors tried their very best, they did *everything* they could."

And often, that would be a lie. Perhaps a comforting one, but nevertheless a lie. Not a little white lie, not a slight twist on the truth, not an innocent or even deliberate misrepresentation. *A lie.*

Stay In Your Lane!

Physician training – medical school and residency/fellowship programs – are closely coordinated in the US. Curricular planning and escalating clinical responsibilities are designed to produce graduates with reasonably consistent skill sets and adequate judgment for patient care situations. Sadly, this regimentation also narrows the viewpoints of most new physicians, who obviously seek to gain favor and approval of their faculty or practice seniors.

One worrisome correlate is a uniform suspicion of technologies to which they were not exposed in their class work, clinical experiences, journals, or continuing education conferences. CME credits, controlled tightly by "AMA-types," are granted to groups and programs that meet oftimes rigid criteria that discourage deviation from "the norm," only accrediting the topics from approved teaching and work experiences. Hospital "quality control/ utilization review" investigations can be a powerful incentive for every physician to conform – or to come to heel if possibly stepping out. Membership on the medical staff or privileges granted for hospital activities can be imperiled as a more serious gradient. Another enforcement option: whether the insurance carrier will approve reimbursement for something different, something new, which brings to bear efforts of administrative officers or colleagues to discourage any "deviations."

Who's Holding Up Traffic?

Galen of Pergamon (129–ca. 200 AD, Greece), for all his observational and analytical skills, so dominated and influenced Western medical science that his teachings retarded advances in physiology for 1300 years. The scenario can be encapsulated as "See one, do one, teach *only the same*." Understanding the actual circulation of the blood in a circuit through the heart and to the brain and body and back would wait until William Harvey (royal Physician Extraordinary to James I and Physician in Ordinary to Charles I of England) boldly parted with tradition. In 1628 he rather easily demonstrated the correctness of his explanation. His detractors insured that his social prestige and professional stature suffered dearly and enduringly.

All too often now, local colleagues and professional organizations successfully suppress questions, research, or practices that could lead to more perfect understandings. When a questioning "transgressor" meanders too far astray of the "prevailing manifesto," senior staffers can always report such deviations to the state medical board to rein in performance that could disturb the status quo. Sadly,

a clear majority of articles published in "indexed" medical publications (those 5300+ cataloged for computer searching [since 1966] in Medline/PubMed – out of 13,000+ biomedical journals worldwide) reinforce "*the* way to do things," as they are sponsored by major pharmaceutical companies with branded products to hawk and more than just a commercial bias as well. All in all, the profession does a respectable job of insuring that the same uninspired level of clinical care is offered by most every local physician, generalist, and specialist, both town and gown.

My Way or the Highway

In such an oppressive hospital, clinic, or office environment, how are recent advances to be integrated into the practice setting? Whenever journal articles or CME conferences introduce different approaches, they *might* slowly become adopted. Resistance, though, is often high, especially if the postulates appear at radical variance to standard practice, or if in-depth learning is required, or if a complicated and expensive technology must be employed. Only slowly does the cadre of practitioners become trained and skilled and then, of course, "Everyone knows that *this* is the way to do it." As the German philosopher Arthur Schopenhauer (1788–1860) succinctly noted: "All truth passes through three stages. First, it is ridiculed. Second, it is violently opposed. Third, it is accepted as being self-evident."[1]

Marked resistance flared against breast "lumpectomy" espoused by Harvard-educated Cleveland Clinic surgeon George Crile Jr., MD, from the 1950s until its reluctant adoption over 30 years later. He is said to have stated, "I came home from World War II convinced that operations in many fields of surgery were either too radical, or not even necessary. Universal acceptance of a procedure does not necessarily make it right."[2]

With the adoption of pretended "evidence-based" protocols, promulgation of "standards of care" by specialty societies, and "compliance documentation" by reimbursement-driven checklists embedded in electronic medical records, the regimentation in clinical practice ever more successfully ostracizes divergence from the "expert"-asseverated norms.

Heart Hospital – Next Exit

Two specialties that conspicuously reveal the head-on clash of values that needlessly costs lives and promotes suffering are the care of the leading killer in the US, heart and circulatory diseases, whether by medical or surgical means. Skilled physicians who venture into cardiovascular approaches that integrate "alternatives" into (or in place of) conventional care schema are often astounded at their new level of success in controlling or resolving complex problems. Since robust function of the heart and blood vessels is critical to survival and preservation of mental activities and physical capabilities, the comparison of treatment results is easy to demonstrate. Any dalliance into a different way of thinking and treating will bring swift and sure retaliation from their colleagues. Not much has changed in 40 years – even now, conventional physicians and regulatory medical boards foolishly discourage "changing lanes" to pursue honest inquiry, despite clear signals from state and federal courts:

> The courts have rather uniformly recognized the patients' rights to receive medical care in accordance with their licensed physician's best judgment and the physician's rights to administer it as it may be derived therefrom. ... In *People v. Privitera*, Cal.App., 141 Cal.Rptr. 764, 774 (1977), the court ... stated that,
>
> "To require prior State approval before advising prescribing administering a new treatment modality for an informed consenting patient is to suppress innovation by the person best qualified to make medical *progress. The treating doctor, the clinician, is at the cutting edge of medical knowledge.* To require the doctor to use only orthodox 'State sanctioned' methods of treatment under threat of criminal penalty for variance is to invite a repetition in California of the Soviet experience with Lysenkoism [false science accepted as real only because *politicians* endorsed and enforced it]. The mention of a requirement that licensed doctors must prescribe, treat, 'within State sanctioned alternatives' raises the spector [sic] of medical stagnation at the best, statism, paternalistic big brother at worst. It is by the alternatives to orthodoxy that *medical progress* has been made. A free, progressive society has an enormous stake in recognizing and protecting this right of the physician."[3] (emphases added)

NB: Both Drs. Privitera and Evers have long been champions of chelation therapy and nutritional approaches to help those suffering with cardiovascular diseases – and they both weathered several attacks.

Sadly, the *crash* of such values, which doggedly discourage even a passing exploration into so-called "alternative" approaches, is directly responsible for mangling of bodies, untold suffering, and avoidable death on a daily basis.

Merge Now – Right to Your Bypass or Stent

Assessment and treatment of coronary artery disease is a senseless and bloody battlefield between conventional care and EDTA chelation therapy.[4] Rather than adopting chelation, a nonsurgical technology, as complementary and contributing to survival and enhanced patient comfort, cardiologists and surgeons often resort to tacit intimidation. "You're a ticking time bomb, so we need to operate as soon as possible. We can do your operation this Thursday only because our scheduled patient didn't believe his condition was serious." This was a classic line, likely still used today. A study by the National Institutes of Health concluded that patients who resorted to chelation therapy (for removal of toxic metals and improved circulation) had less faith that conventional medications could prevent worsening of their heart disease, increase the quality of life, and give a feeling of control over heart disease.[5] Of concern is that major heart bypass studies – from the 1970s and 1980s! – suggest a situation quite the opposite from that described by heart surgeons. The Veterans Administration Cooperative Study, US CASS study, and European CASS study demonstrated that having to endure the side effects and risks of bypass surgery is essential for survival only in about 16% of cases, especially those with left main or left anterior descending (LAD) obstruction.[6–8] The remaining 84% of patients can expect to live on and thrive without operative intervention, often for many years.

Are surgical techniques and survival better now? Probably – and I hope so!

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In 1991, a study of 222 patients showed that bypass grafts gradually accumulated blocking plaque from the very first year, to where 75% of survivors showed "disease" at 10 years after surgery; only 17% of grafts were healthy at 10 years.[9] A large Duke University study of coronary stents shows no increase in long-term patient survival.[10]

Harvard cardiologist Thomas Graboys, MD, reported his famous "Second Opinion" studies in the early 1990s: patients who had declined bypass (or even angiography with the prospect of stents) survived surprisingly well, generally *better* than those who chose operation.[11,12] Technological improvements have helped to reduce the risks of death and major disabilities from operative procedures. Even now, the majority of patients resorting to medical (drug and diet) treatments can safely delay surgical interventions without increasing their risk for untimely death. Those who also choose to undergo chelation therapy might improve so much that they even defer the risks of surgery for years ... and years. Given the number of "redo" bypasses or repeat placement of stents, is it odd that conventional specialists have ignored referring their patients to chelation therapy after recovering from successful lifesaving surgery for acute events?

The key to long-lasting relief from cardiovascular blockage, especially often fatal coronary artery obstructions, always involves a nutritional support approach, not just a simple dietary change along with surgery and drugs. Conventional physicians and surgeons seem to loiter in the fast lane at 35 or 40 miles per hour, preventing those who might want to find new roads from easily passing them by. The science, though, is clearly published in well-respected journals and alternative physicians pass along to patients these tactics with ease. While antioxidant approaches have long been valued, only in recent years has cardiovascular obstructive disease been characterized as a debilitating development from chronic ascorbic acid (vitamin C) deficiency – yes, scurvy.[13]

Your Ticket for Failure to Drive Safely

"My doctor is the very best." I sure hope so! Despite (sometimes deserved) broad criticism of the profession, most patients are trusting that their own personal physician is exceptional, that he or she really is competent, knowledgeable, and trustworthy.[14] As one practitioner so keenly stated years ago, "You better find and trust the very best, because your cardiologist doesn't get buried in your casket." But ... what if your doctor simply hasn't kept up with the latest advances in care? Or what if she never quite mastered the skill set required to treat complex problems (or even simpler ones) that you have? Or ... what if he hasn't ever heard about or studied or understood effective alternative therapies such as chelation, oxygen, nutritional support, even appropriate dietary interventions? My friend and mentor Richard Brennan, MD, explained that professional attacks and crushing criticisms could be encapsulated by a quote from R. Stanton Avery, inventor of peel-off adhesive labels: "You're always down on what you're not up on."

Congestive heart failure, an increasing problem in recent years, is a diagnosis encompassing a wide variety of cardiomyopathies, where the heart muscle itself is ailing and underperforming. In the year after initial diagnosis, more than a third of patients with conventional care are likely to die.[15] A search for underlying conditions – hyperthyroidism, anemia, chronic tachycardia, and much more – is always essential. Many physicians-in-training learn the "basics" of emergent intervention: bed rest, diuretics, oxygen. Medication management has become intensely complicated, adapted to diverse presentations and evolving condition. In the old days – yes, I have enough gray hairs to state with certainty – we were taught to use digitalis preparations to improve heart contractility and, thus, ejection fraction. Unless acute infarction, rhythm alterations, rupture of a papillary muscle, valvular incompetence, or septal defect were discovered and required surgical intervention or other care, improved circulation dynamics usually resolved the episode in days. Restoring satisfactory heart function led to discharge home, usually with more medications.

A more recent technology is ECP (external counterpulsation), which uses pneumatic cuffs placed around the legs with inflation/deflation timed with the EKG rhythm, to decrease the afterload that the heart has to pump against, and increase the preload that fills the heart, increasing the cardiac output. Patients with more severe failure are candidates for an implantable defibrillator to reduce mortality associated with ventricular arrhythmias that are likely.

So what could possibly be wrong with this picture?

In the labor-relations field, blame is always directed at "management." And in this case, I squarely hold management responsible! Some find it reassuring that today's physicians rely on objective data – laboratory tests, imaging studies, published reports of treatments, and so on – to diagnose and "manage" patients. "Happily," such an approach rarely requires touching (examining!) the patient or even taking a detailed and illuminating history. (This would be an unwarranted sarcastic remark – but think back to recent doctor visits.) The next "objective" step is to write prescriptions. The patient on half a dozen "meds" might even receive instruction (counseling!) on their treatment program ... then they're promptly sent home for a later return-to-office. (Remember: a patient on two or more prescriptions is already an "experiment," and results and adverse effects or interactions remain to be seen.)

What's wrong with this management? Doctors become skilled at ordering tests and writing prescriptions – listening to and examining patients have become lost arts, as has training in managing certain complex physiologic medications. Why? Because management is time consuming! You have to "fiddle" with dosages and respond to patient complaints and concerns. Who has time for those phone calls or extra test reports coming through? And insurance won't pay for extra ("unneeded"?) office visits that would make such management techniques more convenient for the physician. Management of digitalis is a classic example; too little doesn't work and the patient could die; too much is toxic and the patient could die. "Just right" is the "sweet spot" that has to be individually determined for each individual – and it changes over time. If a physician fails to understand or appreciate the complexities involved in effective prescribing of digitalis, he shies away from using it. Happily for "him," the "standards of care" now do little to encourage its use, instead favoring a beta

blocker and/or a diuretic, or other recent cardiac/hypertension medications, despite rational arguments that have been advanced for continuing its usage.[16,17] (See sidebar, p. 72.)

Repeat episodes of congestive failure are taxing on body systems and lead to shorter survival times. So if digitalis isn't used as much by conventional physicians as would be desirable, why could it represent a dangerous or deadly clash of values? A large number of "alternative/integrative/complementary" physicians have practiced for dozens of years. They were trained to use digitalis. They actively manage various aspects of their patient's condition. They listen. They examine. They teach valuable tricks for home monitoring, such as daily weight, pulse, blood pressure, and assessment of dependent edema. They usually respond to patient concerns between office visits and readily adapt their treatments to changing circumstances. And many of them quite handily manage the use of digitalis to keep their patients out of congestive failure.

One last note on the clash of values: integrative physicians might reach for medications, but they'll also depend on adequate intake of magnesium and balance of potassium (both depleted by diuretics), and cardiac performance enhancers such as D-ribose, coenzyme Q10 and idebenone, pyridoxine (vitamin B6), cholecalciferol (vitamin D3), and iodine, to name a few. A number of herbs can be helpful as well: hawthorn, garlic, curcumin, bilberry, others. Increased vegetable intake (colored, often raw) along with reduction of sugar and starch intake have been shown since 1960 to be invaluable as well, especially with emphasis on low sodium, high potassium, and high water intake.[18,19] Interestingly, "diastolic dysfunction" in heart failure is often documented on the EKG ... and few physicians recognize that as a sign of intracellular magnesium deficiency.[20]

You're Driving Me Up the Wall!

Let's bust another myth; namely, that daily stresses drive blood pressures up. Sure, that can happen – especially with chronic magnesium deficiency – but many patients (and their physicians) misunderstand what stressors are and the simple nondrug techniques to better cope with them, such as easily learned and readily practiced meditation (not medication).[21] Even worse, many physicians poorly appreciate the gradual worsening of mental and physical performance associated with aggressive control of blood pressure. The adult ideal, of course, is about 120/80 mm Hg. Elevations above 140/above 90 attract lots of attention and often lead to "the usual" medication programs. Patients come in with home pressures below 110/below 60 and are told by their cardiologist, "That's fantastic." But many of them awaken tired, are fatigued easily, have difficulty thinking clearly, and have little if any physical endurance.

The physiology usually is not difficult to understand. Arteries and tiny arterioles have muscular and elastic layers, both of which slightly resist expansion when impacted by the bolus of blood pulsing through during systole. By returning to their preferred "no tension" baseline state during the pause of diastole, they contribute "just a bit more" to distal tissue perfusion. Not merely the brain but all other organs as well depend upon a basal volume and pressure of flow to meet their survival needs, ➤

Head-On Collision

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with an increased level obviously needed to perform functions. When one is lying down, the heart is pumping blood "horizontally," with little effort. Any upright position, especially standing, imposes a gravitational load on the now-vertical columns of blood, requiring more "punch" (stronger contractility, even a more rapid pulse and greater ejection fraction) by the heart. Beta blockers, diuretics, and other blood pressure medications can impair physiologic reflexes and thereby severely limit cardiac responses to increased demand. Simply stated, many alternative practitioners are mindful of fine-tuning control, sometimes allowing systolic pressures to reach or breach 150 and diastolic to reach 95. Those higher levels, so long as tolerated without cardiac strain or peripheral distress, have only a marginally increased risk of infarct, aneurysm, or hemorrhage – but the beneficial effect on patient comfort cannot be underestimated.

So what is the collision with conventional care? Desirable cardiovascular conditioning becomes achievable only when a patient can tolerate (even enjoy) a tailored and graduated exercise program. Obviously, hardened vessels (arteriosclerosis) or flow-limiting blockage by plaque (atherosclerosis) reduce the younger-age contribution of arteriolar distension and resistance, so the heart by itself must work harder for *any* result. Integrative physicians will reach for medications as needed – but they'll also depend again on minerals and vitamins, dietary factors, and herbs for cardiac support, as noted above.

Before we exit the "stress highway," reflect on the oft-forgotten work of Canadian experimental surgeon Hans Selye, MD, who first characterized the phenomenon of "stress" within the body. Studies on doctors-in-training showed work-pressure can lead to a surge in white blood cells, which apparently clump and promote clot formation that reduces distal blood flow. This finding led to experiments with mice that placed under chronic stress conditions, associated with higher levels of noradrenaline. The results show that mice developing atherosclerosis in their arteries make plaques that very closely resemble those known to be most at risk of rupturing and causing heart attacks or strokes in humans.[22] (Relax, pull over, take time to smell the roses?)

A Duke University study of 6000 white patients with a history of heart disease – two-thirds of them men – showed 13% had a simple genetic mutation (one base-pair in one gene coding for the serotonin receptor) that led them to overreact to stress. They found double normal circulating cortisol levels and a 38% greater risk for heart disease and

Window View, Bathtub Leak

Physician training encompasses a wide range of topics that need some degree of mastery. With the explosion of new drugs in the past several dozen years, younger doctors have even more to learn. Sadly, that might omit the finesse with which certain (often older) medications must be managed. First, you have to understand the mechanism of action and the degradation pathways. Second, you have to account for your patient's unique circumstances. Only then can you initiate and then manage the dose of certain medications.

My father was maintained on Lanoxin (trusted brand of digitalis) for the last 14 years of his life, staying out of congestive heart failure despite multiple health challenges. During his final course, his attending physicians refused to order Lanoxin – "We don't do that anymore." "But he's been stable for years, it works well for him." "No, we mostly use beta blockers and diuretics." "If you don't put him on Lanoxin, he'll likely slip into congestive failure in the next 4 or 5 days." And he did. Three separate times over 5 months. Their modern response was "admirable": he was urgently taken by ambulance from the "skilled nursing" (don't ask!) to the hospital in frank congestive failure (dyspnea, tachypnea, tachycardia, edema, elevated BNP, the whole show). And, of course, a man in his 90s *must* be entered into the standard treatment protocol that includes fourth-generation antibiotics "for pneumonia." "But ... he doesn't *have* pneumonia." "Protocol requires him to be on presumptive treatment." "But ..." It was a fruitless battle.

Lanoxin and Coumadin (brand of warfarin) share a common feature with regard to dosing for desired effect. The loading dose needs quickly to achieve a therapeutic level – not too low (below the bottom sill of a window) and not too high (above the horizontal part forming the top) but "just right," (enjoying the view through the window). A new factor then becomes central: maintenance dosing for "continued viewing through the window" needs to replace drug lost to metabolism or excretion ("leaking" out the bathtub drain, so the level eases down). A variety of factors – comorbidities, liver function, cholestyramine (Questran) for Lanoxin, "green" vegetables for Coumadin, and so on – influence the decline of drug level. Testing is easy for either drug ... *but* the prescribing physician needs to manage the dosing, sometimes several times between office visits to achieve reliable levels. Some doctors are just too busy ("taking care of patients"), others simply aren't interested in making the extra effort, and maybe many (or most?) never understood the physiology, so they simply don't know how.

Not to mention numerous drug–drug interactions with Coumadin and Lanoxin, even by commonly prescribed items. Food choices matter as well: foods rich in vitamin K can reduce the anticoagulant effectiveness of Coumadin. These include beef liver, broccoli, brussels sprouts, cabbage, collard greens, endive, kale, lettuce, mustard greens, parsley, soybeans, spinach, Swiss chard, turnip greens, watercress, and other green leafy vegetables, and to a lesser extent asparagus, avocados, dill pickles, green peas, green tea, canola oil, margarine, mayonnaise, olive oil, and soybean oil, and even some vitamin products. Similar to impaired absorption by cholestyramine, Lanoxin levels can be reduced by high-bran/high-fiber foods, such as certain breakfast cereals.

Last but not least, there's the problem of the "protocols" or enforced "standards of care" often arriving by mail from large mail-order pharmacies. And, additionally, we are always coping with scanty insurance reimbursement for essential lab testing, "overly frequent" office visits, and prescribed drugs. Help me to understand: Exactly who is responsible for managing the patient?

early death.[23] There you have the scientific future of health enhancement for each individual patient: the better your map, the more you'll enjoy the trip, and the easier to get to your destination.

Keep on Truckin'

Our autonomic (automatic) functions are reliably monotonous or unconsciously responsive to changing conditions. Pulse is usually so "straight and steady" that rarely is someone aware of his heartbeat – until it seems to be jerking or racing along or pounding hard. Arrhythmias are frustrating disturbances, and some can create dangerous or fatal problems. Atrial fibrillation – seemingly much more frequently seen than in past years, now affecting more than 2 million Americans – is especially troublesome. Advances in electrophysiology and cardioversion have rapidly ushered in the new and often effective specialty of interventional cardiology. Sadly, some patients remain stubbornly out of rhythm control or easily or frequently relapse. Antiarrhythmic medications sometimes have troublesome side effects and are no guarantee of normalized rhythm. Alternative physicians are keenly aware of the critical contribution of minerals and vitamins, dietary factors, and herbs for cardiac support, as noted above.

