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## **'Stealth' Viruses and Eastern Medicine**

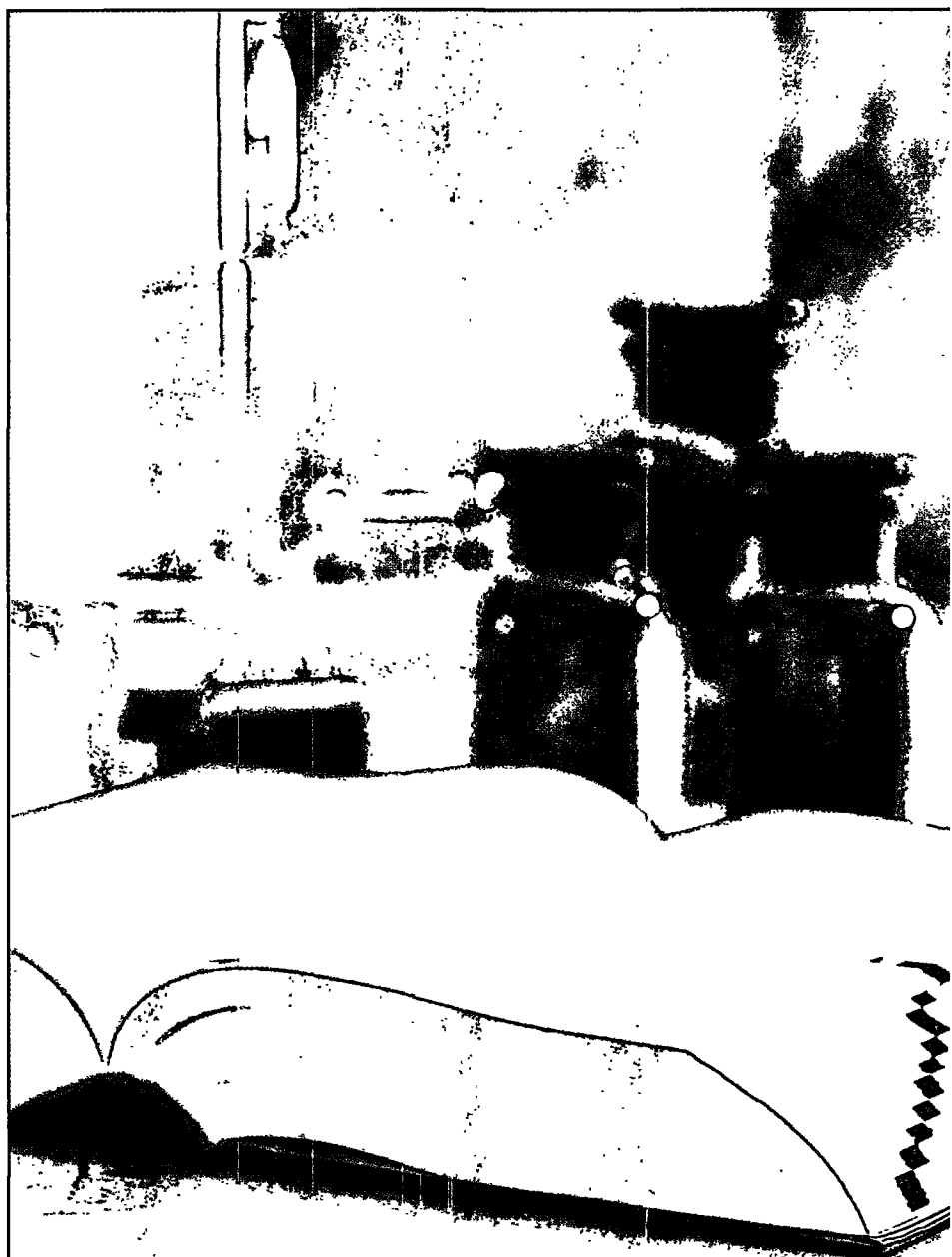
Tools for Integrative  
Practice

## **Low-Dose Allergen Immunotherapy**

Comparison with Other  
Methods

## **Hormones and Autoimmune Diseases**

The Missing Piece in  
Treatment



**Freedom of Homeopathy at Risk  
REGULATIONS UNDER SCRUTINY**



**ISSUE #383  
JUNE 2015  
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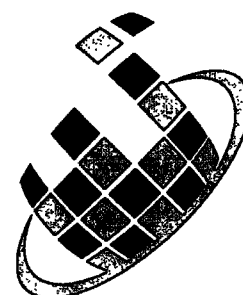
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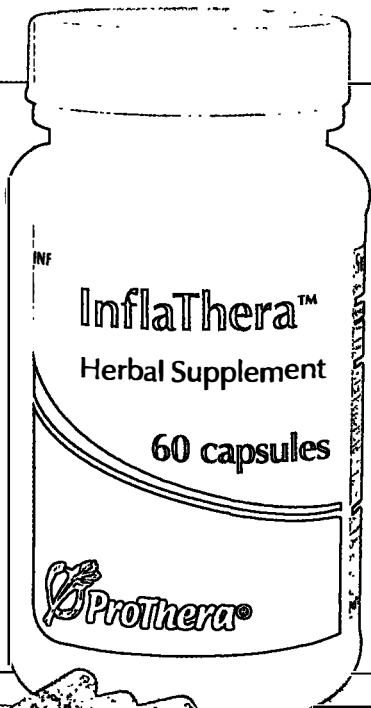
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### Homeopathy Under Review by the FDA

Monday mornings are never my best, but it was a warm spring day, and I was braced to face a pile of charts, nurse queries, and prescription-refill requests. While enjoying some pleasantries with

## *From the Publisher*

the hospital staff and drinking some coffee, I was requested to see Dr. E., the medical chief. This was not the usual routine, and I became a little anxious and sweaty walking through the hallway to his