Perhaps of greatest concern is the prospect of arrhythmia-related coagulation, with the very real likelihood of resultant myocardial infarcts (heart attacks), transient ischemic attacks or frank cerebrovascular accidents, optic nerve or retinal infarcts leading to vision degeneration, kidney failure (possibly obstruction of renal artery flow, creating a Goldblatt kidney that leads to ischemic renin–angiotensin–aldosterone system-mediated hypertension), mesenteric ischemia or infarct, peripheral ischemia and even gangrene. The list is ominous – and survival is squarely challenged by any of these pathological blood clots. Although related to different mechanisms in the post-capillary circulation, deep vein thrombosis (DVT) and pulmonary embolism (PE) are similarly calamitous.

For the fearless driver, here's an interesting detour: infarctions can occur without any clot being found in the artery;

Head-On Collision

a clot can form in a coronary artery days or even weeks before a myocardial infarction; a clot can fully obstruct a coronary artery without causing an infarction.[24] And why does plaque not form in your veins or your pulmonary artery, exposed to almost all of the same "risk factors" as coronary arteries? The story is gigantically complex, not merely as simple as, "Start here, turn there, and *X* marks your destination." Quite possibly it is an infarction that first occurs and *then* the clot forms. With all the emphasis on the cholesterol hypothesis, kick *these* tires: systemic lupus erythematosus (SLE) increases the risk for cardiovascular disease 83 times (8300%!) more than having an elevated level of LDL cholesterol.[25] Answering these challenging issues will provide future treatment strategies.

Conventional physicians have long relied on Coumadin to impair clotting tendency of the blood. The annual market for anticoagulant drugs is estimated to be over $10 billion in the US. Side ➤

effects of Coumadin are not trivial: brain hemorrhages and other forms of internal bleeding, making it one of the leading causes of emergency room fatalities. More recently, Eliquis, Pradaxa, and Xarelto have emerged as drug "favorites," claiming that frequent blood testing (PT, protime assessment of the in vitro time to reduce fibrinogen to an intact fibrin clot or the derived INR [international normalized ratio]) is not needed nor are dietary limitations (such as salads, green leafy vegetables containing forms of vitamin K that competitively interfere with the blocking of liver production of fibrinogen by Coumadin). I have long advocated dosage levels that achieve 18 to 20 seconds (PT) or about 1.8 to 2.2 (INR) for many patients, to reduce bruising/bleeding risks while providing a desirable anticoagulant effect.[26] Comfort and convenience certainly are promoted for the newer drugs, so long as the side effects can be ignored: unexpected or uncontrolled bleeding leading to injury or death. The list of common drugs that interact with these recent medications is long indeed. Taking aspirin or other over-the-counter or prescription NSAIDs while on *any* anticoagulant prescriptions can dramatically raise the risk of deadly bleeding. (Remember 1-800-BAD-DRUG? In May 2014, a short 3½ years after Pradaxa was introduced, the manufacturer reportedly settled more than 4000 lawsuits for $650,000,000.)

Alternative physicians need not rely solely on conventional prescription drugs to create desired effects. We often look to nutritional supplements that improve blood rheology (viscosity relating to ease of flow, such as ketchup versus syrup) and reduce inflammatory (oxidant) reactivity of the blood compartment (whether circulating constituents or endothelial lining). Sadly, some conventional doctors strongly protest or discourage their patients from taking "any vitamins or such" that they unknowingly surmise would "cause problems." Critical examples of useful natural substances are fibrinolytic enzymes – classically nattokinase (subtilisin, produced by bacteria from boiled/fermented soybeans), serrapeptase (from bacteria found in the silkworm intestine), and lumbrokinase (enzymes from earthworms) – along with nonesterified tocopherols/tocotrienols (vitamin E), carotenoids and beta-carotene with vitamin A activity, ascorbic acid (vitamin C), omega-3 fatty acids (EPA and DHA) from marine sources, even ubiquinone, liposomal glutathione (GSH), L-carnitine, alpha-lipoic acid, curcumin, Pycnogenol from grapeseeds or tree bark, and several bioflavonoids..

How many conventional physicians strongly discourage pro-inflammatory foods – not just sugars and starches but also those processed, preserved, stabilized, enhanced, and other "foods of commerce"? The standard American diet ("SAD") is a simmering cauldron, ready at any moment to slide you off the road to healthy as easily as a wet oil slick kills your traction on pavement.

Where appropriate, physicians skilled in the management of Coumadin readily rely on that valuable prescription (see sidebar). In my almost 40 years of clinical care, I never have needed to severely reduce vegetable intake; all I do is have the patients stay on a reasonable fresh food diet (always limiting sugars and starches!) and then adjust Coumadin dosage *around* their personal food choices. After optimizing antioxidant status, erythrocyte deformability, platelet reactivity, endothelial function, and blood viscosity, some patients can be reduced in prescriptive dosages or even removed from such support.

Screeching Halt

Talk about a deadly accident! Deep vein thrombosis (DVT) and thrombophlebitis have grabbed the attention of the public more recently due to the television ads for the recent (expensive) anticoagulants noted above. Lest we forget that some emergencies really are life-threatening and might require urgent surgery, a high index of suspicion must be maintained by all physicians so that dire consequences can be avoided. When ultrasound or other modalities confirm the presence of an obstructive pattern, hospital care is often most advisable. At discharge, however, the routes take different directions: conventional cardiologists and cardiovascular surgeons often pursue a treatment plan similar to that outlined above for disturbing arrhythmias.

Successful treatment merely begins when your patient is stabilized and recovering for discharge. Alternative physicians follow the same map outlined above for arrhythmias, but they emphasize a plan to reduce inflammation and improve rheology (flow characteristics). More importantly, they devise a program of inquisitive investigations trying to explain how this "accident" developed in this individual at this time. The answers could suggest the direction to be pursued as foundational treatment, aimed at reducing the chances of recurrence in coming months or years. Surprisingly, each search might turn up a different "answer," since we're sleuthing for the specific pathways by which this particular patient finally hit the wall and suffered such a potentially catastrophic event. Not just the high road, not just the low road, many "roads lead to Rome"!

Perhaps it goes without saying ... diagnostic and treatment programs for cerebrovascular accidents (strokes) and TIAs (transient ischemic attacks), gangrene, and retinal or optic nerve occlusions are pursued by alternative physicians in very much the same way as for DVTs. Although the "theme" is the same, a personalized program will be designed for each suffering patient.

Brand names are trademarks of their respective owners.

John Parks Trowbridge, MD, has long been regarded for his incisive thought and broad perspectives. Recognized as a Fellow of the American College for Advancement in Medicine in 1990 and honored with a Lifetime Achievement Award by the International College of Integrative Medicine in 2014, he has lectured around the world on integrative medicine topics and is listed in over five dozen volumes of *Who's Who*. He maintains an active office practice in Humble (Houston), Texas. Phone: 800-FIX-PAIN.

Due to space limitations we are not able to print the full text and references of "Head-On Collision." Please look on our website, www.townsendletter.com, under the contents for the May 2016 issue for the hyperlink to the unabridged article.

Head-On Collision

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Calcium Fructoborate: A New Mineral Complex with Anti-Inflammatory Action

by Jerry Stine and Nancy Faass, MSW, MPH

The role of inflammation is well established as a major contributing factor in chronic illness and aging. Consequently, the management of inflammatory process has become an important goal in both integrative and standard practice. Clinicians in functional and longevity medicine address this issue with specialized lab testing, diet, and a range of supplementation strategies. Here we review a new, but well researched natural supplement, *calcium fructoborate*, an agreeably tolerated, easily absorbed, moderately-priced mineral compound affecting a number of fundamental processes integral to human health, including the reduction of *inflammation*.

Calcium Fructoborate (CF). CF is a boron-based mineral complex composed of calcium, fructose, and boron in a patented formulation, with more than a dozen research studies showing the potential to affect functional dynamics in the body, including:

- Inflammation—reduces CRP levels consistently in all studies by approximately 40%
- Markers of cardio risk—lowers TChol, LDL, and IL-6, and raises HDL
- Incidence of angina—50% reduction in angina episodes in a clinical trial
- Important indicator of congestive heart failure—reduces N-terminal prohormone of brain natriuretic peptide, a marker of left ventricle function
- Joint health and osteoarthritis—reduces markers of inflammation such as CRP, IL-6, and IL-1, and users report improved comfort and flexibility
- Bone health, including osteoporosis—reduction of inflammatory markers and bone resorption
- Possible cancer prevention—in vitro studies show enhanced apoptosis of cancer cell lines and moderation of oncogene expression

Why Boron?

Boron is a nutrient essential for human health. Epidemiological studies of population health and boron content in soil show higher rates of arthritis in areas with low-boron soil levels. These findings have stimulated research on the biochemistry of boron in living systems and the effects of various boron compounds in different types of experimental situations.[1] This has led to the identification and study of calcium fructoborate, a naturally occurring boron compound present in small amounts in many fruits, vegetables, legumes, herbs, and wine. CF is readily synthesized, well-absorbed, and non-toxic, and has demonstrated beneficial impact on several metabolic processes that underlie osteoarthritis, osteoporosis, and other chronic conditions.

Of special interest is the finding that CF reduces some biochemical markers of inflammation such as CRP and IL-6, but does not reduce levels of another key indicator of inflammation, COX-2. Recent research has highlighted the importance of COX-2 in the natural process of inflammatory resolution and the problems caused by blocking this important enzyme.

The Dark Side of Anti-inflammatories: The COX-2 Story

A vastly more detailed understanding of the natural process of inflammation resolution has emerged from a series of meticulous studies on inflammation by Charles Serhan, PhD and his team at Harvard.[2,3] While an in-depth review of their findings is beyond the scope of this article, a key take-home is the realization that we have been looking at only half of the inflammation story. Studies from this Harvard team demonstrate the way in which NSAIDs and certain natural remedies actually interfere with healing. The use of calcium fructoborate avoids this dilemma.

The Two Phases of Inflammation. The initial phase of inflammation is defined by release of numerous cytokines such as CRP, IL-6, and COX-2. Reducing the levels of these key inflammatory cytokines has been the target of anti-inflammatory drugs and certain botanical products found to provide pain relief. Although this may seem logical, it is here that the problem begins.

Serhan's group examined the underlying processes by which episodes of inflammation are resolved in a healthy, well-nourished body. An extensive range of experiments identified new classes of substances termed resolvins and protectins that occur naturally in inflammatory states and set

the stage for the body, tissues, and organs to heal. Researchers described inflammation as a process with two general phases: initiation and resolution. Initiation occurs after an insult or attack on the body such as infection, an injury, or a metabolic imbalance. At this point, inflammation is initiated, and inflammatory cytokine levels are elevated. This research found that the initial process of inflammation lays the foundation for a second phase of healing and ultimately for resolution of damage to the tissue. The second or resolution phase begins when the elevated levels of inflammatory cytokines trigger the release of resolvins and protectins, which direct the immune system to alter its function. In this second phase, the system destroys any infectious material, cleans up debris, and triggers the healing of tissues and organs.

The Catch-22. The high level of cytokines in the initiation phase, particularly COX-2, is what triggers the resolution phase. However, current anti-inflammatory drugs and certain supplements are designed to reduce this key cytokine. The production of resolvins and protectins is required for the natural progression of the resolution phase. Consequently, blocking COX-2 impedes healing, contributing to chronic inflammation.

This dynamic helps to explain situations such as the Vioxx disaster. Vioxx was a powerful, selective COX-2 inhibitory drug. It was very successful commercially because it caused fewer stomach problems than any previous NSAID and reduced pain effectively. However, this potent drug, particularly at higher doses, blocked COX-2 activity which impeded the body's natural repair processes, resulting in damage to the heart, circulation, and kidneys. It is estimated that between 90,000 and 300,000 heart attacks can be attributed to Vioxx, many of them fatal. The final cost to the drug company was more than $4 billion.

Calcium Fructoborate Research

The discovery of boron carbohydrate complexes with a range of anti-inflammatory and anti-oxidant effects has led to the reassessment of boron's therapeutic applications. A natural sugar-borate ester, CF is a source of soluble boron, biologically active at the intracellular level as free boric acid and at the extracellular level as fructose borate, diester, and monoester. CF has demonstrated beneficial effects on oxidative metabolism and cell apoptosis.[4] Clinical effects demonstrated in the research include reductions in CRP levels by 30% to 40% and the stimulation of superoxide dismutase activity by more than 70%.[5]

Cardiovascular Health. There are two studies of real significance in this area. The research of greatest clinical relevance was a randomized, double-blind trial that tracked four groups of middle age men (n = 116) with stable angina pain.[6] In addition to usual care and treatment provided to all patients, those in group 1 received resveratrol, group 2 received resveratrol plus calcium fructoborate, and group 3 received calcium fructoborate alone. Outcomes included a marker of left ventricle function (N-terminal prohormone), CRP, lipids, and the number of angina attacks per week.

CF and resveratrol were provided in combination, because resveratrol is rapidly degraded in the GI tract. CF protects resveratrol from deterioration in the gut, supporting higher levels of resveratrol absorption and longer effective time in the body. Additionally, as this study demonstrated, there is a synergistic effect of taking these two supplements together. The most significant outcome of this clinical trial was a 49.8% reduction in angina episodes after 60 days.

The second study of relevance to cardiovascular issues is research evaluating the effects of CF on blood parameters and proinflammatory cytokines in healthy subjects. This randomized, double-blinded, placebo-controlled trial tracked responses after 30 days of a placebo or CF at a dose of 56 mg/day or 112 mg/day.[7]

Parameters tested included C-reactive protein, homocysteine, total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, interleukin 1b, interleukin 6, and monocyte chemoattractant protein-1. The most noteworthy results were achieved with 30 days of CF supplementation at 112 mg, which reduced C-reactive protein, interleukin 1b, and MCP-1 each approximately 30%.

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Table 1. Effects of calcium fructoborate and resveratrol on cardiovascular markers and angina.[6]

Groups (n = 29 per group)	Decrease in CRP	N-terminal prohormone at 60 days	Lipids	Angina Attacks
1. Resveratrol		<59.7%		
2. Resveratrol plus calcium fructoborate	<30.3%	<65.5%		<49.8% in 60 days
3. Calcium fructoborate	<39.7%	<52.6%	<5.9% TChol <9.2% LDL >5.1% HDL	
4. Controls				

Table 2. Effects of calcium fructoborate at two different dosages on markers of cardiovascular health.[7]

Group	CRP	Homocysteine	TChol	TG	LDL	HDL	IL-1b	IL-6	MCP-1
Placebo									
CF-1 112 mg day	<31.3%	<5.5%	Significant reduction	<9.1%	<9.8%	Increased	<29.2%	Significant reduction	<31%
CF-2 56 mg day				<8.8%	<9.4%				26%

Osteoarthritis. A number of studies have looked at the role of key inflammatory cytokines in osteoarthritis and the effect of CF on cytokine chemistry:

- ***Knee pain.*** A double-blind, cross-over study of 60 people with osteoarthritic knee pain tracked patients for 15 days. CF showed consistent reduction in inflammatory markers and improved comfort and flexibility.[8]
- ***CRP and calcitrol.*** In another double-blind, cross-over study involving 10 subjects for 15 days, CRP levels dropped 37%. Subjects also showed a 19% increase in calcitrol, the active form of vitamin D3, and this was without any increase in the amount of vitamin D3 supplementation.[9]

Osteoporosis (OP). Review studies report that CF appears to be useful in preventing and managing OP.[10] The literature indicates that the majority of osteoporosis cases involve bone resorption (osteoclast) that is too rapid relative to bone building (osteoblast). There is clear evidence that inflammation is a significant component of this process. One of the inflammatory compounds found to be central to osteoporosis is termed RANKL (receptor activator of nuclear factor kappa-b ligand). Increases in RANKL directly cause bone resorption. Given the improvement observed in osteoporosis with the use of CF, we can presume that levels of RANKL are simultaneously being reduced.

Cancer Prevention. Boron has been investigated for its impact on cancer, and CF has been specifically evaluated through in vitro research. A study comparing the effects of CF and boric acid found both effective in inhibiting breast cancer cell growth (MDA-MB-231 cell line) in a dose-dependent manner. However, only CF increased and normalized apoptotic activity. Treatment with calcium fructoborate (but not with boric acid) was found to reduce p53 and bcl-2 proteins levels, markers that reflect pro-cancer genetic expression. We look forward to seeing more research on this aspect of CF.[11]

Clinical Applications

Systemic inflammation presents a major challenge in the management of chronic conditions such as cardiovascular disease and osteoarthritis in which inflammation interferes with the body's normal repair and regulatory processes. Consequently, the utility of calcium fructoborate in reducing total body inflammation makes it relevant to a broad range of clinical applications. At Lifespan, our experience bears this out.

In the management of chronic conditions, clients may be taking an excellent support protocol of supplements, but not getting the desired results. Lab findings with elevated CRP, IL-6, or other inflammatory markers indicate that systemic inflammation is a primary interfering issue (but possibly not the only factor). Reducing total body inflammation can unencumber the body's natural healing processes, maximizing the benefit of nutritional supplements and facilitating recovery. CF has strong potential application in these common situations.

Functional programs for chronic issues usually rely on specialized lab tests, leaky gut protocols, low antigenic diets, and a number of supplements. Major drawbacks to this approach have been complexity, cost, the need to make substantial lifestyle changes, and the gradual nature of improvement, particularly in conditions that have persisted for years or even decades. Calcium fructoborate appears to be a useful adjunct to the anti-inflammatory tool box of functional nutrition.

Cardiovascular Support

The medical literature identifies elevated CRP levels as a contributor to essentially all aspects of cardiovascular pathology. Outcomes are worse if CRP levels are higher or uncontrolled in resistant hypertension, coronary artery disease, congestive heart failure, atrial fibrillation, and diabetic vascular complications. CF, particularly in conjunction with resveratrol, appears to be a basic adjunct to a functional cardio support program.

In our cardio protocol at Lifespan, we utilized this combination in the nutritional support of a client with congestive heart failure (CHF), following a resveratrol protocol for CHF from the literature. The resveratrol was taken in combination with CF, as in the angina clinical trial. The subjective response in this case was perceived improvement in endurance and in recovery from moderate exercise.

Osteoarthritis

Our most extensive experience in the use of CF has been the provision of nutritional support for arthritis and joint problems. A number of different functional impairments can be at play in this common, but difficult-to-manage problem:

- Bone morphogenic protein. Age-related decreases in bone morphogenic protein (BMP) slow the repair and production of joint tissue in conjunction with increased systemic inflammation. We support BMPs with Ostinol® and Chondrinol®.
- Inflammation. Increased inflammatory cytokines and systemic inflammation appear to block many natural healing processes. Frequently, inflammation must be reduced before other products can work effectively. In our protocols, CF is always combined with connective tissue support products.
- Autoimmunity. In these cases, there are not only high levels of inflammation, but also immune activity targeting the tissues of the body. Given the complexity of these conditions, we utilize testing from Cyrex to focus our programs. Basic products are selected to support T-regulatory activity include glutathione, super oxide dismutase, fish oil, and vitamin D.
- Microcirculation impairment. This refers to blockage of fine capillaries in the vicinity of a painful joint or injury. Constriction of capillary circulation compromises the

tissues' ability to function and repair. Products such as Yan's Heng Fa #1®, Herbal Yuth®, or lumbrokinase can be employed to support microcirculation.

Osteoporosis

In support programs for osteoporosis, we combine CF with bone morphogenic proteins (Ostinol®). However, we do not find high calcium doses to have substantial impact on osteoporosis. Rather, OP seems to be primarily an issue of inflammation and lack of BMPs.

Conclusion

Calcium fructoborate is a promising new tool for functional nutrition practitioners. This supplement offers a modest price point, convenient dosing, and a broad range of uses in health conditions with an inflammatory component. CF can be effectively integrated in many functional medicine programs, reducing inflammation without disrupting natural inflammatory resolution and healing. Already well-studied, more research is underway that will further determine usefulness in difficult and painful chronic conditions.

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Resources: Product Details

Calcium fructoborate is sold under the name FruiteX-B and comes in 120 capsule bottles. Each capsule contains 108 mg of CF. This product is manufactured by FutureceuticalsDirect.com. For consumer sales, see www.LifespanProducts.com or Contact Lifespan at:
Phone: 707-421-2143
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The Neurology of Meditation: Implications for Meditation Therapies

by Gérard V. Sunnen, MD

Abstract

The perspective of this article favors the concept of the existence of neuronal brain networks that are not only more specialized than others in the creation of awareness but also capable of expansion, both in their anatomical configurations and in the output of their electrochemical activity. Herewith explored are meditative practices as activators of awareness development.

Awareness is a term that carries different meanings. While to most people it refers to the capacity to be conscious of oneself, herewith it is also applied to the property of the nervous system to generate energies that make such self-awareness possible. As such, awareness ultimately takes root in the nervous system's capacity to create energy, which is a core expression of life itself.

This article examines awareness from a neurological perspective, then as it applies to the practice of meditation, aiming to enhance the many promises that it embodies. Meditative therapies thus may enhance not only the creation of new neuronal networks, but also stimulate the corresponding creation of new dimensions of awareness, both quantitative and qualitative.

Knowing about mechanisms of awareness is important because it satisfies the rational mind's quest to understand all that surrounds it. Reasons for meditation thus gather greater logical impetus.

Introduction

Awareness is the experiencing of life in the very instant of time and space, in wakefulness, and also in dreams. Experiencing, if one focuses on its flow, is poignant, intense, and relentlessly ongoing, whose only respite is possibly dreamless sleep. Awareness, in its streaming of thoughts and emotions, is felt in unique ways by each individual. And although awareness changes its outward expression as it courses through life's stages from infancy onward, there is shared universality in its very essence.

The question has been posed a thousand ways: How can the gray mass of the brain reconcile with the evanescent substance of its flame, awareness? The mind/body problem thus posed is as beguiling today as it was thousands of years ago when early anatomists doggedly dissected the most obscure body recesses seeking the magic home of the sentient soul ... only to come out empty handed.

Cracking the code of awareness will not be easy, because awareness is the very tool that is used to study itself. This can be somewhat problematic (if not a bit embarrassing) for the field of science, which, in its sustained attempts to explain life's highest elixir, awareness, has so far only yielded conjectural mazes whose exits invariably return to their entrance.

Focusing solely on its extremes will likely not solve the mind/body problem: the body's matter on one extreme, and the ungraspable substance of mind on the other. These poles are conceptually far apart, and logic thus perennially fails to see their links. The mind/body dichotomy is in fact so polarized that awareness, as it lives in its physical body, has often been referred to as "the ghost in the machine."

Brain is indeed matter, but it is matter that embodies the electrical phenomena of its individual cellular elements and of its greater neuronal networks. Quantum perspectives also respect the energies of brain's atoms and the forces that give them structure and motion: Forces that bind atomic nuclei together, such as electromagnetism, gravity, and the "weak" and "strong" nuclear forces. Fundamentally, all brain matter, as all matter, can be translated to energy and vice versa, and the brain, with and beyond its electrochemical properties, respects that rule.

On the other extreme, awareness, in all its evanescence, can also be seen as an energy form. In the Tibetan Buddhist perspective, the ultimate stuff of awareness belongs to a substance called the *subtle body,* which, with a minor stretch of imagination, can be conceived as belonging to a yet unidentified energetic dimension.

The mind/body problem can thus be grasped so that it is no longer a duality, but rather a continuum in a panoramic spectrum linking the electromagnetism of neuronal elements to the energy form that we all experience while experiencing: awareness itself. It may

be that brains, as specialized organs, have evolved to bridge these disparate forces, allowing them to be expressed as the fundamental fabric of life.

Awareness in the Brain

The magical quality that is awareness remains a cardinal conundrum. Gathering all current knowledge about how neurons work, what makes possible the leap to experiencing? And where can all this awareness be located in the nervous system?

Despite the concerted forays in the labyrinthine soft fortress that is the brain, via anatomical dissection, neurological mapping, medical imagery, and decades of pondering by means of various psychotherapies on how thoughts and feelings dynamically flow in the mind, the fundamental riddle remains: How does the material substance of brain relate to awareness? What purpose does awareness have? Can evolution's demand for adaptation be invoked, or does the existence of awareness correspond to other imperatives?

Arguably most developed and refined in humans, this fundamental elixir of life is nevertheless shared in some manner by the spectrum of higher animal life, perhaps crossing all species' boundaries to kindle all life. Awareness, for lack of a better word denoting the very substance of life's energy, is fundamentally all permeating.

Awareness brings to life the messages of the senses, vivifies emotions, and personalizes the uniqueness of every thought. Moods are background awareness symphonies, complex mélanges of affective colors and thought, all unique in their individual configurations. Every feeling in mind space is paired, in physical brain space, with the activation of corresponding neuronal circuits, and each thought, in theory – and increasingly in fact – can be identified by a unique neuronal chain reaction, from one neuron's span, to the billions of neurons in the most complex mental processes.

Raw nervous system energy feeds the brain's cortical circuitry. The elements of higher self, such as personhood, depend on networks fueling the brain with neuronal force. An approximate metaphor is for the brain's power supply to be likened to a generator outputting electrical amperage and voltage. Connected to the generator can be myriad appliances performing any number of tasks: lamps, microphones, speakers, rechargers, fans, and so on. Hence the difference between awareness nature (as in electricity) and awareness content (as in the appliances).

The reticular activating system (RAS), as its name implies, is a core contributor to the basic tonus of awareness. Composed of billions of neurons with trillions of interconnections, with beginnings in the bulbous upward continuation of the spinal cord, the medulla oblongata, and moving higher through the brain, it looks, under high magnification, like a packed dense and diffuse cellular net (Greek: *reticulum*, net), coursing into ancient brain structures (pons, mesencephalon, thalamus), eventually lighting up the cortical landscape.

Like an island in a vast sea, awareness floats on an ocean of brain activity that is not granted cognizance, the unbounded domain of the unconscious. Indeed, most bodily activities, most thinking, most emotions, and increasingly recognized, most decisions take place in the more surface pre-conscious, and the more unattainable unconscious. Nature has rationed conscious perception. Floating on this subterranean unconscious mass is the atoll of awareness, the "experiencer," embodying the conscious kernel of "me."

Networks linked to conscious awareness, appear in scans as clouds of mostly cortical neurons, with neuronal filaments reaching out into the brain. The shape of these neuronal nebulae shift with attention and focus. Meditations inviting visual imagery, for example, will also involve occipital cortical areas. Proposed is that neurons in this network be called *A* (awareness) neurons.

Like memory, which gathers from all neurons for complete reconstruction, awareness, in its final expression, receives contributions from pan-neuronal networks. The *A* neuronal networks, however, are more specialized than others in the generation of awareness. *A* neuron networks are all important in the practice of meditation because the crux of meditation lies in the sustained kindling of awareness.

Regardless of the nature of its essence, awareness is closely connected to proper neuronal functioning. Could awareness ever exist without a nervous system? Many spiritual schools seem to think so; modern science, however, is highly skeptical.

***A* Neurons, Awareness Content, and Awareness Essence**

Meditation centers on igniting awareness to new levels. Staying with the experiencing of awareness is fundamental to most, if not all, forms of meditation. In fact, devoid of a sustained focus on awareness, no practice can properly be called meditative. The thrust of meditation is centering on awareness. Once awareness is brought to the foreground, where may it be channeled? Choices exist, and this accounts for the different styles of meditation.

The many styles of meditation all aim to prime awareness. Meditative focus, in such priming, can center on a physiological process such as breathing, on a bodily space such as an energy plexus, on internal sensations such as heat and light (Tummo meditation), on a movement sequence as in tai chi and qi gong, on the vibrations of a mantra, or on the illumination of a global feeling state, such as joy, peace, love, and compassion. The art of meditation resides in electing an optimal personal meditation style.

In autogenic training, a Western style of meditation, awareness is channeled to sensory experiences, such as feelings of bodily heaviness and warmth, and eventually to coolness of the forehead (Luthe 1965).

Certain meditation practices develop the ability to distinguish awareness content from awareness nature. Any thought, any emotion, any memory

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manifesting in consciousness belongs to awareness content. Beyond all content, there is essence. In *zazen* meditation, all mental constructs are seen as clouding the perception of pure awareness.

While neuronal *A* circuitry is activated in meditation, one other network is needed to make that happen. Willfulness is an essential ingredient. Willfulness pipelines attention's thrust into awareness networks. Gentle sustained willfulness activates *A* circuitry. Highly developed in humans, the neuronal conglomerate generating willfulness mainly resides in the brain's frontal lobes and its connections. The partnership and synergism linking these two networks form the crux of meditation's contribution to awareness expansion.

Meditative Therapies, Brain Growth, and Awareness Extension

What happens to the brain's circuitry when meditation is consistently practiced? In light of discoveries showing the capacity of neuronal generation (Duan 2008; Gould 1999; Gage 2013; Guo-li Ming 2005; Kaneko 2011; Zhao 2008), is it possible to incite awareness's neuronal networks to expand its brain demographics? Can the voluntary arousal of awareness, as in meditation, increase this *A* population, the sum total of its connectivity, and therefore the sheer energetic output of awareness neurons?

Research shows that meditation can indeed alter the morphology of selected brain components (Fox 2014; Lazar 2005; Luders 2015; Vestergaard-Poulsen 2009; Xue 2011). What are the implications of these findings? Can mental mechanisms that engage awareness networks stimulate neuronal connectivity, or even neurogenesis? What happens to the experiencing of awareness when its physical components are transformed through meditation?

Meditation Therapies: Stages and Promises

The term *meditation therapies* implies that techniques of meditation have the capacity to redress disharmonies of well-being. Indeed, this is so. Numerous studies have reported on meditation's therapeutic action in a spectrum of psychological conditions (Schmidt 2014; Brown 2015; Cvetkovic 2011). Meditation therapies also show beneficial influence on the body's functioning. Of particular interest are meditative studies of cardiac reactivity, the tendency of the cardiovascular system to become nefariously activated in response to stress (Travis 2009; Barnes 2004). This type of research is, in essence, symbolic of the calming effects of meditation on autonomic nervous system networks.

Meditation therapies address dysphoric symptomatology. Symptoms relative to anxiety, in the anxiety/apprehension/fear/worry spectrum, are the first to be mollified. The meditator is often surprised that formerly gripping anxiety has gradually dispelled and that new vistas of relaxation are revealed. Learned experientially is that relaxation has many subjective layers, seemingly limitless in their reach. Also assuaged by meditation therapies is the irritability/anger/aggression spectrum. Angers can be dissolved with consistent meditation, as are the unfortunate sequelae that derive from them. New landscapes of peacefulness are opened. Also bolstered by meditation is the self-esteem/self-image/self-confidence dimension. Distressing feelings that connect to this dimension have to do with the mind's tendency to compare self with others. Feelings of inadequacy give way to new perceptions of personal centeredness and social equipoise.

Especially pertinent to meditation therapies is their capacity to highlight the immediacy of life. The empathy/sensitivity/love spectrum is involved. Meditators find themselves with new capabilities to capture the intensity of interpersonal contact, to resonate with others emotionally, and to project expressions of goodwill, friendship, and love. In the context of meditation, there often begins an awakening to the fact that awareness of one's awareness is a reckoning of the existence of fundamental life energy, and with it, a revelation that this energy – and conceptually, spirit – is not only always positive but also profoundly immutable. Revelations often feature the fact that awareness nature is ever more fundamental than awareness content.

Meditation therapies invite the development of dimensions of the psyche that correspond to higher, if not the highest of personal aspirations. They open portals to experiencing states of mind that ordinarily surpass us, belonging to domains of the "Overself" (Brunton 1965).

Conclusion

Techniques that develop heightened entente between mind and body can easily complement contemporary psychotherapies. In fact, to be maximally effective, psychotherapies need to be integrated into the body's networks. *Meditation* is a generic term for a variety of techniques that center on the activation of awareness. Sustained priming of awareness independently leads to positive personal transformations, in the psychological, the psychosomatic, and the transcendent dimensions of being.

Research has shown that consistent meditation correlates with actual and measurable physical modifications in the nervous system. In turn, awareness tends to shift toward relaxation, psychological harmony, organ balance, and importantly, toward states of experiencing that, like a staircase ascending, invite novel realizations of the Self.

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Review: The Clinical Utility of Urinary Biogenic Amines and Other Neurotransmitters

by Andrea Gruszecki, ND

Abstract

Central and peripheral nervous system functions depend on normal synaptic transmission, which is mediated by a variety of neurotransmitters, including the biogenic amines (the catecholamines dopamine, norepinephrine, epinephrine, serotonin, histamine; Eisenhofer 2004; Rothman et al. 2012). Analysis of urinary biogenic amines and other neurotransmitters may provide a noninvasive assessment of neurotransmitter metabolism. Urinary neurotransmitters are easily collected by patients and the results may be readily integrated into current practice patterns. Urinary neurotransmitter evaluations may be used to identify neurotransmitter imbalances and evaluate the function of enzymes on synthesis and catabolic pathways (Fryar-Williams 2015). Alterations in neurotransmitter metabolism may reflect the neurological effects of environmental exposures to toxicants and may serve in the assessment of a variety of physiologic conditions (Castro-Diehl 2014; Kaidanovich-Beilin 2012). They provide a noninvasive means of assessing a patient's ability to synthesize and metabolize neurotransmitters, and may be used to evaluate patient responses to supportive nutritional therapies (Marc 2011). A review of the current scientific literature evaluates the utility of urinary neurotransmitters for clinical assessment.

Introduction

A recent review of biomarker development for neuropsychiatric disorders (Enaw 2013) stated in its conclusion, "The need for biomarkers in the field of psychiatry is clear, but progress towards their development has been limited." In the article's conclusion, Enaw and Smith claim that "the successful identification of biomarkers will advance the field of psychiatry towards the goal of biological tests for diagnosis, symptom management and treatment response." The review failed to consider urinary neurotransmitters as a viable biomarker for neurologic health, despite the associations between urinary neurotransmitter levels and some mental health conditions that have been documented in scientific literature (Marc 2011). Enaw and Smith may have legitimate skepticism regarding urinary neurotransmitters, perhaps due to the fact that less than 20% of measured neurotransmitter metabolites in peripheral circulation originate in the central nervous system (CNS; Eisenhofer 2004). Or perhaps due to reports from some laboratories claiming, in spite of the evidence, that urinary neurotransmitters may be directly correlated with CNS neurotransmitter levels? If the notion that urinary neurotransmitters are a direct assessment of CNS neurotransmitter levels must be discarded, how might urinary neurotransmitters be of clinical value? Urinary neurotransmitter evaluations may be used to identify neurotransmitter imbalances, evaluate the function of enzymes on synthesis and catabolic pathways, monitor the effect of therapeutic interventions, and serve in the assessment of a variety of physiologic conditions. Given the recent advances in the understanding of nutritional biochemistry, inheritance, epigenetics, and environmental toxicology, as well as improved sensitivity and specificity in the analysis of urinary neurotransmitter levels (Li 2014), it may be time to reconsider the clinical utility of urinary neurotransmitters in functional medicine.

Urinary Neurotransmitters

Normal function of the central and peripheral nervous systems depend on the transmission of electrical signals from one neuron to another across the synapse, or gap, between neurons. Neurotransmitters convert the electrical information into chemical information that can cross the synapse and stimulate or inhibit the next neuron (Hyman 2005). There are many types of neuroactive substances. "Classic" neurotransmitters are called small molecule neurotransmitters or biogenic amines (Eisenhofer 2004). Some amino acids obtained from the diet or synthesized in the body may act as neurotransmitters or neuromodulators (Berry 2007; Eisenhofer 2004; Paul 2002). A neuromodulator alters a nerve cell's response to a neurotransmitter signal. Other essential amino acids serve as precursors for neurotransmitter synthesis (Cansev 2007). Many neuroactive molecules are synthesized by gut bacteria, such as gamma-aminobutyric acid (GABA; Dhakal et al. 2012; Saulnier et al. 2013), and many hormones have neuroactive properties (Lyte 2013). Some nerve cell metabolites may also act as neurotransmitters or neuromodulators. Other metabolites have no known function and are simply excreted from the

body by the liver and kidneys. Currently under investigation are several gases, such as nitric oxide, that may also modulate the action potentials of neurons (Kakizawa 2013).

Because enzymes are expressed differently in various body tissues, circulating levels of the neurotransmitters and their metabolites may have distinctive sources. In the periphery, the catecholamine epinephrine is synthesized in the medulla of the adrenal glands; the majority of norepinephrine is synthesized in the sympathetic nerves that surround blood vessels (Goldstein 2003). Serotonin synthesis occurs primarily in the enteric nervous system of the gastrointestinal (GI) tract (Hansen 2003) but may also de novo in blood vessels and renal proximal tubules (Watts et al 2012). Dopamine is released from the peripheral nervous system when sympathetic noradrenergic nerves are stimulated to release norepinephrine (Goldstein 2010). Up to 45% of peripheral dopamine may be synthesized in mesenchymal organs and the digestive tract; however, the dopamine found in urine is primarily synthesized de novo in the kidneys (Eisenhofer 2004). Many biogenic amines are actively taken up and stored by platelets, which have no neurotransmitter synthesis capacity of their own (Audhya et al 2012). Evaluation of platelet levels may offer an excellent assessment of the cellular active transport mechanisms necessary for normal neurotransmission, but will offer little insight into the synthesis or metabolism of neurotransmitters (Jedlitschky 2012).

Urinary levels of neurotransmitters primarily reflect the activity of the peripheral and GIT enteric nervous systems. The majority of the neurotransmitters excreted in the urine reflect peripheral metabolism (Eisenhofer 2004). However, with the exception of tryptophan-5-hydroxylase, the enzymatic machinery for neurotransmitter synthesis and metabolism is often similar (if not identical) on both sides of the blood–brain barrier (Cansev 2007). Urinary neurotransmitter analysis may be clinically useful to identify neurotransmitter imbalances, evaluate enzyme function, and in risk assessment.

Urinary Neurotransmitters May Identify Imbalances

Plasma epinephrine concentrations increase markedly in response to hypoglycemia, hemorrhagic hypotension, asphyxiation, circulatory collapse, and, importantly, *emotional distress*. Other catecholamine neurotransmitters do not elevate like epinephrine (Goldstein 2005). A 2004 epidemiologic study of posttraumatic stress disorder (PTSD) found significantly higher mean urinary levels of dopamine, epinephrine, and norepinephrine in those with lifetime PTSD, when compared with controls in the community without PTSD (Young 2004). Other research indicates that specific urinary neurotransmitter levels may correlate with neuropsychiatric conditions such as depression (Marc 2010) and attention deficit/hyperactivity disorder (ADHD; Dvorakova 2007).

Evaluate Function

Enzyme function. Catecholamines are metabolized by enzymes such as monoamine oxidase (MAO) and catechol-O-methyl transferase (COMT; Goldstein 2005). Inherited or acquired factors may affect enzymatic activity. Mutations (Hyland 2007) or single nucleotide polymorphisms (SNPs) may alter enzyme function and affect the metabolism of neurobiogenic amines. Mutations and SNPs have been associated with neurodegenerative (Dorszewska 2013) and neuropsychiatric disorders (Inoue 2003) in the scientific literature.

Defects in enzyme functions may be evident in neurotransmitter analysis as elevations or deficiencies. Neurotransmitter levels have been associated with symptom severity in some disorders. For example, patients with MAO-A deficiency have low plasma 3,4-dihydroxyphenylacetic acid (DOPAC) levels and may have an increased tendency to violent antisocial behaviors. Patients with MAO-B deficiency exhibit normal behavior and have normal DOPAC metabolite levels (Goldstein 2005). Addison's disease, secondary adrenocortical insufficiency, and severe 21-hydroxylase deficiency all have impaired adrenal secretion of epinephrine, and plasma levels are decreased (Goldstein 2005); it is possible that these findings might be reflected in urine.

MAO-A metabolic pathways work in conjunction with aldehyde/aldose dehydrogenase and aldehyde/aldose reductase enzymes; MAO-A is the first step in a two-step enzymatic process (Eisenhofer 2004). Some aldehyde metabolites of catecholamine metabolism, such as formaldehyde, may cause neurotoxicity if the aldehyde dehydrogenase and reductase enzymes are deficient (Marchetti 2007). Analysis of neurotransmitter metabolites in urine may indicate which enzyme pathways are compromised. For example, the catabolism of the catecholamine neurotransmitters epinephrine and norepinephrine into metanephrine and normetanephrine (respectively) primarily occurs in the same cell where they are synthesized. The metabolites are then released from the cell for excretion in the urine (Eisenhofer 2004). Many of the enzymes in the neurotransmitter synthesis pathways require various nutrient cofactors and the presence of SNPs may further affect nutrient requirements (Stover 2006).

Nutrition. The assimilation and absorption of nutrients requires a healthy digestive tract and a healthy microbiome (the presence of expected and beneficial microbes in the gastrointestinal tract). Bacteria in the microbiome synthesize neuroactive compounds as part of normal gut-brain-microbiome crosstalk. Imbalances in the gastrointestinal microbiome may affect mood and behavior (Lyte 2013). The addition of probiotics has been shown to be beneficial in some types of neuropsychiatric disorders. A 2009 double-blind placebo-controlled study of emotional symptoms in chronic fatigue patients reported that the addition of a *Lactobacillus* probiotic improved emotional symptoms (Rao 2009).

In addition, gastrointestinal disorders may *result* from imbalances in neurotransmitter synthesis or metabolism (Hansen 2003) or may contribute to nutritional deficiencies that may then affect enzyme functions and neurotransmitter levels. Neurotransmitters arise from the precursor amino acids phenylalanine and tyrosine. The kidney is the primary source of circulating tyrosine; approximately 50% of phenylalanine-to-tyrosine conversion occurs in the kidneys. Renal disease may affect the levels of neurotransmitters in urine, and renal function should be evaluated prior to urinary neurotransmitter testing (Eisenhofer 2005).

Response to therapy. Normalizing urinary neurotransmitter levels based on test results has been shown to improve

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some mood and behavior symptoms (Marc 2010). Urinary neurotransmitter levels may be altered by nutrient or pharmaceutical supports. For example, urine serotonin levels may be increased by the addition of neurotransmitter precursors such as tryptophan or 5-hydroxytryptophan (5-HTP; Trachte 2009). The treatment of ADHD with Pycnogenol in a randomized, double-blind, placebo-controlled study resulted in a statistically significant decrease in urinary dopamine and a trend of decreasing norepinephrine and epinephrine levels (Dvorakova 2007).

Risk Assessment

The use of urinary neurotransmitters to diagnose carcinoid tumors and pheochromocytoma is well established (Goldstein 2005). The use of urinary neurotransmitters to evaluate the effects of other health conditions is more recent. Accumulating evidence indicates that insulin levels may be critical to normal CNS neuron function, and insulin dysregulation may contribute to the development of neurodegenerative disorders such as Alzheimer's disease (Kaidanovich-Beilin 2012). Altered levels of urinary neurotransmitters have been documented in health conditions such as sleep apnea (Kherahdish-Gozal 2013), gastrointestinal tumors (Eisenhofer 2004), and inherited disorders of neurotransmitter metabolism such as phenylketonuria (Hyland 2007). Urinary catecholamines and cortisol levels have been measured to evaluate the effects of socioeconomic and psychosocial factors on the risk for atherosclerosis (Castro-Diehl 2014). An epidemiologic study of PTSD found significantly higher mean urinary levels of dopamine, epinephrine, and norepinephrine in those with lifetime PTSD, when compared with controls (Young 2004). The study also described an increase in urinary catecholamines for study subjects with no PTSD but with major depressive disorder. Alterations in urinary neurotransmitters have been reported in studies of ADHD (Marc 2010), and decreased levels of urine amino acids important in neurotransmission, such as glutamate, phenylalanine, tyrosine, and tryptophan, have been reported (Ghanizadeh 2013). A 2015 study (Fryar-Williams 2015) reports elevations in urinary norepinephrine, epinephrine, dopamine, and histamine in schizophrenic patients compared with controls; the results also correlated with the subject's symptom intensity ratings.