office. "Take a seat," I was told. "I've been informed that you asked the pharmacy to prescribe a homeopathic remedy to one of the patients." I had just returned from a conference and training in Dallas, and I had been impressed with the safety and effectiveness of

homeopathic medicine – I wanted to add homeopathy to my treatment repertory.

"Yes," I told Dr. E.

"Well, the pharmacy has informed me that you prescribed arsenic to the patient," he countered.

"Yes, well, no, yes, I did prescribe a homeopathic remedy, but it was Arsenicum, not arsenic, and homeopathic remedies are very low dosage, miniscule in dosage," I stammered.

**continued on page 6 >**

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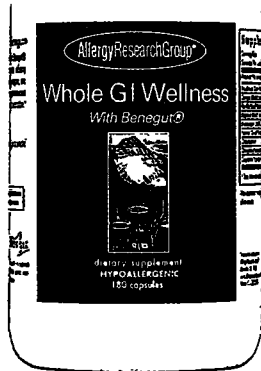
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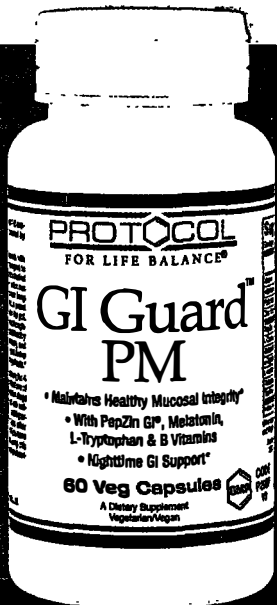
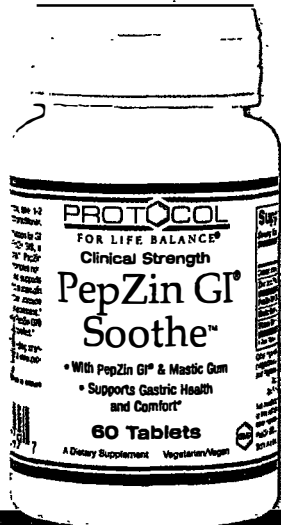
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### Letter from the Publisher ► continued from page 4

"What do you mean? Arsenic is a poison – and you are prescribing a poison to the patient," Dr. E. responded sternly.

"Uh, no, yes, it is derived from arsenic, but it has been diluted over and over, repeatedly, so that in fact there is no arsenic. All that remains is the carrier, a milk sugar pill and the arsenic's energetic imprint, but there is no arsenic, so it is not a poison, there is no poison in the remedy," I tried to explain.

"What do you mean!" Dr. E. yelled, "Arsenic is arsenic, it is a poison, and you prescribed this to the patient!"

By now I was flustered, trying to give a quick synopsis of homeopathy and homeopathic prescribing; but Dr. E. was neither impressed nor agreeable. "I don't want you to prescribe homeopathy to any of our patients," he demanded, and I was excused from his office.

Homeopathy was not the only unconventional medical treatment that I had been administering in the Carville, Louisiana, leprosy hospital in 1977. I had begun to prescribe nutritional supplements, herbs, and chelation. The leprosy patients, most of whom were being treated with one or more pharmaceutical medications, were definitely interested in homeopathic and herbal remedies. Asked to use these products, most were quite eager to add them to their program. None of the patients experienced adverse effects using the remedies. Nevertheless, Dr. E. was not impressed with my explanations and asked me some time later to find a clinic elsewhere for my alternative medicine practice. (The US Public Health Service closed the leprosy hospital in the 1990s; it was used briefly by the state of Louisiana as a prison, and now it serves as a museum.)

I was later to learn that what I had been prescribing is known as "classical" homeopathy. Classical homeopathy is based on a single material, be it plant, animal, mineral, or other substance, serially diluted to create a remedy of low potency or high potency. Homeopathy's most powerful remedies are diluted repeatedly so that the strongest homeopathic is diluted the most, the weaker homeopathic is diluted less. Neither a strong or weak potency actually contains the original material; in fact, for most remedies, the amount of dilution is thought to exceed the limit of Avogadro's number in terms of the presence of chemical molecules in the dilution. For chemists and pharmacologists, if there is no detection of the original chemical molecule in the remedy, the remedy contains nothing and can have no therapeutic activity. However, homeopathy is based on the fact that while the chemical molecule is no longer in the remedy, there is an "energetic imprint" of the material retained that exerts a therapeutic effect. If this explanation does not make sense, it is because homeopathy is predicated on "activating" the body's innate healing, not on drugging the system. For those who insist that healing can only ensue with the administration of a

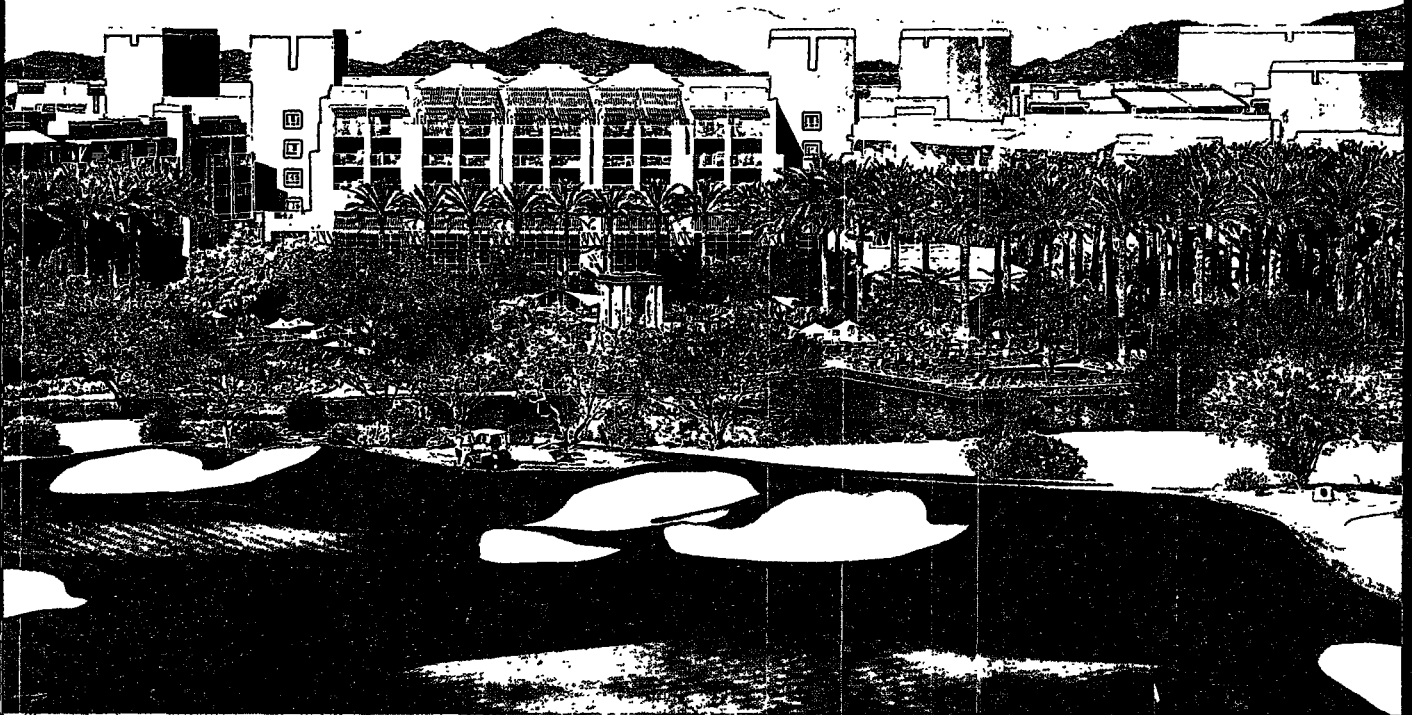
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**Letter from the Publisher**  
➤ continued from page 6