Exposures to environmental toxicants may also alter urinary neurotransmitter levels and may be associated with neuropsychiatric symptoms. A statistically significant increase in 5-hydroxyindoleacetic acid (5-HIAA), compared with nonexposed controls, was found in Chinese welders exposed to manganese (Yuan 2006). In a study designed to monitor the health effects of industrial exposure to polychlorinated biphenyls (PCBs), urinary concentrations of the dopamine metabolite homovanillic acid (HVA) and the epinephrine/norepinephrine metabolite vanillylmandelic acid (VMA) were analyzed over a 3-year period (Putschögl 2015). The study documents alterations in HVA and VMA for different types of PCBs, with effects dependent upon the degree of chlorination within the chemical. Increasing levels of exposure to all PCBs reduced urinary HVA and VMA levels. The findings are consistent with many animal studies that document decreased levels of dopamine in the central nervous system after PCB exposure. Coke oven workers exposed to benzo[a]pyrene (B[a]P) had decreased urine levels of dopamine, norepinephrine, serotonin, and HVA with elevated levels of 5-hydroxyindoleacetic acid (5-HIAA; Niu 2009). According to the World Health Organization Neurobehavioral Core Test Battery (NCTB), memory and learning capacity were reduced in the exposed workers.

Methodology and Technical Considerations

While there are multiple methods available for the measurement of catecholamines, liquid chromatography (LC) coupled with tandem mass spectrometry remains the gold standard (Li 2014) for these and many other biological analytes (Grebe et al. *Clin Biochem Rev.* 2011 Feb;[32]:5–31.). The proper collection and handling of urine specimens prior to laboratory receipt is of the utmost importance for accurate results. The kidney functions in the synthesis of not only amino acids, but also peptides and proteins. Thomas et al. (2010) report that, for urinary proteins, relative standard deviations were lowest for 24-hour collection and first morning collections, while second collection and spot urine samples had much higher variability. The same may or may not be true for urinary neurotransmitters; research is needed in this area. As an important site of amino acid synthesis (approximately 50% of plasma tyrosine is synthesized in the kidneys), renal synthesis also contributes to the plasma concentrations of the neuroactive amino acids glycine and glutamate (Van de Pol et al. 2004).

At Doctor's Data, a small study (n = 10) performed to assess the utility of 24-hour urinary neurotransmitter testing, as specified by Mayo Clinical Laboratories, was shown to be more clinically relevant when compared with second morning void samples. The second morning void samples showed 3 clear outliers with elevated catecholamine levels, when their 24-hour results demonstrated no such increase in the excreted catecholamines. When diet and lifestyle information was reviewed and input, the 3 subjects with elevated second morning catecholamines had all experienced long commutes to work, when compared with the rest of the cohort! As the purpose of urinary neurotransmitter testing is to evaluate clinically significant elevations or deficiencies in neurotransmitter status, it appears that either true first morning void (i.e., after being in bed without arising × 8 hours) or 24-hour urine neurotransmitters may be more clinically relevant.

A study of PTSD subjects (Young et al. 2004) used a novel method of collecting 24-hour urine catecholamines for study, choosing to collect urine in 8-hour increments. Urine collection for a 32-

Detailed Flow Tables of "Neurotransmitters" as well as "Neurotransmitter Synthesis Nutrient Cofactors" are available at our website: www.townsendletter.com. Please look for the contents of the May 2016 issue for the hyperlink for the "Urinary Biogenic Amines" article.

hour stay at a sleep center was made in four parts as Young et al. report: "The first collection covered the first night, the second collection covered 8 hours from rising to early afternoon, the third collection covered the late afternoon and evening, and the fourth, the second night. The procedure provided total 24-hour measures and had the added capacity to provide separate timed measures that captured the morning surge (in the 8 AM hour) and the evening low (in the 8 PM hour) for an examination of effects related to diurnal phase." This method of collection and analysis requires further study, and may ultimately prove clinically useful.

The ingestion of certain foods may affect the results of urinary neurotransmitter testing, and the avoidance of specific foods is recommended by the Mayo Clinic Medical Laboratories and other medical laboratories analyzing neurotransmitters. Any medication meant to affect neurotransmitters (such as reuptake inhibitors, etc.) may alter neurotransmitter levels from baseline levels; it is the clinical decision of the prescribing physician whether to discontinue (by safely tapering off) any such medications prior to testing.

New methods, such as capillary electrophoresis, electrochemical detection, enzyme immunoassay, chemiluminescence detection, and fluorescence detection, are being developed but may not have sufficient large-scale clinical studies yet to assist with the clinical interpretation of results (Tsunoda 2006). None of these technologies has been found superior to the LC-tandem mass spectrometry gold standard. In addition, different methodologies often use different reference values, which make the comparison of a result using one set of reference values to a result using a different set of reference values virtually impossible and clinically questionable (Katayev 2010).

Conclusion

Urinary neurotransmitters provide an overall assessment of a patient's ability to synthesize and metabolize neurotransmitters, which must occur in both the peripheral nervous system and behind the blood–brain barrier. Altered patterns of urinary neurobiogenic amines may highlight the need for precursor amino acids or nutritional cofactors essential for synthesis and metabolism. Alterations in urinary neurotransmitter status may result from a variety of conditions, including metabolic disorders, mood/behavioral disorders, environmental exposures, or (rarely) the presence of certain tumors. Evaluation of neurotransmitters may provide the clinician with increased clarity about patient health, functional status, and nutritional needs.

Disclosure

The author, Andrea Gruszecki, ND, is employed in the Scientific Support Department at Doctor's Data Inc.

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Food Reactivity Testing: The Leukocyte Activation Test

by Andrew W. Campbell, MD

Introduction

The world has advanced vastly in technology, but also in increasing prevalence of chronic illnesses.

For thousands of generations, we ate food shortly after it was harvested and when it was in season. Meat was occasionally consumed and much of it was caught in the wild. Fish was fresh, never frozen and shipped. All food was organic: there was no other choice. Then, starting right after World War II, our diet changed dramatically, especially in industrialized countries and in urban areas. What we eat now, as compared with the diet of even two or three generations ago and back to the beginning of human history, is vastly different.

Each person in America eats approximately 1 ton of food per year, including 220 pounds of protein. Add to this the chemical additives such as artificial food colorings, flavorings, preservatives, and sweeteners both in foods and liquids we consume. In this mixture of foods we eat are new strains of wheat, rice, soy, and corn; in the United States, we eat more GM crops than the rest of the world combined. Our vegetables and fruits contain residues of insecticides, pesticides, and fungicides. The cattle, hogs, chickens, and turkey in concentrated animal feeding operations (CAFOs) are fed and injected with antibiotics and hormones. CAFOs use ractopamine to increase the meat content in cattle and pork: it is a ß-agonist drug that is known to augment protein synthesis and is banned in 160 countries, including China, the European Union, Taiwan, and Russia. Our dairy products contain recombinant bovine growth hormone (rBGH), which is given to cows to increase their milk production; it is banned in the European Union, Canada, and other countries. We use plasticizers such as bisphenol A (BPA) in food and beverage containers that leach out and get into our bodies. Tally up with all this the medications that we take, the antibiotics, antacids, proton pump inhibitors, histamine 2 blockers, and other drugs, many of which are available over the counter – many of these are found in the water supply of most cities. The majority of Americans include processed food in their diet. How we cook has also changed: our ancestors did not have microwave ovens nor coated pots and pans.[1–3]

All of the above and more have contributed significantly to a dramatic increase in many chronic diseases, such as obesity, gastrointestinal disorders, cancer, stroke, and cardiovascular diseases, with inflammation as a predominant central cause. Part of this inflammation is due to the massive amounts of food and liquids along with their chemicals that our gastrointestinal tract is exposed to, which can bring on an immune reaction.

Our Defense Mechanism

Our defense mechanism against this relentless and incessant bombardment of xenobiotics is our immune system. It is divided into two parts: our innate immune system and our adaptive immune system, also known as the antibody mediated (specific) immune system. One main difference between the two is that the cells of the innate system recognize and respond to pathogens, whereas the adaptive immune system confers long-lasting protective immunity. The innate immune system is our first line of defense against invading organisms while the adaptive immune system acts as a second line of defense and affords protection against re-exposure to the same pathogen.

The innate immune system remains unchanged from birth and consists of neutrophils, dendritic cells, macrophages, natural killer cells, complement and various other neutralizing proteins, and physical epithelial barriers like the skin. It is our "firewall," is the first respondent, and is non-specific. The major functions include activation of inflammation, activation of NK cells, removal of antigen-antibody complexes, and complement activation, with its pathogen opsonization and membrane attack complex functions, among others.

The innate immune system responds to infection or irritation with inflammation via chemical factors released by injured cells. These include histamine, bradykinin, leukotrienes, and prostaglandins, and produce vasodilation of the blood vessels in the direct vicinity, as well as the attraction of neutrophils, which make up 60% to 75% of white blood cells in the circulation. These neutrophils migrate through the blood vessels, passing through interstitial tissue to the site of injury or infection via chemotaxis mediated by interleukin-8 (IL-8), C5a, fMLP, and

leukotriene B4. The bone marrow of a healthy adult produces approximately 100 billion neutrophils daily, and 10 times that amount during an acute inflammatory reaction. Neutrophils phagocytize the offending substance and release factors that summon other leukocytes and lymphocytes. Cytokines produced by the innate immune system mediate the inflammatory response via TNF, IL-1, and others. The results of inflammation are well known classical signs: redness due to locally increased blood circulation; increased local temperature or internally a fever; swelling of the affected tissues; increased production of mucus; pain; and dysfunction of the affected tissues or organ.[4]

With all the above, we can readily see how a person may undergo inflammation as a result of intolerance or sensitivity to foods or other substances with the subsequent activation of the innate immune system followed by neutrophil reactions.

The adaptive immune system develops later on and consists primarily of lymphocytes and their products, including antibodies and cytokines. It adapts as new substances are encountered and has memory for antigens it has come across before. The adaptive immune system is a specific response, induced by an antigen that targets that specific antigen. It has memory, and provides long-lasting protection, as when a person recovers from measles and is now protected against measles for their lifetime. There are two main responses, the antibody responses and the cell-mediated immune response that are carried out by B cell lymphocytes and T cell lymphocytes. In the first, B cells are activated to produce antibodies, also known as immunoglobulins, and bind to the foreign antigen inactivating it or rendering it more accessible to phagocytes. Various cytokines and chemokines mediate this process, where there is collaboration between antigen presenting cells and CD4 T lymphocytes and B-lymphocytes.

Classical allergies are part of the adaptive immune system, are an IgE antibody hypersensitivity reaction, and include atopic dermatitis, asthma, hay fever, food allergies, and anaphylaxis. Common symptoms are itchy rash, runny nose, and wheezing. These occur quickly and very shortly after exposure. However, food intolerance and sensitivities are not part of classical allergies.

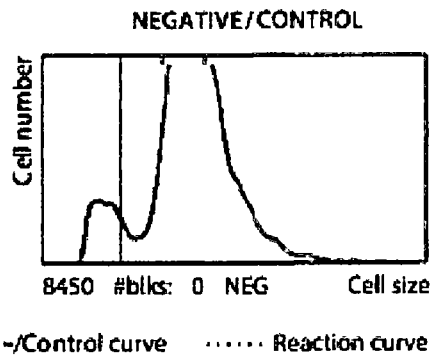
Testing for Food Reactivity

The challenge is to find the right way to test for food reactivity. Hippocrates is quoted as saying: "Let food be thy medicine and medicine be thy food." Maimonides, the 13th-century physician and scholar, is believed to have said, "Anything that can be treated by diet should be treated by diet." Each person is unique, and their immune system is unique; therefore diets should be personalized.

In searching to elucidate which food or foods could be causing an adverse reaction or intolerance in a patient, the gold standard still remains the double-blind, placebo-controlled oral challenge test, with each challenge of food separated by 3 days. This method is cumbersome, impractical for clinical practice, and would take months if not years to test all the foods that we eat today. Furthermore, this would be a very costly undertaking. However, there is another method that correlates very well with oral challenges and is cost efficient and convenient.

The Leukocyte Activation Test

The leukocyte activation test, known as the ALCAT (antigen leukocyte cellular antibody test), is a laboratory method to identify immune reactions by leukocytes, mainly neutrophils, to food and other substances. Leukocytes are stimulated by foods, chemicals, herbs, food additives, common medications, molds, and others. These reactions are mediated by the innate immune system rather than by the adaptive immune system, therefore the testing is done on live leukocytes rather than on serum. This is a functional response test, rather than an antibody test, and therefore is not subject to cross-reactivity with other substances, nor is it affected by molecular mimicry, both of which yield false-positive results. An important notable factor of the ALCAT is that it uses organic food processed in house rather than purchasing reagents from a supplier. This assures purity of the food, as well as not having pesticides or other chemical contaminants, which would perhaps give false-positive results. The ➤



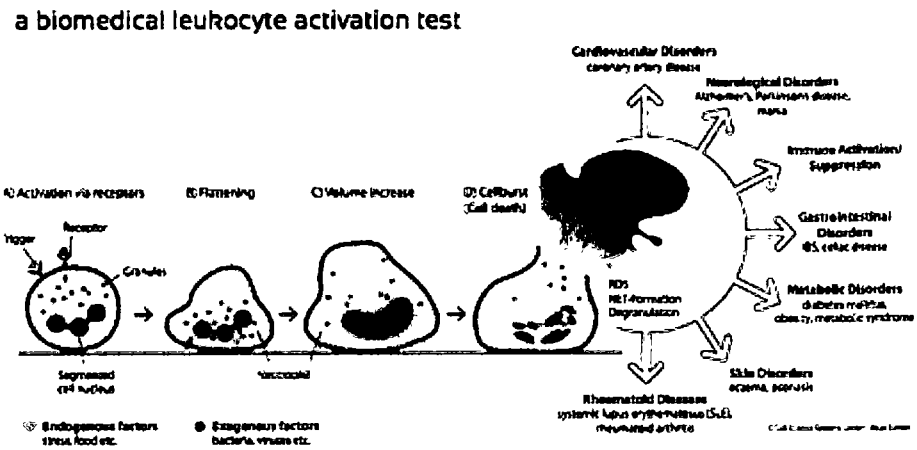


Figure: Reaction of polymorphonuclear (PMN) cell (here, a neutrophil) and potential associated diseases.

The Leukocyte Activation Test

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ALCAT measures changes in cell size and volume after incubation with foods or other substances, including the swelling of the cell, the decrease in cell numbers with degranulation of neutrophils, and the respiratory burst, releasing activated NADPH oxidase, generating superoxide anion and hydrogen peroxide, which then give rise to reactive oxygen species. These free radicals can damage tissues and induce apoptosis in other immune cells, leading to inflammation and disease processes. These changes to neutrophils and a histogram of the reaction, with the cell size on the *x*-axis and the number of cells on the *y*-axis, are shown in the 2 figures above (p. 89).

Analysis of blood instead of serum offers a significant advantage in that it contains not only all the cellular elements, but also the immune system elements. There is always some mediator release in a reaction to a food or other substances, so if a leukocyte begins to swell or progresses to a respiratory burst of reactive oxygen species, which is a crucial reaction to degrade internalized particles, these morphological changes can be accurately measured by the ALCAT. These measurements are of the immune reaction to a specific food or substance by live leukocytes and denote what that patient is reacting to. It's worth noting that the resulting symptoms from the reaction may not occur quickly, as this test is does not measure allergic reactions. Rather, the symptoms may be delayed by a few hours to a few days, and tend to be vague, such as fatigue, bloating, muscle and joint aches and pains, and abdominal discomfort. The sustained activation of leukocytes by substances leads to chronic inflammation, giving rise to common problems such as: gastrointestinal complaints, skin diseases, metabolic disorders, obesity, neurological disorders, and musculoskeletal disorders. The ALCAT is therefore a valuable tool for practitioners for identifying dietary and environmental triggers of inflammation. A review paper by Pietschmann showed how the ALCAT is a useful clinical screening tool to identify substances at the root of inflammatory disorders and how the diet provided by the results can restore immune homeostasis.[5]

A recent study by researchers at Harvard University, including Dr. Alessio Fasano, and the National Institutes of Health, reported real-time microscopic observations of gluten-induced neutrophil activation in the duodenal tissues of laboratory animals.[6] Other research has yielded important facts regarding the ALCAT. Researchers at Yale School of Medicine have discovered immunological specific markers associated with food intolerance using the ALCAT method. They found that severe intolerance on the ALCAT was linked with an upregulation of the CD11b on CD4+ and CD8+ T cells, a known inflammatory marker. [7]

In a controlled study, carried out at Baylor Medical College, analyzing 100 overweight patients, an 80% decrease in body fat was observed in the group following a diet based on ALCAT results when compared with the control group. Furthermore, there was a significant improvement reported by the ALCAT group on a 20-item Disease Symptom Inventory Self-Report.[8]

There have been a number of studies showing improvement in gastrointestinal diseases such as IBS, as well as arthritis, skin problems, and others. Double-blind studies have shown the clinical usefulness of the ALCAT in identifying food additives and food sensitivities in patients.[9–15]

IgG Antibodies to Food

With IgG food testing, there can be a lack of correlation between results and actual symptoms. This increases the risks of unnecessary food avoidance and thereby developing a lack or deficiencies of certain nutrients, escalating the potential harm from the results of this test. In addition, there is no published clinical evidence to support the use of IgG tests to determine the need for vitamins or supplements. IgG antibodies indicate exposure to foods, not allergy, and may be markers of food tolerance rather than intolerance or adverse reactivity. IgG is a "memory" antibody; it is normal for the adaptive immune system to make IgG antibodies to foreign proteins, and IgG antibodies to a food is a sign of a normal adaptive immune system. IgG antibodies to food is a test that relies on only proteins; antibodies cannot be made against any other substance. Due to molecular mimicry, there can be high antibody levels to foods that do not provoke any clinical symptoms.[16] For example, a patient's diet might be strictly kosher, but may react to pork and other nonkosher food due to cross-reactivity.

Irritable bowel syndrome (IBS) is the most common gastrointestinal disorder with prevalence rates in the US of 10% to 15%, with annual physician visits between 2.4 and 3.5 million. Two-thirds of subjects with IBS relate their symptoms to the foods in their diet. Many of these patients modify their diet after getting their IgG test for foods, and, as a result, some of them have an inadequate diet.[17] However, IgG antibodies to food antigens may be detected in the serum of normal healthy individuals as well as patients with IBS. In a case-controlled study in the general population with abdominal complaints and their intake of common food items, IgG and IgG4 antibodies were measured. There were 269 subjects and 277 controls. The study concluded that there was no evidence that the use of IgG or IgG4 antibody to food testing is a method to diagnose food hypersensitivity.[18]

In another example, 42 bakers and 20 controls were measured for IgG antibodies to wheat flour. IgG antibodies were significantly higher in the bakers than in the unexposed group, but none had symptoms. The conclusion of the study was that IgG antibodies reflect exposure, but are not related to any specific clinical situation.[19]

A study conducted in China on 5394 participants and published in

2013 looked at IgG antibodies to 14 foods and the symptoms associated with these positive antibodies. The authors concluded: "Although testing for the presence of food-specific IgGs has been regarded as a potential tool of the diagnosis of food allergy/ intolerance, it's the accuracy and clinical utility of such testing [that] remain unclear." Also: "Chronic symptoms were negatively associated with the concentrations of a few food-specific IgGs, and were positively associated with the concentrations of other food-specific IgGs." This large study indicates that IgG testing for foods is not clinically relevant in regard to symptoms, and that the clinical utility of this type of testing is uncertain.[20] In a study titled "Blood Testing for Sensitivity, Allergy or Intolerance to Food," the author concluded: "Immunoglobulin G antibodies directed at specific foods can be found in healthy children as well as adults."[21] In a randomized controlled trial of food elimination diet based on IgG antibodies to see if this would reduce migraine headaches, the authors concluded: "Use of ELISA test with subsequent diet elimination advice did not reduce the disability or impact on daily life of migraine like headaches or the number of migraine like headaches at 12 weeks."[22]

In the Diabetes Autoimmunity Study in the Young (DAISY), 260 participants were tested for IgG4 antibodies to dietary foods. The conclusion of the study showed: "Our examination of the individual dietary IgG4 antibody concentrations, as well as our composite measure of ß-lactoglobulin, gluten, and ovalbumin IgG4 antibodies in childhood, provided no evidence of a greater generalized immune response in children developing IA (Islet Autoimmunity) or progressing to T1D."[23]

Conclusion

The clinician looking for answers to treat his patient's complaints such as fatigue, aches and pains, gastrointestinal issues, migraine and other neurological complaints, short-term memory loss, malaise, tremors, sleep disturbance, skin rashes, and others should consider if foods might be the causal factor. The ALCAT can determine this in a reproducible and accurate manner, and has done so for the last 29 years, and in over 1 million patients in the last 10 years alone, throughout the world.

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Dr. Campbell was born of an American father and a Swiss mother in Beirut, Lebanon. He graduated from a Swiss preparatory school at age 14, first in his class. He completed college in 3 years and then graduated from medical school. Dr. Campbell trained at the Orlando Regional Medical Center in Florida and at the Medical College of Georgia before moving to Houston, Texas, where he was the medical director of the Medical Center for Immune and Toxic Disorders for over 20 years. He has held various leadership positions in hospitals in Houston. Dr. Campbell served on the admissions committee for the University of Texas Medical School and as a faculty member. He founded the St. John Vianney Clinic for the indigent 27 years ago. He has served as president or vice president of a number of medical organizations, both national and international. He has also been editor-in-chief, coeditor, associate editor, and on the editorial board of several medical journals. He is currently the editor-in-chief of two peer-reviewed and indexed medical journals. Dr. Campbell has received awards from many organizations, both medical and consumer, national and international. He is fluent in French, Spanish, Arabic, Hungarian, and English. He has been on several television shows, including *20/20*, the *Montel Williams Show*, 24 Hour Investigative News and has been interviewed by NBC, ABC, and CBS affiliates throughout the United States as well as television programs in Canada and Mexico. Dr. Campbell has published over 70 peer-reviewed journal articles and medical textbook chapters.

Subclinical Hypothyroidism: A Review, with Treatment Considerations

by Todd A. Born, ND

Definition

Albeit it is somewhat controversial as to whether subclinical hypothyroidism exists, technically subclinical thyroid disease (SCTD) is defined as serum free T(4) and free T(3) levels within their respective reference ranges in the presence of abnormal serum TSH levels. Most often, patients present with vague, nonspecific symptoms that are suggestive of hypothyroidism, but on many occasion, attempts to identify patients clinically, via laboratory values, have not been successful – conventionally, at least.[1]

Epidemiology

Depending on the source, the prevalence ranges from 4% to 15%.[2] From 1988 to 1994 (I could not locate more current data), in the US National Health and Examination Survey (NHANES III), excluding known thyroid disease, 4.3% of 16,533 people had subclinical hypothyroidism. As we age, prevalence increases. It is present more often in females than males, and lower in blacks than in whites.[3]

Etiology[4]

The causes of subclinical hypothyroidism are the same as those of overt hypothyroidism.

Most patients have Hashimoto's thyroiditis with elevations of antithyroid peroxidase antibodies (anti-TPO). Other major causes include prior ablative or antithyroid drug therapy for Graves' disease; prior partial thyroidectomy; radiation therapy with Hodgkin lymphoma, leukemia, or brain tumors; inadequate T4 replacement therapy for overt hypothyroidism; and drugs impairing thyroid function.[5]

Diagnosis

Diagnosis is based on blood tests. It may occur with the presence or absence of mild symptoms of hypothyroidism.

In my opinion and experience, to increase the precision of the diagnosis, serum TSH, FT3, and FT4 should be tested. However, in circumstances where there is a strong indication for T4 therapy, such as pregnancy or infertility, T4 and/or T3 replacement should be initiated if TSH is elevated and/or the individual is symptomatic.

Consequences of Subclinical Hypothyroidism

A substantial proportion of patients will eventually develop overt hypothyroidism. Studies have shown in 10 to 20 years of follow-up, the cumulative incidence of overt hypothyroidism ranges from 33% to 55%.[6,7]

Subclinical hypothyroidism has been associated with an increase in cardiovascular risk factors, markers of inflammation, vascular reactivity, endothelial function, and carotid intima media thickness.[8–10] Some subjects have been observed to have diastolic dysfunction, along with increased peripheral vascular resistance.[11]

Other comorbidities may also exist. For example, in a cross-sectional study, nonalcoholic fatty liver disease (NAFLD) was correlated with serum TSH levels. Thirty percent of individuals had ultrasonographic findings of NAFLD (versus 20% of controls), while 20% had abnormal liver enzymes.[12]

Management

Virtually all experts recommend treatment with serum thyrotropin (TSH) concentrations >10 mU/L. The routine treatment of asymptomatic patients with TSH values between 4.5 and 10 mU/L remains controversial.[13]

Some groups suggest treatment in patients with subclinical hypothyroidism and TSH levels greater than 10 mU/L, given the data linking atherosclerosis and myocardial infarction, along with increased risk of progression to overt hypothyroidism.

There are few reported data showing benefit or harm of thyroxine (T4) treatment in patients with TSH values between 4.5 and 10 mU/L. A clinical consensus group (comprising representatives from the Endocrine Society, American Thyroid Association (ATA), and the American Association of Clinical Endocrinologists) did not recommend routine treatment for such patients, but recommended monitoring TSH levels every 6 to 12 months.[14]

Treatment Goals[4]

The goal of therapy is to reduce the patient's serum TSH concentration into the normal reference range, as well as improve symptoms. 1.4 mU/L is the mean serum TSH for the general US population, with 90% having serum TSH levels <3.0 mU/L. Many experts recommend a therapeutic TSH target of 0.5 to 2.5 mU/L in young and middle-aged patients, while a TSH target of 3 to 5 mU/L may be appropriate in patients over age 70 years.

Integrative and Holistic Approach

Throughout my training as a naturopathic doctor, I was indoctrinated with "don't treat the numbers, treat the patient." Typically in our view, subclinical hypothyroidism is a mild elevation in TSH (this value varies amongst various CAM providers, but typically ≥2.5 µU/

ml, but less than 10 µU/ml), but may also be based more on clinical symptoms.[15] These patients don't meet the criteria for hypothyroidism via standard hormone tests per se (i.e., free or total T3 and free T4), but yet present clinically as hypothyroid.[16]

The question then arises, to treat or not to treat with thyroid hormone? I believe this needs to be taken on a case-by-case basis, but studies do show that patients generally have an improved sense of well-being, and measurable lipid and cardiac abnormalities tend to improve.[17,18] For those with thyroid autoantibodies, it may also prevent progression of the autoimmune process with thyroid replacement.[19]

In my opinion, investigation of other organic etiologies that overlap hypothyroid symptomatology should be excluded first, before initiating thyroid hormone replacement. Iron deficiency anemia, hypercortisolemia, and adrenal hypofunction are just a few examples.

DHEA-S looks at adrenal function, and the stress hormone cortisol (secreted from the adrenal cortex) inhibits T4 to T3 conversion.[20] T4 to T3 also need cofactors of iron (Fe), zinc (Zn), methylcobalamin (B12), and selenium (Se) to convert.[21] If FT3 is low or low normal, while FT4 is normal, you might consider a cofactor conversion issue. In order for thyroid hormone to be functionally produced, tyrosine and iodine also need to be present.[22]

Once I have ruled out iron deficiency anemia, metabolic syndrome, diabetes and frank hypothyroidism, and the diagnosis "subclinical hypothyroidism," is determined, I institute the following treatments before using thyroid hormones. I have seen improvements in TSH, FT4, and FT3 values in over 100 patients, and more importantly, improvement in most if not all of the patient's health concerns.

- proper sleep hygiene
- stress management
- exercise
- contrast hydrotherapy (water therapy) to regions over the thyroid and suprarenal glands
  - Consists of 3 min hot, 30 seconds cold, in sets of three, three times daily. Always end on cold.
    - The theory is that this acts as a pumping mechanism and stimulates the glands.
- high-potency multivitamin/mineral combination, including RDA of iodine (varies from 90 mcg to 290 mcg depending on age, pregnancy, and lactation)[23]
  - Provides cofactors for T4/T3 conversion.
- adaptogenic botanical medicines (beyond the scope of this discussion)
  - These have traditional use, as well as evidence regarding their efficacy to assist the body's ability to "adapt" to stress, improve stamina, energy, and mood.[24-26]
- DHEA supplementation if DHEA-S is low or low normal for age and gender[27]

Conclusion

Subclinical hypothyroidism is becoming increasingly prevalent in the US, especially when one considers the ubiquity of endocrine disruptors in our environment, role of chronic stress, and poor dietary choices.[28] Many patients seek out integrative/CAM providers because they don't feel listened to and/or their symptoms may be brushed off and ignored.

This article has (hopefully) opened the door to the view that this may be an overlooked etiology for a patient's health concerns, and appropriate treatment may improve not only laboratory values but quality of life.

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Dr. Todd A. Born is a naturopathic doctor, and coowner and medical director of Born Naturopathic Associates Inc. in Alameda, California. Dr. Born is the product manager, head of new product development, and scientific advisor for Allergy Research Group LLC and editor-in-chief of its science *Focus Newsletter*. He is a Thought Leader for the UK-based Clinical Education, a free peer-to-peer service that offers clinicians a closed forum to ask clinical questions and receive evidence-based responses by experts in their fields

Dr Born graduated from Bastyr University in Seattle and completed his residency at the Bastyr Center for Natural Health and its 13 teaching clinics, with rotations at Seattle-area hospitals. His clinical focus is utilizing integrative medicine to treat chronic disease He has a strong interest in difficult and refractory cases, gastrointestinal issues, neurological and neurodegenerative disorders, endocrinology, cardiovascular disease and diabetes, autoimmune disease, development and behavioral issues, HIV/AIDS, and geriatrics. He has extensive knowledge and training in the basic medical sciences, physical medicine (osseous manipulation, craniosacral therapy, hydrotherapy, and physiotherapy), botanical medicine, homeopathy, biotherapeutic drainage, Ayurveda, counseling, pharmacology, and diet and nutrient therapies.

Dr. Born may be contacted via dr.born@bornnaturopathic.com or www.bornnaturopathic com.

When he's not working, Dr Born enjoys spending time with his wife and son, being in the great outdoors, reading, writing, traveling, and playing with his three rescued Persian cats.

Exercise for All Conditions

review by Jule Klotter

The Exercise Cure, by Jordan D. Metzl, MD
Rodale Inc.; www.rodalebooks.com
© 2013; hardback; $26.99; 298 pp.

"Exercise is honest, inexpensive, all-natural medicine," says Jordan D. Metzl, MD. "When formerly sedentary people start moving regularly, miraculous things happen – just as miraculous as any treatment or procedure or drug I've ever seen or prescribed in my medical career." Metzl is a sports medicine physician at New York City's Hospital for Special Surgery. He, along with fitness coach Andrew Heffernan, CSCS, has written *The Exercise Cure* – the most comprehensive and user-friendly book on physical activity that I've come across. The book is divided into four sections: an overview of exercise benefits, specific exercise recommendations for common ailments, a detailed fitness program, and concise advice about diet. The book also includes illustrations and instructions for dozens of stretches and strength-building exercises. Throughout the book, Metzl urges readers to find physical activities that they enjoy rather than making exercise "another obligation on a never-ending to-do list."

Exercise does far more than strengthen muscles and promote cardiovascular fitness. The increased blood flow that comes with movement benefits every cell and organ in the body. Movement of any kind engages areas throughout the brain, including emotional, memory, and decision-making centers. Memory and cognitive function especially benefit when movement is combined with novelty such as walking an unfamiliar route or learning a new dance or sport. Physical activity increases energy, improves mood, and deepens sleep, aiding the body's ability to heal. Regular exercise boosts immune function and reduces chronic low-level inflammation. All in all, physical activity improves quality of life and increases longevity. "The higher your fitness level, the longer you'll live," Metzl writes. People who have the strength, flexibility, and coordination to rise from a seated position on the floor without using their hands or other help live much longer than those who need help to stand up, according to Brazilian research.

> "Give yourself permission to fail, to look awkward, to be a rank beginner. Babies and toddlers learn new physical skills at an astounding rate. You know why? They aren't afraid to stink at something."

The Exercise Cure provides exercise advice for people with various physical and psychological problems and illnesses as well as for healthy folk wanting to take part in marathons and triathlons. People with back pain, for example, are encouraged to find ways to keep moving. "The most important exercise you can do for your lower back is to get up out of your chair as often as you can: Sitting weakens the muscles that surround your spine and leaves you vulnerable to injury," Metzl writes. Special sections on heart disease and cancer give guidelines for safe, beneficial activity for patients. Whether addressing cognitive, psychological, cardiopulmonary, metabolic, hormonal, or musculoskeletal problems, Metzl gives a brief explanation of the physiology, exercise suggestions, and research that backs his suggestions. Each section also includes a note for "When to Call a Doctor."

Too often, exercise is viewed as a one-size-fits-all workout at the gym. *The Exercise Cure* has a more individualized approach, providing basic guidance for encouraging physical activity in people with diverse conditions. It is a great resource for anyone who seeks a better quality of life.

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More than Blood Sugar

review by Jule Klotter

How to Cure Diabetes! by Sherry A. Rogers, MD
Sand Key Company Inc.
P.O. Box 19252, Sarasota, Florida 34276
© 2013; $23.95; 380 pp

For nearly three decades, Sherry A. Rogers, MD, has encouraged patients to take charge of their health and support the body's innate healing ability. Her latest book, *How to Cure Diabetes!*, looks at the shortcomings of conventional treatment and advocates a nutrient-based program. Although pharmaceutical treatments are useful for acute situations, they do not cure diabetes. Rather, they simply lower blood sugar levels without addressing underlying causes. Rogers says, "If your sugars are out of whack, you are deficient in nutrients that regulate sugars in the body." Nutrients, not drugs, are what the body needs to prevent and cure diabetes and related conditions such as neuropathy and heart disease.

Rogers has no patience for "dinosaur doctors" who rely on pharmaceuticals while ignoring nutrient deficiencies. She urges readers to find "dynamo doctors" who appreciate the intricacies of nutrient balance, biochemistry, and mitochondrial function. She highly recommends the 13-page laboratory assay Cardio/ION (Metagenics Inc.) to assess nutrient imbalances and underlying problems. For example, elevated D-arabinitol on the assay can indicate candida overgrowth. "Candida can make an enzyme called thiaminase that destroys the B1 vitamin before it gets a chance to be absorbed," says Rogers. "This silent B1 deficiency can lead to not only heart failure (usually fatal within 5 years), but poor energy, poor recovery from exercise, and worsening of diabetes (with mysterious inability to bring down the [hemoglobin] A1C)."

> "In a nutshell, dinosaur docs do drugs; while dynamo docs focus on cause and cure. Dinosaur docs don't take the time to learn how God designed the body to heal."

From Rogers's perspective, the first step toward healing is to repair nuclear, endoplasmic reticular, and mitochondrial membranes. She says that Cardio/ION results from people with diabetes (and many other diseases) indicate "starving cell membranes." She recommends a combination of cod liver oil, GLA, phosphatidyl choline, vitamin D, vitamin K2, phosphatidylserine, tocopherols (particularly gamma), and tocotrienols from reputable manufacturers that make good-quality supplements. In addition to nutrient deficiencies, phthalates in plastics and other environmental chemicals contribute to diabetes and metabolic syndrome. Rogers says that infrared sauna therapy is the most effective way to remove these chemicals from the body. For more information about detoxification, she refers readers to her book *Detoxify or Die*.

How to Cure Diabetes! does not contain a one-size-fits-all protocol. Rather it offers a series of short, referenced essays that encourage readers to see another way of treating diabetes and comorbid illness. This book is designed to be read, reread, and mulled over with underlining and note-taking; Rogers intentionally refrained from including an index. For the careful reader, *How to Cure Diabetes!* offers a rational basis for choosing a functional nutrient-based approach to treat and prevent diabetes.

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Another Viral Epidemic?

Early in January 2016, US news overflowed with stories about the Zika virus. Researchers had found PCR evidence of Zika virus in two Brazilian fetuses with microcephaly (smaller head circumference than normal due to poor brain development).[1] They believed that the virus might be responsible for Brazil's marked increase in microcephaly in fall 2015. Most cases (about 80%) were clustered in nine northeastern Brazilian states. Known causes of microcephaly include severe malnutrition, exposure to harmful toxins (i.e., alcohol, toxic chemicals, some drugs), and some infections (i.e., rubella, toxoplasmosis, cytomegalovirus), according to the CDC.

While mainstream media eagerly churned out reports about this latest viral epidemic, researchers and physicians were more conservative, pointing out that association is not causation. Zika virus, first discovered in Uganda's Zika Valley in 1947, is carried by the same mosquito species that spreads dengue. Until now, Zika had been viewed as a mild disease characterized by fever, rash, and joint pain. Why would it suddenly affect fetal brain development? And why in those nine states?

In a paper submitted to the *Bulletin of the World Health Organization*, researchers in Paraíba, the second-hardest hit Brazilian state, looked at head circumference data for about 10% of the neonates (n = 16208) who were part of a pediatric cardiology study that started in 2012.[2] The researchers found that the number of microcephaly cases "were greater than expected since the end of 2012 and with its sharpest peak in mid-2014." Incidence ranged from 4% to 8% of children born between 2012 and 2015, depending upon which diagnostic criteria were used. Severe cases have significantly increased within recent months. Zika supposedly entered Brazil in mid-2014 during the World Cup, so it is unlikely that the virus is the sole cause, say the researchers. They note that most cases have occurred in low-income families; malnutrition that comes with poverty is a likely contributor. "Also to be considered is teratogens [sic] exposure," the authors state, "such as vaccines or drugs used in early pregnancy."

In late 2014, Brazil added Tdap (diphtheria, tetanus, pertussis) vaccine to the vaccine schedule for all pregnant women. Following the US CDC recommendations, the vaccine is given late in pregnancy – between the 27th week and 36th week – to prevent pertussis in the neonate. Neither the vaccine manufacturer nor the US FDA has established its safety in pregnant women. Safety studies for pregnant women and their infants are just beginning. (See "Shorts" February/March 2016.) Tdap, like all vaccines, does contain brain-damaging toxins such as aluminum compounds, so the vaccine could be a contributor. However, why would the increase be clustered in just the northeastern part of Brazil when Tdap is given to women throughout Brazil?

Tdap was not the only vaccine to be administered to fertile women in the months before fall 2015, when the northeastern states showed a sharp increase in severe microcephaly. Applied physicist Pliny Bezerra dos Santos Filho, PhD, says that a measles outbreak in 2014 in northeast Brazil led to a widespread MMR (mumps, measles, rubella) vaccination campaign targeting women of childbearing age, beginning in November 2014. The measles epidemic and call for vaccination were covered in Brazilian news. The program continued until mid-April in some areas.[3] As noted above, the rubella virus is a known cause of microcephaly. Women who had just become pregnant or who became pregnant shortly after vaccination would have been exposed to the virus during early pregnancy. Nine months after the MMR campaign started, the incidence of microcephaly began its surge, according to Filho. Furthermore, Filho points out that the season for mosquito-borne dengue/Zika, however, is from mid-February to late April. If Zika were the culprit, the increase would not have commenced until mid-November, with the greatest incidence in January 2016.

Although Brazilian and World Health Organization officials have been quick to deny the possibility, pesticides may also be contributing to microcephaly. The Argentine group Physicians in the Crop-Sprayed Towns and Abrasco, a Brazilian public health organization, believe that the larvicide pyriproxyfen is to blame. Pyriproxyfen was added to drinking water of many northeast Brazilian communities in 2014, to kill off mosquitoes. The larvicide is a hormone disruptor and causes birth defects, according to the Argentine group. Brazilian and WHO officials disagree. They say that some areas with microcephaly have not used the larvicide. Moreover, they say there is "no scientific basis" to support an association between pyriproxyfen and microcephaly.[4] In searching for information on pyriproxyfen, I found one study testing its effectiveness when applied to mosquito netting; I found nothing assessing its safety when consumed by humans.

In addition to pyriproxyfen, herbicides and other agricultural chemicals are used in mass qualities in northeastern Brazil. Brazil uses more agrochemicals than any other country, and many of the pesticides have been banned elsewhere.[5] Pesticide use has been associated with congenital abnormality (p = 0.004), according to a 2010 Brazilian study.[6] In addition, animal research has shown that glyphosate-

based herbicides, used on genetically engineered Roundup Ready crops and cereal grains, have produced "marked alterations in cephalic and neural crest development" as well as microcephaly.[7] Long-term, ongoing use of agricultural pesticides is unlikely to be the primary contributor to the 2015 microcephaly increase, but it may be a contributor to the higher-than-expected incidence reported by pediatric cardiology researchers.

"In the absence of data, we will always make up stories," says Brené Brown in her book *Rising Strong*. "Meaning making is in our biology and our default is often to come up with a story that makes sense, feels familiar, and offers us insight into how best to self-protect." Those who believe that pathogens are the source of disease target the Zika virus, postulate that its sudden virulence is due to viral mutation, and look to a vaccine as prevention. But malnutrition, toxins found in vaccines and pesticides, and perhaps some yet-unidentified factor could be the primary culprit(s). US CDC researchers went to Brazil in late February to help investigate the association between Zika and microcephaly. In addition to asking women about possible Zika infection, they will also ask about exposures to mercury and pesticides, according to a National Public Radio report.[8] I do not know if the researchers will also consider the use of MMR or Tdap, but I hope that they do.

Jule Klotter

Notes

1. Oliveira Melo AS, Malinger G, Ximenes R, et al. Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg? *Ultrasound Obstet Gynecol.* January 2016;47(1):6–7.
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4. Robinson C. Argentine and Brazilian doctors name larvicide as potential cause of microcephaly. *GM Watch.* February 10, 2016.
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8. Stein R. CDC arrives in Brazil to investigate Zika outbreak. *Morning Edition.* February 24, 2016

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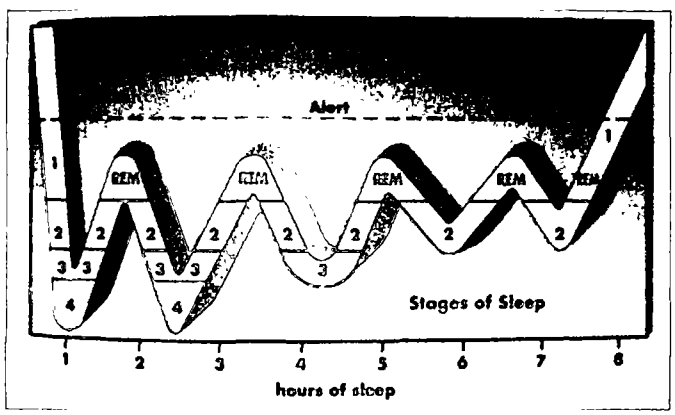
Anti-Aging Medicine

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

An Anti-Aging Approach to Optimal Sleep

Most people are aware of the importance of a healthful diet and exercise, but many overlook the importance of getting enough sleep each night. One of the most crucial components of an anti-aging regimen, is getting the proper amount of sleep on a consistent basis. Inadequate sleep would be counterproductive to an anti-aging regimen, as it may lead to a shortened lifespan. Of particular concern is the fact that just 1 night of sleep deprivation can lead to insulin resistance (equal to 6 months on a high-fat diet) and may promote biological aging in older adults. Sleep loss can affect brain size, which is of particular concern as we age, and can lead to brain shrinkage. Without getting adequate sleep each night, one is leading an uphill battle in the race against aging. Since sleep deprivation affects us mentally and physically, getting enough of it should be a cornerstone in the foundation of achieving optimal health – which is especially crucial with age.