drug, a classical homeopathic remedy makes no sense. Yet strong empirical evidence and studies have established the effectiveness of homeopathy.

If homeopathy had remained "classical" with single, individual remedies, there would probably be little issue with the prescribing and sale of homeopathic remedies. However, over the last several decades, homeopathic companies have hypothesized that if one classical remedy were mixed with a second classical remedy, then the effect of the mixture would provide a different effect and a different and potentially stronger benefit. The problem with this thinking is that classical homeopathy is based on the practitioner's prescribing a single remedy for the patient's current condition. When two or more remedies are prescribed simultaneously, the practitioner is no longer prescribing homeopathy according to classical prescribing, known as "repertorizing." However, when two or more remedies are used, the new homeopathic mixture is thought to have a specific therapeutic effect, such as relieving cough, calming nerves, or easing pain. The homeopathic medicine may now be prescribed based on general symptoms, and the remedy can be sold in the marketplace for that purpose. It is the sale of these homeopathic mixtures that has come to the attention of the FDA; now the FDA wishes to regulate homeopathy.

On the professional level, homeopathic medicine has become complicated by innovations in prescribing practices. Practitioners have acquired devices that measure various energies, or "energetics." A device that has been used for many years is "electroacupuncture according to Voll" (EAV). The EAV device can be used to measure so-called weaknesses or blockages of the chi (qi). Based on measurements provided by the EAV device, a patient may be "diagnosed" with weakness in different body systems, such as the liver, kidney, or lungs. EAV practitioners use the energetic measurements that the device provides to "energize" or "potentize" a water or alcohol or glycerol base with the homeopathic energetic "imprint" needed to overcome the weaknesses or blockages. In other words, the EAV device is being used to create a patient-specific homeopathic remedy.

Homeopathic remedies known as nosodes are used to treat infection and/or inflammation. Nosodes are preparations potentized from pathogens such as viruses, bacteria, and fungi. Once again, without knowledge of homeopathic principles, one can assume that a nosode prescription contains infectious organisms. However, nosode prescriptions are based on homeopathic dilution; there is no pathogen in a nosode prescription. But, it is difficult to explain that a nosode is not infectious nor contains any infectious agents. One can only imagine what the FDA will say about nosode remedies.

**continued on page 10 ➤**

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1) Enhanced glutathione levels in blood and buccal cells by oral glutathione supplementation. J.P. Richie. Published in the European Journal of Nutrition, May 2014

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## Letter from the Publisher

► continued from page 8

In April, the FDA held hearings for two days about homeopathic medicine. Let us hope that the FDA commission is not filled with doctors like Dr. E. who do not understand or condone homeopathy.