The Centers for Disease Control and Prevention has called insufficient sleep a public health problem. It has gone on to state, "Persons experiencing sleep insufficiency are also more likely to suffer from chronic diseases such as hypertension, diabetes, depression, and obesity, as well as from cancer, increased mortality, and reduced quality of life and productivity." The CDC estimates that approximately 50 to 70 million US adults have sleep or wakefulness disorders. The amount of sleep that we need varies from person to person, but adults should be getting at least 7 hours of sleep per night. Many adults do not attain this. In the CDC study "Prevalence of Healthy Sleep Duration among Adults – United States, 2014," researchers found that more than one-third of the adults reported sleeping less than seven hours in a 24-hour period.



Reprinted from Goldman R. *Brain Fitness*. Doubleday Books, 1999

As obtaining adequate sleep is crucial to an anti-aging regimen, sleep hygiene is key. This column reviews recent studies that suggest simple and natural approaches which may assist you in obtaining optimal sleep.

Broussard J Cedars-Sinai Medical Center. Poster abstract presentation at Obesity Society Annual Meeting at ObesityWeek 2015, November 2–6, 2015, Los Angeles, CA

Cedernaes J, Osler ME, Voisin S, et al Acute sleep loss induces tissue-specific epigenetic and transcriptional alterations to circadian clock genes in men *J Clin Endocrinol Metab* July 13, 2015

Centers for Disease Control and Prevention. Insufficient sleep is a public health problem [online article] Sept 13, 2015 http //www cdc.gov/features/dssleep

Liu Y, Wheaton AG, Chapman DP, Cunningham TJ, Lu H, Croft JB Prevalence of healthy sleep duration among adults — United States, 2014. *MMWR Morb Mortal Wkly Rep* 2016;65 137–141. DOI http //dx.doi.org/10 15585/mmwr mm6506a1

Parthasarathy S, Vasquez MM, Halonen M, et al Persistent insomnia is associated with mortality risk *Am J Med* 2014;128(3).268–275.

Sexton CE, Storsve AB, Walhovd KB, Johansen-Berg H, Fjell AM Poor sleep quality is associated with increased cortical atrophy in community-dwelling adults *Neurology* 2014 Sep 3. pii.10.1212/WNL 0000000000000774

Simple Secret to Sleep

As we age, we typically experience declines in the quality of our sleep. Mindfulness meditation is a self-administered approach that intentionally focuses one's attention on the emotions, thoughts, and sensations occurring in the present moment. David Black and colleagues from University of Southern California (US) enrolled 49 men and women, aged 55 years and older, who experienced moderately (or greater) disturbed sleep, who were divided into two groups. One group visited the study center for 6 weekly 2-hour sessions of a course in Mindfulness Awareness Practices (MAPs) for daily living. Those included meditation, eating, walking, movement, and friendly or loving-kindness practices. A certified teacher led the exercises and also instructed participants to meditate for 5 minutes daily, gradually increasing to 20 minutes daily. The other group attended 6 weeks of a sleep hygiene and education course, wherein they learned about sleep problems, self-care methods for improving sleep, and weekly behavioral sleep hygiene strategies. Prior to the start of the 6-week programs, the average sleep quality questionnaire score was

10. At the end of the study period, those in the meditation group demonstrated improvement in their sleep score by an average of 2.8 points, compared with 1.1 points in the sleep hygiene group. Among those in the meditation group, daytime impairments, including symptoms of insomnia, fatigue and depression, were improved as well. The study authors conclude: "Formalized mindfulness-based interventions have clinical importance by possibly serving to remediate sleep problems among older adults in the short term, and this effect appears to carry over into reducing sleep-related daytime impairment that has implications for quality of life."

Black DS, O'Reilly GA, Olmstead R, Breen EC, Irwin MR Mindfulness meditation and improvement in sleep quality and daytime impairment among older adults with sleep disturbances: a randomized clinical trial. *JAMA Intern Med* 2015 Feb 16.

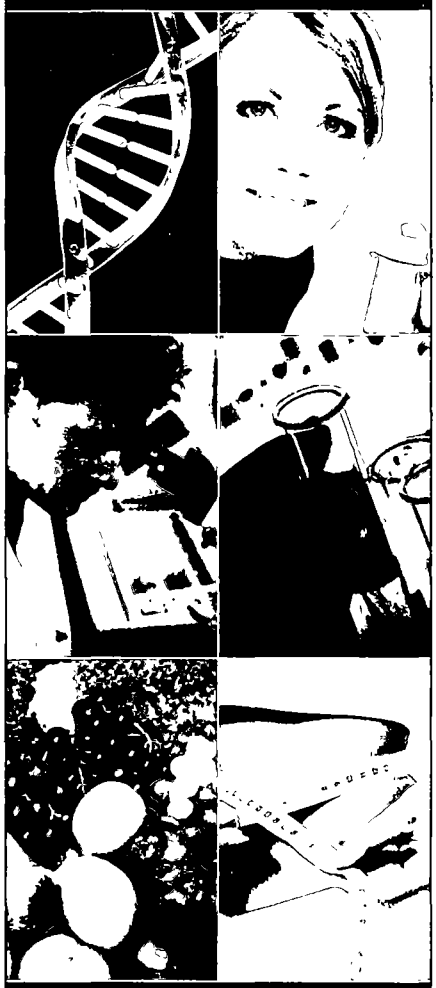
Eight Great Sleep-Enhancing Activities

It is generally established that physical activity associates with restful sleep, and a study by University of Pennsylvania (US) team elaborates on specific types of activities that help to improve sleep quality. Michael Grandner and colleagues analyzed data on sleep and physical activities of 429,110 adults enrolled in the 2013 Behavioral Risk Factor Surveillance System, measuring whether each of 10 types of activities was associated with typical amount of sleep, relative to both no activity and to walking. Subjects were asked what type of physical activity they spent the most time doing in the past month, and also asked how much sleep they got in a typical 24-hour period. All types of activity except for household/child care were associated with a lower likelihood of insufficient sleep, as compared with those who reported that they did not get physical activity in the past month. Specifically, walking, aerobics/calisthenics, biking, gardening, golf, running, weight-lifting, and yoga/Pilates were each associated with fewer cases of insufficient sleep, and household chores and child care were associated with higher cases of insufficient sleep. The study authors submit: "Not only does this study show that those who get exercise simply by walking are more likely to have better sleep habits, but these effects are even stronger for more purposeful activities, such as running and yoga, and even gardening and golf. These results are consistent with the growing scientific literature on the role of sleep in human performance."

Chheda J et al. Physical activity and habitual sleep duration: does the specific type of activity matter?" [Abstract #0246]. Presentation at SLEEP 2015 (Associated Professional Sleep Societies); 8 June 2015

Nature Promotes Sleep

Previous studies report that exposure to the natural environment may improve health behaviors (by encouraging physical activity), as well as improve mental health (including to reduce levels of depression). Diana Grigsby-Toussaint and colleagues from the University of Illinois (US) analyzed data collected by the US CDC's Behavioral Risk Factor Surveillance System, which surveyed 255,171 adult men and women. The team also used a USDA index that scores the country's geographical areas for their natural amenities, using hours of sunlight, which is important in regulating a person's circadian rhythm, and temperature. In response to the survey question about sleep quality in the last month, the researchers found ➤



Anti-Aging Medicine

that the most common answer was that respondents had slept poorly for less than 1 week. Across the entire sample, individuals reporting 21 to 29 days of insufficient sleep consistently had lower odds of access to green space and the natural environment, as compared with those reporting less than 1 week. The relationship between sleep and exposure to green space was much stronger for men than for women, as well as for men and women ages 65-plus. Observing, "Access to the natural environment attenuated the likelihood of reporting insufficient sleep," the study authors submit: "Additional studies are needed to examine the impact of natural environment exposure on sleep insufficiency across various socio-demographic groups."

Grigsby-Toussaint DS, Turi KN, Krupa M, Williams NJ, Pandi-Perumal SR, Jean-Louis G Sleep insufficiency and the natural environment: results from the US Behavioral Risk Factor Surveillance System survey. *Prev Med* 2015 Sep;78:78–84.

Brain-Boosting Sleep Position

The brain's glymphatic pathway is responsible for clearing harmful wastes – particularly amyloid-beta plaques that characterize Alzheimer's disease, during sleep. Employing an animal model, Helen Benveniste and colleagues from Stony Brook University (New York, US) studied the cerebrospinal fluid (CSF)–interstitial fluid (ISF) exchange efficiency – a marker of the clearance capacity of the glymphatic pathway. The team found that sleeping in the lateral position (on one's side) may more effectively remove brain wastes, including amyloid-beta, as compared with sleeping on the back or stomach. The study authors submit: "We propose that the most popular sleep posture (lateral) has evolved to optimize waste removal during sleep."

Lee H, Xie L, Yu M, Kang H, et al The effect of body posture on brain glymphatic transport *J Neurosci*. 2015 Aug 5,35(31) 11034–11044.

Fish Compound Hooks Better Sleep

An ever-expanding library of data suggests a variety of potential health-improving benefits of omega-3 fatty acids – compounds found abundantly in "fatty fish" such as salmon, herring, and sardines. Previous studies have suggested links between poor sleep and low blood levels of omega-3 long-chain polyunsaturated fatty acids (LC- PUFAs), among infants and in children and adults with behavior or learning difficulties. Paul Montgomery and colleagues from Oxford University (UK) assessed sleep in 362 healthy 7- to 9-year-old UK schoolchildren in relation to the levels of omega-3 and omega-6 LC-PUFAs found in fingerstick blood samples. The children who took part in the study were not selected for sleep problems, but were all struggling readers at a mainstream primary school. At the outset, the parents filled in a child sleep questionnaire, which revealed that 4 in 10 of the children in the study suffered from regular sleep disturbances. Of the children rated as having poor sleep, the researchers fitted wrist sensors to 43 of them to monitor their movements in bed over 5 nights. This exploratory pilot study showed that the children on a course of daily supplements of omega-3 had nearly 1 hour (58 minutes) more sleep and 7 fewer waking episodes per night compared with the children taking the corn or soybean placebo. Writing, "Cautiously, we conclude that higher blood levels of docosahexaenoic acid may relate to better child sleep, as rated by parents," the study authors submit: "Objective evidence from actigraphy suggests that docosahexaenoic acid supplementation may improve children's sleep."

Montgomery P, Burton JR, Sewell RP, Spreckelsen TF, Richardson AJ Fatty acids and sleep in UK children subjective and pilot objective sleep results from the DOLAB study – a randomized controlled trial *J Sleep Res*. 2014 Mar 8

To stay updated on the latest breakthroughs in natural approaches that may help you achieve optimal sleep, 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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Calendar

Please submit an announcement of your event 90 days in advance. Event publication must be limited to 25 words or less. Multiple event listings require paid advertising. Contact calendar@townsendletter.com for details.

FELLOWSHIP IN STEM CELL THERAPY – 5-Module Course online and weekends: May 19-21 (Hollywood, Florida), **September 22-24** (Dallas, Texas), **December 9-11** (Las Vegas, Nevada). CONTACT: Metabolic Medical Institute, 561-910-4960; www.mmimedicine.com

APRIL 29-MAY 1: 45th ANNUAL INTERNATIONAL ORTHOMOLECULAR MEDICINE TODAY CONFERENCE in Vancouver, British Columbia. Current advances in orthomolecular psychiatry, paediatrics, oncology and general medicine. CONTACT: 416-733-2117; www.csom.ca/omt/

APRIL 30-MAY 1: 6th ANNUAL INTEGRATIVE AND HOLISTIC NURSING CONFERENCE- Bringing Healing to You and Your Patients in San Diego, California. CONTACT: www.scripps.org/integrativenursingce

MAY 1-6: GERSON THERAPY PRACTITIONER TRAINING – MODULE I (of 2) in San Diego, California. In-depth training in Dr. Max Gerson's principles of dietary healing. CONTACT: 800-838-2256; gerson.org/gerpress/practitioner-training; aonken@gerson.org

MAY 12-14: THE INSTITUTE FOR FUNCTIONAL MEDICINE'S 2016 ANNUAL INTERNATIONAL CONFERENCE – Creating Balance *Between* Motion and Rest in San Diego, California. CONTACT: www.functionalmedicine.org/AIC

MAY 12-15: 20th CLINICAL APPLICATIONS FOR AGE MANAGEMENT MEDICINE in Championsgate/Orlando, Florida. CONTACT: agemed.org

MAY 14: WINNING THE WAR ON ADDICTION IN AMERICA: Understanding the Role of Neurogenetics and Epigenetics in Reward Deficiency Syndrome and Recovery in New York City, New York. CONTACT: 646-367-7411; www.pathfoundationny.org/

MAY 17-20: INTERNATIONAL CONGRESS FOR INTEGRATIVE MEDICINE & HEALTH – Bridging Research, Clinical Care, Education, and Policy in Las Vegas, Nevada. With IHPC, ACCAHC, AIHM and ISCMR. CONTACT: www.icimh.org/

MAY 19-21: 24th ANNUAL WORLD CONGRESS ON ANTI-AGING MEDICINE in Hollywood, Florida. **MAY 18-21:** ABAARM & ABAAHP exams. CONTACT: www.a4m.com/

MAY 19-21: METABOLIC MEDICAL INSTITUTE MODULES on Endocrinology, Clinical Practice Protocols, and Regenerative Medicine with Stem Cells in Hollywood, Florida. CONTACT: www.mmimedicine.com/2016/hollywood/index.html

MAY 20-22: PRECISION LYME TREATMENT WITHOUT ANTIBIOTICS in Kenmore, Washington. Tools, Remedies, Techniques for Brain, Body, & Bugs. CONTACT: 908-899-1650; info@klinghardtacademy.com; www.klinghardtacademy.com/Seminars-Workshops/Lyme-Conference-Biological-Medicine-2016.html

MAY 20-22: 2016 TRADITIONAL ROOTS HERBAL CONFERENCE in Portland, Oregon. CONTACT: traditionalroots.org/2016-traditional-roots-conference/

MAY 21: UNDERSTANDING, ADDRESSING, AND EVALUATING AUTOIMMUNE DISORDERS in Windsor Locks, Connecticut. CONTACT: www.facebook.com/BioticsResearch.

MAY 21-22: MASTERING THE SCIENCES OF INTEGRATIVE BLOOD CHEMISTRY in Los Angeles, California. CONTACT: www.facebook.com/BioticsResearch.

MAY 23-24: 18th INTERNATIONAL CONFERENCE ON COMPLEMENTARY, ALTERNATIVE, INTEGRATIVE MEDICINE & HEALTH in London, United Kingdom. CONTACT: waset.org/conference/2016/05/london/ICCAIMH/

JUNE 3-6: MEDICINES FROM THE EARTH HERB SYMPOSIUM in Black Mountain, North Carolina. CONTACT: 541-482-3016; www.botanicalmedicine.org

JUNE 6-10: APPLYING FUNCTIONAL MEDICINE IN CLINICAL PRACTICE – 5 day foundational course in Austin, Texas Also, **SEPTEMBER 19-23** in Baltimore, Maryland. CONTACT: www.functionalmedicine.org/AFMCP

JUNE 16-18: SOPMED (Society of Oxidative & Photonic Medicine) CONFERENCE near Salt Lake City, Utah. Oxidative, light, and energy medicine. Limited to 300 participants. CONTACT: 517-242-5813; info@sopmed.org;; www.sopmed.org

JUNE 18: ORGANIC ACIDS WORKSHOP FOR DISCOVERING UNDERLYING CAUSES OF CHRONIC ILLNESS with Kurt Woeller, DO in Cherry Hill, New Jersey (near Philadelphia). CONTACT: organicacidworkshop.com

JUNE 23-25: A4M BHRT SYMPOSIUM in San Diego, California. CONTACT: www.a4m.com/2016/june/san-diego/a4m-symposium.html

JUNE 23-25: METABOLIC MEDICAL INSTITUTE MODULES on Weight Management and Compounded Prescriptions in San Diego, California. CONTACT: www.mmimedicine.com/metabolic-medicine-event-schedule.html

JULY 1-3: 3rd INTERNATIONAL CONGRESS ON NATUROPATHIC MEDICINE in Barcelona, Spain. CONTACT: icnmnaturopathy.eu

JULY 15-17: HORMONE ADVANCED PRACTICE MODULE – RE-ESTABLISHING HORMONAL BALANCE in National Harbor, Maryland (DC) CONTACT: www.functionalmedicine.org/Hormone

JULY 15-17: ENERGY REGULATION ADVANCED PRACTICE MODULE – Illuminating the Energy Spectrum in National Harbor, Maryland (DC) CONTACT: www.functionalmedicine.org/Energy

JULY 22-24: 4th COLORADO INTEGRATIVE MEDICINE CONFERENCE – Focus on Mind-Body Medicine & Lifestyle Management in Estes Park, Colorado. CONTACT: 970-310-3030; info@altermedresearch.org; www.altermedresearch.org/cimc2016/

JULY 27-30: AMERICAN ASSOCIATION OF NATUROPATHIC PHYSICIANS' ANNUAL CONFERENCE & EXPOSITION in Salt Lake City, Utah. CONTACT: www.naturopathic.org/aanp2016.

AUGUST 6-7: GREAT PLAINS LABORATORY WORKSHOPS ON ORGANIC ACIDS TESTING AND GENETIC TESTING in San Jose, California. CONTACT: www.gpluniversity.com

AUGUST 10-13: 25th ANNUAL IAACN SCIENTIFIC SYMPOSIUM – Renovation of the Structural Integrity of the Human Body Through Biomolecular Interventions Beyond the Collagen Connections in Jacksonville, Florida. CONTACT: www.iaacn.org/symposium/

AUGUST 11-13: METABOLIC MEDICAL INSTITUTE MODULES on Gastroenterology and Toxicology & Detoxification in Las Vegas, Nevada. CONTACT: www.mmimedicine.com/metabolic-medicine-event-schedule.html

SEPTEMBER 3-9: HEALTHY BIRTH, HEALTHY EARTH @ Findhorn Foundation, Scotland. CONTACT: www.findhorn.org/programmes/healthy-birth-healthy-earth

SEPTEMBER 9-10: INTERNATIONAL ACADEMY OF ORAL MEDICINE AND TOXICOLOGY (IAOMT) ANNUAL CONFERENCE & JOINT MEETING WITH IABDM in Reno, Nevada. CE credits. CONTACT: iaomt.org.

continued on page 112 ➤

Study Shows Role For Alpha-Stim Technology In Treating PTSD – Cranial Electrical Stimulation (CES) Helped Reduce Symptoms In Active-Duty Soldiers Being Treated For PTSD

Electromedical Products International Inc. (EPI), a manufacturer and developer of devices that utilize electric waveforms for therapeutic purposes, announces the publication of a report, "Effects of Integrative PTSD Treatment in a Military Health Setting," which outlines the effectiveness of the Warrior Combat Stress Reset Program (Reset) in reducing symptoms of post-traumatic stress disorder (PTSD) among active-duty military personnel.

The Reset Program, an innovative intensive outpatient behavioral health program conducted using cranial electrical stimulation (CES) with EPI's Alpha-Stim® technology, trauma-focused behavioral health techniques, and complementary and alternative medicine (CAM), demonstrated significant reductions in PTSD symptoms, as well as anxiety, depression, and pain, in a cohort of 764 active service members treated at the Carl R. Darnall Army Medical Center at Fort Hood, Texas. Using a verified PTSD scoring system, the Reset Program yielded an average 10-point improvement in PTSD scores from pre- to post-treatment over the 5 years of the program, with improvement as high as 14 points in the last years.

"This report shows the value of including complementary and alternative treatment approaches, including CES, in a vulnerable and at-risk population of patients. The Reset Program used CES to address the neuropsychological precursor of PTSD symptom clusters as well as the resulting symptoms of PTSD-induced stresses, providing further demonstration of the broad applications for electromedicine," said Jerry Wesch, PhD, former director of the Warrior Combat Stress Reset Program, Fort Hood, Texas, and one of the authors of the report. "Soldiers with PTSD are complex. Most have Chronic Pain Syndrome, at least 80% have headaches and about 40% have concussion histories. CES is significantly useful in all three, plus depression and anxiety. CES (Alpha Stim) should be standard first-line care in this population."

The program evaluation report, which was published in the November issue of *Energy Psychology*, highlights that as many as 28% of American soldiers develop PTSD as a result of combat stress. Traditional approaches to managing PTSD have focused on cognitive-behavior and exposure theory. However, researchers have begun to focus on more holistic intervention programs that also incorporate CAM and mind-body treatments. In the Reset Program, CES with EPI's Alpha-Stim® technology was used to both attenuate hyperarousal—a state of psychological tension known to potentiate PTSD symptom clusters—and to reduce intrusive symptoms, such as sleep disturbance, pain, headaches, avoidance and residual post-concussion symptoms.

The Reset Program combined conventional allopathic and alternative/complementary techniques in a stepwise intervention among a large group of group of soldiers diagnosed with moderate to severe combat PTSD:

- Phase 1 involved strategies intended to reduce hyperarousal through use of CAM, CES, and active self-regulation strategies, including breathing exercises, muscle relaxation, and mindfulness.
- In Phase 2 patients continued with CES while adding neurofeedback training, acupuncture, massage, yoga, tai chi and Reiki practice to reduce symptoms such as sleep disturbances, pain and headaches. In addition, trauma memories were directly targeted for interventions via 1:1 therapies and group procedures.
- In the third and final Phase, patients received help in identifying triggers of traumatic stress and were trained to help them manage such instances. Trauma-focused group and individual psychotherapy continued through all phases.

The researchers demonstrated year-over-year improvements in symptom scores with high patient satisfaction and extremely low dropout rates. Using various verified scoring algorithms, the researchers noted statistically and clinically significant improvements in measurements of PTSD symptoms (up to -14 pre- to post-treatment), depression (mean difference -9.0 pre- to post-treatment), anxiety (mean difference -6.3 pre- to post-treatment, pain (mean difference -2.4 pre- to post-treatment) and resilience (mean difference +6.8 pre- to post-treatment).

According to the report, "The Reset Program appears to have been very successful in meeting its stated goals and objectives." The researchers noted that it was difficult to identify the contributions of the individual techniques to the improvements noted, but concluded the outcomes were likely due to the holistic synergy of the program. The authors recommended ongoing studies to understand each element of the treatment protocol and its influence on addressing PTSD and its symptoms.

"The results of the Reset Program were both statistically and clinically significant, but we think the patient population provides an additional level of impact of these data," said Tracey B. Kirsch, president, Electromedical Products International Inc. "The care of our veterans should constitute a high priority for our healthcare system, and we are most proud of EPI's ability to contribute to this important research."

About Alpha-Stim

Alpha-Stim is a clinically proven intervention that uses a proprietary electrical waveform pattern to modulate cell signaling in the central nervous system (CNS). Studies show that electrochemical signaling in the CNS has a significant impact on pain, anxiety, depression and insomnia, among other disorders The Alpha-Stim has been validated in over 95 independent, controlled research studies since it was first introduced in 1981, and has proven to be a safe, efficacious and cost-effective intervention for a variety of disorders originating in the CNS.

About Electromedical Products International, Inc. (EPI)

Electromedical Products International, Inc. (EPI) was formed in 1981 to develop, manufacture and market Alpha-Stim® technology worldwide. The original device weighed over 40 pounds; today, because of advancements in electronics and computer technology, the Alpha-Stim® is portable and accessible to patients. EPI is fully committed to supporting its products and customers through ongoing research, education and clinical support.

To date, EPI has received regulatory approvals in numerous countries. Alpha-Stim® products and accessories are FDA-cleared in the United States for marketing, and have obtained the CE mark for regulatory approval in Europe (through the European Medical Device Directive). EPI has also been awarded the UL (Underwriter's Laboratory) safety listing. EPI has been licensed by TGA (Australia) and is approved throughout Asia—including China, Japan, and Korea—and most of the world. EPI provides owner's manuals and product brochures in 19 languages, in order to service all of our patients and practitioners—no matter where they live or what language they speak

For more information on how EPI is pioneering a new paradigm for treating pain, anxiety, depression and insomnia, please visithttp //www alpha-stim.com/.

Libretto, S, Hilton, L, Gordon, S, Zhang, W & Wesch, J Effects of integrative PTSD treatment in a military health setting Energy Psychology 7 2, November 2015

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Monthly Miracles

by Michael Gerber, MD, HMD
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Vascular Modalities

Stroke

When the stroke gods are generous and only mild or moderate impairment is experienced by the patient following a CVA, it provides an opportunity for remedial therapy. Neural therapy is a great first-line tool to improve memory, disorientation, headache, disequilibrium, diplopia, vision loss, and peripheral motor paralysis. Procaine was first synthesized by Einhorn in Germany in 1905. It is made by combining PABA (para-aminobenzoic acid), a B vitamin, with DEAE (diethylaminoethanol) and has the capacity to restore the action potential to damaged nerves and detoxify chemically injured neurons. Your compounding pharmacy can provide you with a 1% solution of procaine without preservatives adjusted to a pH of 7 with potassium hydroxide.

Crown of Thorns

The crown of thorns (COT) is employed using 30-gauge or 27-gauge needles and injecting ¼ cc subcutaneously around the greatest circumference of the head at about 1 inch intervals. Commence injecting at the third eye, GV 24.5, and avoid the superficial veins. If you hit the skull, it may have a better effect and serves to faster dull the needle, which makes a crunching sound as it goes through the skin. This is usually well tolerated and not too painful. Add Traumeel or other medicaments that test well. I always test the procaine and other meds with EAV or ART testing. Some people's systems don't want it, and it helps to gauge the frequency of injections, which can easily be done weekly or more frequently until no further improvements are noted.

Usually a change in the patient's countenance is immediately apparent. They become more alert and diplopia can resolve. Adding injections to LI 4 in the web between the thumb and index finger is helpful, as well as BL 10 two fingerbreadths on each side of the occipital notch, especially for headaches. Intradermal wheals and trigger points at GB 21 on top of the shoulders, as well as any other Ah Shi points (ouch points), can also be beneficial.

The COT is also indicated for any head injury, concussion, and so on, and seizure disorders. Acute strokes can also benefit from high-dose *Arnica montana* 1M or 10M, as it tests well. Chronic head injuries also do well with Natrum Sulfuricum. Don't forget IV vitamin C to lower intracranial pressure.

Natural Anticoagulants

Although coagulation is an extremely dense topic, there is one herb that I have used to great effect for over 40 years. Herbal-grade cayenne pepper (capsicum) I find truly miraculous. Since 1975 I studied with renowned herbalist John R. Christopher (Nature's Herbs); he said, and I agree, that it will stop most angina, TIAs, acute bleeding, seizures, and some ocular migraines by the count of 10 (or within 5 or 10 minutes). It has scores of therapeutic applications.[2] Open the cap and pour into a little warm water and drink, or open capsule directly in the mouth. If one swallows the caps, it takes a few minutes longer. It contains capsaicin 0.25%, a salicylate, and coumarin anticoagulant, which is also classified as a stimulant with heat units from 40,000 to 100,000. Old cooking cayenne can become rancid and is not as powerful. Cayenne balances the circulation in the body and shunts blood away from damaged areas. It can burn coming and going for the first 3 days and can be contraindicated in acute gastritis patients. Christopher would increase the dose up to 1 tablespoon 3 times per day for hypertension or hypotension.

Although there are many herbs, vitamins, fatty acids, and enzymes that support fibrinolysis and platelet disaggregation, stopping drug anticoagulation should be approached with caution, even though patients don't like the drugs. Other favorite anticoagulants include Regulat, a fermentation of 10 fruits and vegetables and 10 spices from around the world prepared over 6 years in a cascade fermentation process from Dr. Niedermaier's Laboratory in Germany; gamma-linoleic acid from primrose oil; borage oil; vitamin E; vitamin D; fish oil; garlic; nattokinase; chocolate; lumbrokinase; and pancreatic proteolytic enzymes. ➤

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Anticoagulant salicylate-containing foods and supplements include cinnamon, turmeric, curry powder, oregano, peppermint, ginger, paprika, thyme, dill, blueberries, cranberries, grapes cherries, strawberries, nectarine, tangerines, oranges, honey, vinegar, black and green tea, pineapple juice, white and red wine.[1]

Blood-thinning coumarin-containing plants and herbs include alfalfa, aniseed, arnica, artemisia, chamomile, chicory, dandelion, fenugreek, horseradish, licorice root, parsley, and red clover.

Heart Applications for Failure, A-Fib, and other Arrhythmias.

Beside chelation therapy for arteriosclerosis and heavy metal toxicity (Flint, MI), magnesium for arrhythmias, CoQ10 and B vitamins for failure, there are a host of wonderful homeopathics to help. Homeopathic digitalis in all of its dilutions is terrific for atrial fibrillation. *Crataegus oxyacantha* (hawthorn berry) is very helpful for angina, arrhythmias, and heart failure in the tincture and all dilutions. *Cactus grand.* and *Convallaria majalis* are wonderful homeopathics to treat chronic heart conditions.

For venous issues, *Aesculus hippocastanum* (horse chestnut) is very valuable. We like the Nestmann preparation from Marco Pharma. There are many more adjunctive therapies for vascular disease treatment and prevention. These are some of my favorites.

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The Next Issue...

In the June issue of the *Townsend Letter*, Bob Frost interviews integrative physician and stem-cell researcher David Steenblock, DO, about his study of ALS (Lou Gehrig's disease).

Steenblock's work with dozens of ALS patients has revealed that most have sustained trauma to the neck that eventually degenerated into a breach in the spinal cord. Toxins from the intestine are carried into the cerebrospinal fluid. The cumulative effect of the toxins leads to injury and ultimately death of motor neurons, eventuating in ALS.

Steenblock's interview provides important insights into ALS's causation and clues for recovery.

Curmudgeon's Corner

by Jacob Schor, ND, FABNO
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Free Radical Theory of Aging – Fact or Fiction?

I find myself attracted by ideas that that stretch the way we see things, what one might call paradigm breakers. Thus I am fascinated by a theory that explains why living things age. This theory caught my attention recently in part because it suggests that our view of antioxidants and of omega-3 fats requires expansion. The theory, called the mitochondrial free radical theory of aging (MFRTA), is now the most accepted theory that explains aging.[1]

In treating conditions wherein free radical damage is a suspected cause of illness, we have reasonable confirmation that antioxidants or omega-3s are efficacious, but little evidence that such supplementation promotes longevity. What follows is not a final answer, but rather an invitation to consider that the influences on longevity are more complex than we have assumed.

The length of an individual life, one's longevity, is similar within a species yet ranges widely between species. Some animals live only a few days while some live much longer. A mud clam currently holds the animal age record; a member of the species *Arctica islandica* was 507 years old when dissected. A theory of longevity must explain why natural life spans vary so much: whales live 200 times longer than shrews and men live 30 times longer than mice. For an individual, life expectancy depends on environment, not genes; but the rate that an individual ages depends solidly on genetics.

Paul Bert was probably the first to advance the idea that free radical stress accounts for aging. Back in 1878 he reported that oxygen is toxic at high concentrations, particularly to warm-blooded animals. He demonstrated that this toxicity varies with ambient temperature in cold-blooded animals, a method to alter rates of metabolism.[2]

In 1908 Max Rubner observed that longevity of mammals increases with body size and that the rate of metabolism of mammals decreases with increases in body size. He combined these two measurements in five mammal species (guinea pigs, cats, dogs, cattle, and horses) to calculate their "life time energy potential," a fairly constant value across these species.[3]

In 1928 Raymond Pearl reported, in an experiment reminiscent of Bert's, that he had shifted the life span of fruit flies by changing the temperature of their cages, and thus their metabolic rates, or to use his term, their "rate of living."[4]

The MFRTA

In 1956 Denham Harman proposed an early version of the mitochondrial free radical theory of aging, writing that "aging and the degenerative diseases associated with it are attributed basically to the deleterious side attacks of free radicals on cell constituents and on the connected tissues."[5] He expanded his theory in the 1970s to suggest that mitochondria are the source of these free radicals.[6] As most chronic diseases are associated with aging, the obvious thought was that if the aging process is slowed, the onset of such diseases would also be slowed.

Denham's ideas led to an early hypothesis that increasing internal antioxidant levels, either through food or supplements, would quench free radicals, slow the aging process, and so prevent chronic disease.[7] This was a reasonable theory at the time. Antioxidants became the focus of research for decades. Antioxidant levels are relatively easy to measure, and there was something compelling about the idea that antioxidant levels might correlate positively with longevity. Unfortunately, over the decades researchers have thoroughly disproved the idea; in fact the opposite is true: the association is negative.[8]

Longer-lived animals have fewer endogenous antioxidants in their tissues than shorter-lived animals.[9] For example, hamsters make 20 times as much glutathione peroxidase in their livers as humans do.[10] In 1998 Pérez-Campo et al. reported that of 27 measured correlations between antioxidant production and longevity, 21 showed a negative association, while the remaining 6 were not associated. No example was found wherein there was a positive association between higher endogenous antioxidants and longer life expectancy.[11]

In a 2011 review Pamplona and Constantini reported, "Among a total of 79 correlations between endogenous tissue antioxidants and longevity, 72 were negative, 6 did not show

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significant differences, and only a single one was positive."[12] Animals that live longer do not do so by producing more antioxidants.

Multiple trials were performed during the 1970s and 1980s giving dietary antioxidants to various animals, seeking to show an increased life span. Greater longevity was seen in about half the trials, but antioxidants did not increase maximum longevity. Mean life span increased in some short-lived animals (life spans <3 years). Antioxidants just appeared to protect the animal from early or premature death – their survival curves look more rectangular with antioxidants – but maximum survival did not increase. This is what happened to humans in the last century. More people live to 100, but new age records are rarely set. Our life expectancy has increased, but our rate of aging remains constant.

Antioxidants protect against oxidative insults that life hits us with but they do not slow the clock of aging.[13]

"In any case, a final goal of gerontology is to increase human longevity, and it is now reasonably clear that antioxidants do not increase longevity in mammals. ..." (Gustavo Barja)[14]

Mitochondrial ROS production

This failure of antioxidants to extend life gave rise to an alternate hypothesis based on energy economy. Producing antioxidants is a metabolically expensive process. Long-lived animals economize by limiting reactive oxygen species (ROS) production. Current thought is that the rate of production of reactive oxygen species by the mitochondria (mtROSp) in an animal is the critical factor determining aging.[15]

The association of low mtROSp and greater longevity has been demonstrated in a wide range of animals, with comparisons between short-lived rodents and birds that live 7 to 9 times longer yet weigh the same.[16] In the 1970s, it was thought that this ROS production occurred in complex III of the mitochondrial electron transport chain, but it is now believed that this occurs in complex I.[17,18] This puts the generation of ROS in closer proximity to the mitochondria's DNA (mtDNA). While other sites within the cell may produce ROS, it is the quantity of ROS produced in close proximity to the mtDNA that is correlated with lifespan.

This seeming paradox, that highly localized mitochondrial production influences longevity but systemic antioxidants have little effect, results from how we visualize a cell's interior. Our view is often oversimplified; we imagine cells as balloons of undifferentiated cytoplasm, when in fact a cell's contents are highly compartmentalized. Measurements of the global oxidative stress of homogenized cells do not tell us what is actually going on when it comes to aging, even if the results do help us predict near-term survival.

The concentration of ROS varies by cell compartment, particularly in the mitochondria, and the proximity to complex I reactions that generate ROS outweighs general antioxidant levels in the cell.

These processes that generate ROS need to be viewed on the micro level, not the cellular level, and certainly not on the organism level. Damage to the mtDNA determines age, and antioxidants have little protective effect against locally generated ROS. Antioxidants may offer global protection, but we age locally.

The scientists and researchers have moved on. The theory has evolved past believing that antioxidants will be the panacea for aging and chronic disease. Reactive oxygen species have been misjudged: "... contrary to their conventional image only as toxic agents, ROS at a non-toxic level function as signaling molecules that induce protective defense in responses to age-dependent damage."[19]

PUFA

There is second aspect to the MFRTA at odds with our worldview. A positive association exists between cellular membrane fatty acid saturation and longevity. This is firmly established, studied multiple times with consistent results. This is considered proven fact. The longer a species lives, the smaller the number of fatty acid double bonds in its cell membranes. The fewer unsaturated fatty acids, the more resistant these membranes are to lipid peroxidation, a highly destructive process that produces both mutagenic and toxic metabolites within the cell.

In 1996, Pamplona et al. reported: "Liver mitochondrial membranes of especially long-lived species show both a low level of free radical production and a low degree of fatty acid unsaturation as important constitutive protective traits to slow down aging."[20]

Since then at least 23 additional studies have reported similar findings.[21,22]

Membrane fatty acid composition varies with body size in mammals. Comparing tissue extracts from mammals that varied in body mass by 9000-fold (mice to cattle) showed that "There were significant inverse allometric relationships between body mass and the proportion of docosahexaenoic acid ... in heart and skeletal muscle." (The greater the mass, the lower the DHA levels.)[23]

This "exponential relationship between docosahexaenoic acid of cardiac phospholipids and the heart rate" was first reported in 1978.[25] The relationship is not restricted to heart tissue but exists in most important mammalian tissues. The bigger an animal is, the lower the DHA content in its membranes: DHA content of cell membranes decreases by 12% to 24% for each doubling of body mass in mammals. [26]

This relationship between low PUFAs and longevity is now a key concept in the MRFTA: "... the fatty acid composition of cell membranes varies systematically between species, and this underlies the variation in their metabolic rate. When combined with the fact that 1) the products of lipid peroxidation are powerful reactive molecular species, and 2) that fatty acids differ dramatically in their susceptibility to peroxidation, membrane fatty acid composition provides a mechanistic explanation of

the variation in maximum life span among animal species. ..."[27]

ROS injure many types of molecules in cells. They attack protein and modify DNA, but perhaps the biggest worry is that they damage membranes. Vulnerability of fats to oxidative damage varies by two things: First, where the reactions occur. Oxygen and other free radicals are more soluble in lipid membrane bilayers than in aqueous solution. Second, not all fatty acid chains are equally susceptible to damage. This is key to understanding these relationships. [28]

DHA is a highly polyunsaturated omega-3 PUFA. With six double bonds, it is vulnerable to oxidation and is 8 times more vulnerable to peroxidation than linoleic acid, which has only two double bonds. DHA is 320 times more susceptible to peroxidation than the monounsaturated oleic acids in olive oil. Long-lived species reduce the amount of PUFA in their cell membranes, making them more resistant to ROS injury.[29]

This information obviously raises the question of whether supplementation with fish oil may have detrimental effects and accelerate aging. Tsuduki reported in 2011 that feeding mice fish oil increased oxidative damage and shortened their life span.[30] But those are mice; what about people?

In 2014 Kelley et al. reviewed 22 published human studies to determine whether omega-3 PUFA supplementation affected lipid peroxidation levels (LPO): "... nine found no change, eight a decrease, and five an increase in markers of LPO." Thus the majority showed either no increase or a reduction in lipid peroxidation. [31] So far it appears that fish oils act differently in humans than in mice.

There is certainly an abundance of published studies which suggest that fish oil supplementation provides health benefits. Heart disease and psychiatric disorders are examples of two conditions in which supplementation appears to bring benefit.[32] The brains of all species have similar levels of unsaturated fats despite variations in lifespan. The brain's distinctive requirements for high PUFAs may explain in part fish oil's benefit for age-related cognitive decline. [33]

(We should be mindful that any benefits of antioxidants on increasing average life span are seen only in short-lived species and not in animals that survive longer than three years. This should be kept in mind when translating research findings from animal studies to clinical practice.)

The hypothesis that supplemental antioxidants will increase maximal lifespan has been solidly disproved, yet it remains firmly entrenched in general belief. The value of antioxidants may only be to compensate against damage caused by suboptimal living conditions or specific damage. Antioxidants may extend life for those who might otherwise die prematurely but may not act as the panacea to slow the process of aging.

Is the universal high regard for polyunsaturated fatty acids, in particular DHA, undeserved? If the current MFRTA proves true, high doses of PUFAs may, because they increase vulnerability to oxidation of cellular membranes, leave us more susceptible to aging. At this point, the evidence has not definitively suggested that this occurs in humans.

Caloric restriction increases longevity probably because it decreases the rate of mtROS generation.[34] Similar changes are seen with methionine depletion without caloric restriction. Severe methionine restriction in long-lived animals may also decrease membrane unsaturation.[35] Alternate day feeding increases longevity also by lowering mtROSp.[36] Restricting only carbohydrates or only fats does not increase longevity.[37] Protein restriction appears to be responsible for about half of the life-extending effects of caloric restriction. Attention is now focused on depleting specific amino acids in isocaloric diets, especially methionine depletion.

Methionine appears to be the only amino acid that when restricted lowers mtROSp to increase longevity.[38]

This mitochondrial free radical theory of aging questions some of our basic assumptions about antioxidants and polyunsaturated fatty acids, in particular DHA. We practice on the assumption that all people should be getting regular doses of both. We have faith that using these supplements is right. We forget that these ideas were based on a hypothesis, one that is disproven.

This is confusing. Supplementing with antioxidants and PUFAs is a primary strategy in natural medicine, and yet it would appear that nature has taken an opposite strategy to preserve life. This is more than confusing; it should be troubling, as our desire in naturopathic medicine is to mimic nature's practices.

When I shared some of my confusion over these matters with a colleague, she responded, "I have faith in antioxidants."

Medicine is not a religion, and faith should not hold us hostage. We humans like explanations for our world and our experiences in it. Once we find an explanation that works for us, we adopt it and hold tight. This tendency appears to be shared both between some who profess religious belief and those who claim that their ideas are based on science. Religious believers may hold fast to outdated worldviews; and we should grace them with a margin of tolerance, as who among us has not at times professed ideas that others consider magical beliefs?

Scientific understandings evolve; knowledge progresses over time, and the fittest explanations endure. The scientific explanations of many phenomena are different now than they were a century ago, or even 10 years ago. Science does not bring a finished theory but a process for advancing understanding. We need to be sure that our beliefs keep pace with the science. As medical practitioners, we need to keep up with the science and question past assumptions as often as necessary.

Curmudgeon's Corner

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Women's Health Update

by Tori Hudson, ND
womanstime@aol.com

New Studies on Blood Pressure, Weight Loss, and Lowering Triglycerides

Flaxseed Reduces Blood Pressure

Fiber and omega-3 fatty acids have been shown to have at least modest antihypertensive benefits, but research on flaxseeds for this purpose have been conflicting. Flaxseed constituents include fiber, an omega-3 fatty acid alpha-linolenic acid (ALA), the peptide KCI-F1, and perhaps best known, the lignans. The purpose of this research was to do a systematic review and meta-analysis to evaluate the effect of flaxseed on blood pressure in humans.

Databases were searched for randomized trials and blood pressure, using flaxseeds. Studies that were selected for inclusion in the review and meta-analysis were those that had a flaxseed and a control group, a duration of at least 2 weeks and those with a case-control or crossover design.

Out of the 622 studies that the search yielded, 15 studies met the inclusion criteria and were thus included in the meta-analysis, which then had a total of 1302 subjects. A total of 618 were treated with flaxseed, 140 were treated with other therapies, and 544 with placebo. Studies included spanned Canada, Brazil, China, India, Australia, Denmark, Finland, and Greece.

The formulations used in these 15 trials were 1.2 to 15 g/day of alpha-linoleic acid (ALA), flaxseed oil 360 to 600 mg/day of flax lignan extract, or 28 to 60 g/day of flaxseed powder. Studies ranged from 4 to 12 weeks.

Comment: This meta-analysis showed that only the flaxseed powder treatment had a significant reduction in systolic and diastolic blood pressure and that the flaxseed powder and flax oil had a significant effect on reducing diastolic blood pressure. Lignan extract therefore had no effect on either systolic or diastolic blood pressure, and the flax oil only had an effect on reducing diastolic blood pressure.

Some of the studies had a small number of and lack of homogeneity in participants, and a variety of dosages, forms, and even kind of flaxseeds used (i.e., brown or golden).

In this meta-analysis, there was a decrease of 2.85 systolic pressure and 2.39 diastolic pressure with the flaxseeds. A decrease of 3.3/1.4 mmHg has been associated with a 22% decline of relative risk of cardiovascular mortality and this meta-analysis is showing the flaxseeds could be meaningful in reducing death from cardiovascular disease.

There are many reasons to include flaxseed powder in the diet (e.g., constipation, irritable bowel, breast health, cardiovascular mortality, polycystic ovarian syndrome, insulin resistance), and specifically a small but meaningful effect on lowering both systolic and diastolic blood pressure. An easy method of delivery is to add 30 to 60 g/day to a smoothie.

Ursoniu S, Sahebkar A, Andrica F, Serban C, Banach M, Lipid and Blood Pressure Meta-analysis Collaboration (LBPMC) Group Effects of flaxseed supplements on blood pressure A systematic review and meta-analysis of controlled clinical trial *Clin Nutr* Epub May 29, 2015. doi 10.1016/j clnu 2015 05 012

Rye Bread Enriched with Green Tea Extract Lowers Blood Pressure and Reduces Metabolic Syndrome Markers during Weight Loss Maintenance

This pilot study was established to determine whether the consumption of rye bread enriched with green tea extract could improve weight loss maintenance and control of metabolic syndrome abnormalities in obese men and women after treatment for weight loss.

A total of 66 obese men and women were recruited, aged 49 to 65 years, with a body mass index (BMI) between 30.0 kg/m^2 and 49.9 kg/m^2. After being screened for entrance criteria, 11 subjects were excluded.

During the first 4 weeks of the study, 11 subjects dropped out and 44 completed the study with a mean age of 53.0 and a mean BMI of 35.0.

The weight-loss phase of the study included a balanced, low-calorie diet providing 600 to 700 kcal daily less than the individually estimated daily energy expenditure. There was then a 12-week weight-maintenance phase that had increase in calories but still below the baseline energy intake. During this maintenance phase, the subjects were randomly assigned to either the control rye bread (n = 21) or the green tea rye bread containing 1.1% green tea extract per 100 g of flour (n = 23).

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Many measurements were taken at baseline, and at the end of the weight-loss phase and weight-maintenance phases, including blood pressure, anthropomorphic measurements, high-density lipoprotein cholesterol (HDL-C), triglycerides (TGs), and fasting blood glucose (BG), as well as resting metabolic rate (RMR) and respiratory quotient (RQ). The International Diabetes Federation criteria were used to diagnose metabolic syndrome.

The daily bread that was consumed by all individuals during the weight-maintenance phase was 280 g for women and 360 g for men. The macronutrient content of the bread (energy, protein, fat, total fiber, insoluble fiber, and soluble fiber) is described in the study. During the weight-loss phase, men and women from both groups lost a significant amount (7.6 ± 3.5%) of their original body weight. Fat mass and waist circumference also decreased significantly in both groups during the weight-loss phase.

After the weight-maintenance phase, the average body weight increased by 1.5 kg (3.3 lb) in the rye bread (RB) group and by 0.6 kg (1.3 lb) in the green tea rye bread (GTRB) group; however, body weight in both groups remained significantly lower than before any weight loss. Waist circumference and fat mass also increased during the weight maintenance phase but remained significantly lower than at baseline. The increase in waist circumference in the GTRB group was significantly less than in the RB group. Systolic blood pressure, diastolic blood pressure, and blood sugar decreased significantly after weight loss in both groups while HDL-C and TG levels did not change in both groups.

Systolic and diastolic blood pressure increased in both groups but was lower in the GTRB group after weight maintenance. BG levels increased in both groups during weight maintenance but were significantly lower in the GTRB group, and lower than baseline. HDL-C levels did not change in the RB group after weight maintenance but increased in the GTRB group compared with baseline.

The number of metabolic syndrome characteristics dropped more in the GTRB group in the weight-loss phase and only increased slightly in the weight maintenance phase while it returned to baseline in the RB only group. Adherence to the diet was similar in both groups throughout the study.

Comment: In the current study, the daily intake of more than 280 g of GTRB as part of a weight maintenance diet did not improve HDL-C, TG, or BG concentrations better than the control RB; however, individuals in the GTRB group did maintain lower blood pressure levels and reduced their characteristics for metabolic syndrome significantly. Both catechins and caffeine are found in green tea and are thought to effect weight loss through mechanisms of increased thermogenesis and fat oxidation. Obesity is one of the most challenging issues in women's health care. No single strategy produces consistent results in all women. Nutritional modifications, exercise programs, behavioral therapy, and agents that can affect insulin resistance, fat burning, fat oxidation, and metabolic rates occupy central roles in efforts.

Bajerska J, Mildner-Szkudlarz S, Walkowiak J Effects of rye bread enriched with green tea extract on weight maintenance and the characteristics of metabolic syndrome following weight loss: a pilot study *J Med Food* 2015,18(6) 698–705.

Vitamin D Treatment Reduces Triglyceride Levels in Postmenopausal Women with Type 2 Diabetes

The primary outcome of this study was to assess the effect of vitamin D supplementation on serum lipids in overweight and obese postmenopausal women with type 2 diabetes. This study was a randomized, double-blind, placebo-controlled trial evaluating the effect of vitamin D supplementation on serum lipids carried out in Mexico. Women were recruited from the Health Workers Cohort Study (HWCS); of the 731 adult HWCS women who had type 2 diabetes, 329 were invited to be screened for the current study because they were postmenopausal (aged 45–65) and had type 2 diabetes without complications and a body mass index ≥ 25 kg/m^2. After women were excluded due to a history of kidney or liver disease, cancer, taking vitamin D supplementation, on insulin or lipid treatment, and a BMI > 40 kg/m^2, a total of 104 were included in the current study.

Women were randomly assigned to one of two groups; group 1 was given 4000 IU per day of vitamin D3 (n = 52) and group 2 placebo (n = 52). Eligible participants took their respective treatment once daily for 6 months. Lab measurements were taken at baseline, 3 months, and after 6 months and had fasting glucose checked once per month. All women received individualized dietary and physical activity counseling, and a physical exam. Ninety-nine completed the study.

Results: At baseline, 46% of the women in the placebo group were vitamin D deficient (≤50 nmol/L) and 44% were at the end of the study. At baseline, 35% of the women were vitamin D deficient in the vitamin D group vs. only 4% at the end of the intervention. Serum triglycerides decreased in the vitamin D group – 34.24 mg/dL. No significant effects were observed for total cholesterol (TC), low density lipoproteins (LDL), and high density lipoproteins (HDL) at the end of the study period. There was a significant effect on serum triglycerides (TG) of –20.4 mg/dL at 6 months. Serum vitamin D levels improved by 25.5 nmol/L in the treatment group.

Comment: Observational studies on the impact of vitamin D on serum lipids and lipoproteins have been inconsistent, confirmed by a meta-analysis or randomized trials. (Wang H, Xia N, Yang Y, Peng D. Influence of vitamin D supplementation on plasma lipid profiles: a meta-analysis of randomized controlled trials. *Lipids Health Dis*. 2012;11:42.) At 6 months, postmenopausal women with type 2 diabetes had lower triglyceride levels after treatment with vitamin D 4000 IU per day compared with placebo, and independent of any effects on other lipid levels. One proposed mechanism of this effect is that vitamin D increases calcium absorption, thereby reducing fatty acids in the gut, increasing fat absorption and lowering triglycerides levels.

Munoz-Aguirre P, Flores M, Macias N, et al The effect of vitamin D supplementation on serum lipids in postmenopausal women with diabetes A randomized controlled trial *Clin Nutr*. 2015;34.799–804

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Iron Deficiency and Congestive Heart Failure

Iron deficiency is a common and sometimes overlooked factor in patients with congestive heart failure (CHF), and is associated with a poor prognosis. Research indicates that testing CHF patients for iron deficiency, and supplementing with iron when appropriate, could increase functional capacity, improve quality of life, decrease the number of CHF-related hospitalizations, and possibly decrease mortality.

Iron is a component of hemoglobin, which delivers oxygen to the tissues. In addition, iron is a cofactor for the enzyme cytochrome oxidase, which plays a role in mitochondrial ATP production via the electron-transport chain. ATP is essential for the pumping action of the heart; therefore, iron deficiency could exacerbate heart failure whether or not the patient is anemic. Patients with CHF are prone to iron deficiency for a number of reasons. CHF may be associated with poor appetite, which can lead to multiple nutritional deficiencies. In addition, gastric acid plays a role in iron absorption, and a large proportion of CHF patients have hypochlorhydria, either due to their age and their disease, or to the use of proton pump inhibitors or other acid-blocking drugs.[1] Many patients with CHF also have bowel wall edema (secondary to the backup of fluid from the heart), which can impair nutrient absorption. Moreover, some patients with CHF have impaired delivery of iron to their metabolically active cells, even though their iron stores are normal or even increased. This is known as functional iron deficiency (as opposed to absolute iron deficiency).

Patients with CHF are considered to have absolute iron deficiency if their serum ferritin level is below 100 µg/L. This cut-off level is well above that used to diagnose iron deficiency in healthy individuals. The higher value takes into account the fact that CHF is associated with chronic inflammation, and that serum ferritin levels rise in response to inflammation. CHF patients are thought to have functional (as opposed to absolute) iron deficiency if their serum ferritin level is between 100 and 300 µg/L (which is frequently seen in patients with chronic inflammatory diseases) and their transferrin saturation is below 20%. Blood tests for iron deficiency are not as reliable as bone marrow biopsy, but the blood tests are generally preferred in clinical practice because they are noninvasive.

In a prospective cohort study of 1506 patients with chronic CHF, 753 patients had absolute or functional iron deficiency according to the above definition. During a median follow-up period of 1.92 years, 29.2% of the patients died. Iron deficiency was a strong predictor of mortality ($p = 0.001$). In multivariable analysis, iron deficiency (but not anemia) remained a strong and independent predictor of mortality (hazard ratio = 1.42; $p = 0.002$).[2] Similar findings were reported in another study.[3]

In a double-blind trial, 459 patients with chronic CHF (New York Heart Association [NYHA] class II or III), a left ventricular ejection fraction (LVEF) of 40% or less for NYHA class II, or 45% or less for NYHA class III, and iron deficiency as defined above were randomly assigned to receive intravenous iron (200 mg per dose, as ferric) or placebo (saline).[4] The total iron dose required for repletion was calculated at baseline, according to Ganzoni's formula.[5] The dosing frequency was weekly until iron repletion was achieved and then every 4 weeks (starting at week 8 or week 12, depending on the time required for repletion). At baseline, in the group that received iron, the mean serum ferritin level was 53 µg/L and the mean transferrin saturation was 17.7%. At 24 weeks, the proportion of patients who reported being much or moderately improved was significantly higher in the iron group than in the placebo group (50% vs. 28%; $p < 0.001$). At 24 weeks, the proportion of patients in NYHA class I or II was significantly higher in the iron group than in the placebo group (47% vs. 30%; $p < 0.001$). Significant improvements were seen in the iron group compared with the placebo group for distance walked in 6 minutes and health-related quality of life. The beneficial effect of iron was similar in patients with and without anemia. The death rate was nonsignificantly lower by 38% in the iron group than in the placebo group. No serious side effects were seen.

In another double-blind trial, 304 patients with CHF and iron deficiency according to the above definition were

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Editorial

randomly assigned to receive intravenous iron (as ferric carboxymaltose) or placebo (saline) over a 52-week period. Iron was given in dosages based on body weight and initial hemoglobin levels, with the aim of correcting iron deficiency and subsequently maintaining iron sufficiency. Compared with placebo, iron supplementation resulted in sustained improvement in functional capacity, symptoms, and quality of life; these differences were statistically significant from week 24 until the end of the study. The frequency of hospitalization for worsening heart failure was significantly lower by 61% ($p < 0.01$) and the death rate was nonsignificantly lower by 14% in the iron group than in the placebo group.[6]

The clinical trials discussed above used intravenous iron, because oral iron preparations are sometimes poorly absorbed and frequently cause gastrointestinal side effects. In contrast, intravenous iron is generally well tolerated, although anaphylactic reactions have occurred on rare occasions. However, intravenous iron is substantially more expensive than oral supplements, and is also not widely available in some places. Oral iron does improve iron status in CHF patients, but it may not be as effective as intravenous therapy. A retrospective study was conducted on 105 patients with CHF and iron deficiency (as defined above) who had received oral iron at a mean daily dose of 130 mg (range, 65–150 mg). After a median treatment period of 164 days, the median value for serum ferritin increased from 39 µg/L to 75 µg/L, transferrin saturation increased from 10% to 21%, and hemoglobin increased from 10.4 g/dl to 11.6 g/dl ($p < 0.0001$ for all). When compared with the changes in CHF patients who received intravenous iron in one of the trials cited above, the increases in transferrin saturation were similar, but the increases in ferritin levels were markedly greater with intravenous iron (mean for oral iron: 40 µg/L at baseline, increased to 72 µg/L; mean for intravenous iron: 53 µg/L at baseline, increased to 312 µg/L).[7]

Iron supplementation of nondeficient patients is not risk free. Because it is a prooxidant, iron may increase oxidative stress, which could exacerbate various chronic illnesses. In addition, iron overload can impair blood glucose control. However, when administered according to the laboratory guidelines described in this article, patients with CHF could benefit greatly, with minimal risk of serious side effects.

Alan R. Gaby, MD

Notes

1. Furbetta D et al. Behavior of hydrochloric acid secretion in cardiopathies *JAMA*. 1951,146.1615
2. Klip IT et al Iron deficiency in chronic heart failure An international pooled analysis *Am Heart J* 2013,165·575–582 e3
3. Jankowska EA et al Iron deficiency· an ominous sign in patients with systolic chronic heart failure *Eur Heart J*. 2010,31.1872–1880
4. Anker SD et al Ferric carboxymaltose in patients with heart failure and iron deficiency *N Engl J Med*. 2009,361.2436–2448.
5. Total iron deficit – Ganzoni equation [Web page] PharmCalc.com http://www.al-nasir.com/www/PharmCalc/mob_exec_calc.php?ID=ganzoni
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Calendar *continued from page 101*

SEPTEMBER 15-18: 2016 ACAM & AAPMD JOINT ANNUAL MEETING – An Interdisciplinary Approach to Advanced Prevention in Tucson, Arizona. CONTACT: www.acam.org/ACAM2016

SEPTEMBER 16-18: 14TH ANNUAL INTERNATIONAL RESTORATIVE MEDICINE CONFERENCE - Cutting-edge Protocols for Treating Chronic Conditions: Practical Clinical Skills You Can Use Monday Morning in Hilton Head, South Carolina. CONTACT: restorativemedicine.org/aarm2016/

SEPTEMBER 19-23: APPLYING FUNCTIONAL MEDICINE IN CLINICAL PRACTICE - 5 day foundational course in Baltimore, Maryland. CONTACT: www.functionalmedicine.org/AFMCP

SEPTEMBER 21-24: A4M BHRT SYMPOSIUM in Dallas, Texas. Also, ABAARM & ABAAHP exams. CONTACT: www.a4m.com/conference-schedule.html

SEPTEMBER 21-24: METABOLIC MEDICAL INSTITUTE MODULES on Neurology, Autoimmune Disease, Cardiovascular, & Stem Cells in Dallas, Texas. CONTACT: www.mmimedicine.com/metabolic-medicine-event-schedule.html

SEPTEMBER 29-OCTOBER 2: 7TH ANNUAL INTEGRATIVE MEDICINE FOR MENTAL HEALTH CONFERENCE in Reston, Virginia (near D.C.). CONTACT: www.immh2016.com/

SEPTEMBER 30-OCTOBER 1: A4M SYMPOSIUM in Washington, D.C. CONTACT: www.a4m.com/2016/washington-dc/a4m-symposium.html

SEPTEMBER 30-OCTOBER 2: 10TH ANNUAL MICROCURRENT CASE CONFERENCE in St. Pete Beach, Florida. CONTACT: microcurrent.info.

SEPTEMBER 30-OCTOBER 2: KLINGHARDT EUROPEAN NEURAL THERAPY & INJECTION TECHNIQUES in Kenmore, Washington. A transformative workshop: basic to advanced skills. CONTACT: 908-899-1650; info@klinghardtacademy.com; www.klinghardtacademy.com/Seminars-Workshops/Injection-Techniques-and-Skills-2016.html

OCTOBER 6-9: AMERICAN ACADEMY OF ENVIRONMENTAL MEDICINE ANNUAL MEETING – The Role of Mitochondria in Health & Disease near San Diego, California. CONTACT: AAEM, 316-684-5500; www.aaemconference.com

OCTOBER 22-23: 10TH AUSTRALIAN HOMEOPATHIC MEDICINE CONFERENCE in Brisbane, Australia. CONTACT: www.homeopathyconference.com

OCTOBER 28-30: DETOX ADVANCED PRACTICE MODULE – Biotransformation and Toxicity in Chicago, Illinois. Live Streaming Available. CONTACT: www.functionalmedicine.org/Detox

NOVEMBER 5-6: GREAT PLAINS LABORATORY WORKSHOPS ON ORGANIC ACIDS TESTING AND GENETIC TESTING in Dallas, Texas. CONTACT: www.gpluniversity.com.

DECEMBER 8-11: A4M WORLD CONGRESS ON ANTI-AGING MEDICINE in Las Vegas, Nevada. Also, ABAARM & ABAAHP exams. CONTACT: www.a4m.com/conference-schedule.html

DECEMBER 8-11: METABOLIC MEDICAL INSTITUTE MODULES on Endocrinology, Clinical Practice Protocols, Weight Management, & Stem Cells in Las Vegas, Nevada. CONTACT: www.mmimedicine.com/metabolic-medicine-event-schedule.html

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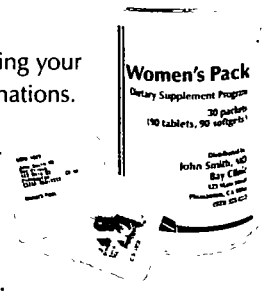

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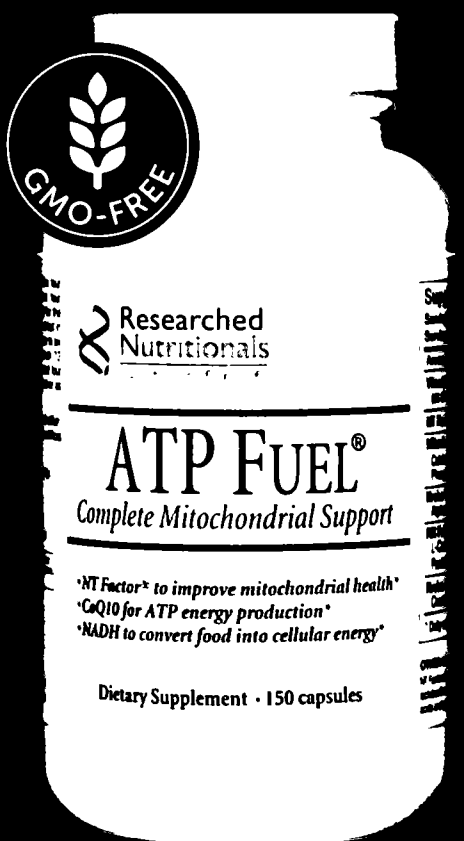

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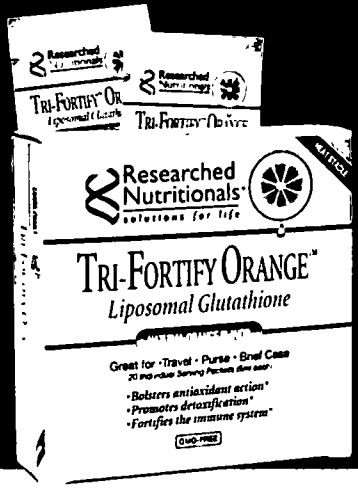

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