### The Hypertension Game

For the healthy population, two medical conditions are fraught with a possible lifetime of medication: hypercholesterolemia and hypertension. Neither condition poses any symptomatic concern for the patient; hence the patient takes it upon good faith that the prescription is necessary as well as safe and effective. For an elevated cholesterol, the pharmaceutical du jour has become the "statin." For high blood pressure, there is no single drug that is paramount; an antihypertensive recipe may call for a diuretic, ACE inhibitor, calcium channel blocker, beta blocker, vasodilator, or other agent. In fact, the "need" for a "statin" as well as one or more antihypertensive medications has become the bread and butter of cardiology practices. Medical protocol requires that there be adequate treatment of elevated cholesterol; the recent necessity that the "LDL" score be 70 mg/dl or less has compelled patients to swallow ever-higher doses of statins. However,

with sufficient dosing of statins, this end point is usually achieved easily. Hypertension treatment is a more complex matter, given the broad number of drugs available for treatment and the need for polypharmacy. What makes blood pressure treatment challenging is that despite the use of one or more drugs, many patients fail to lower their blood pressure adequately, defined as a reading below 140/90 mmHg. For the cardiologist, this turns hypertension into a weird science experiment with ever-increasing doses of medication, as well as an increasing combination of meds. Most patients can tolerate high-dose polypharmacy, but part of the cardiologist's treatment program is to "manage" the potpourri of side effects. The big problem is when an elderly patient is being treated for not only hypercholesterolemia and hypertension but also depression, osteoporosis, diabetes, urinary incontinence, osteoarthritis, and atrial fibrillation.

In the office I see another aspect of the hypertension game – the blood pressure measurement. I still use the out-of-fashion blood pressure cuff with sphygmomanometer manually inflating the cuff and auscultating the sounds to measure blood pressure. Many physicians' offices are using electronically inflated cuffs that record blood pressure

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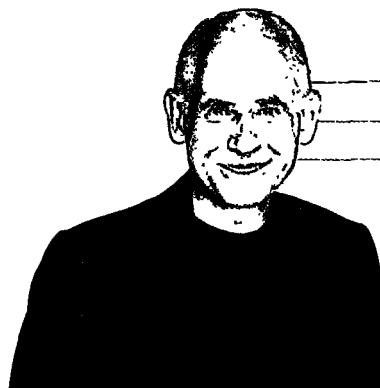


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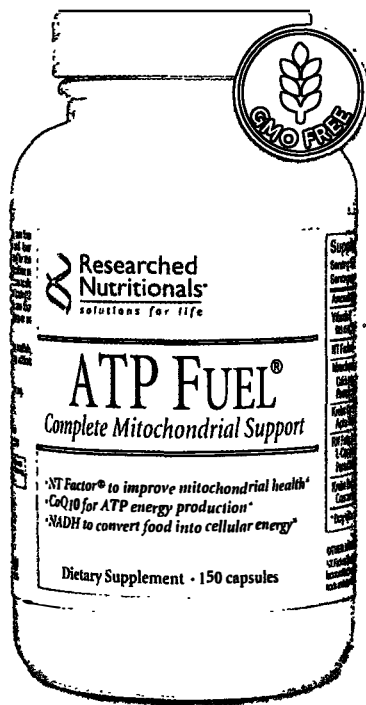
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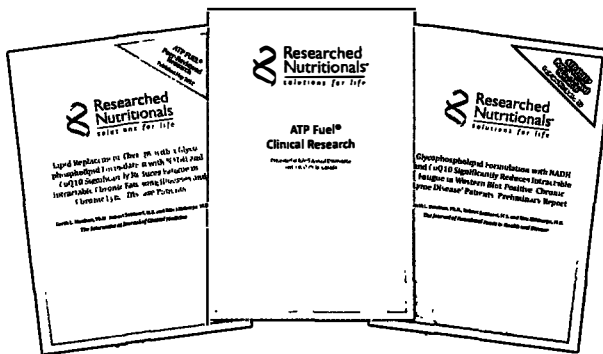


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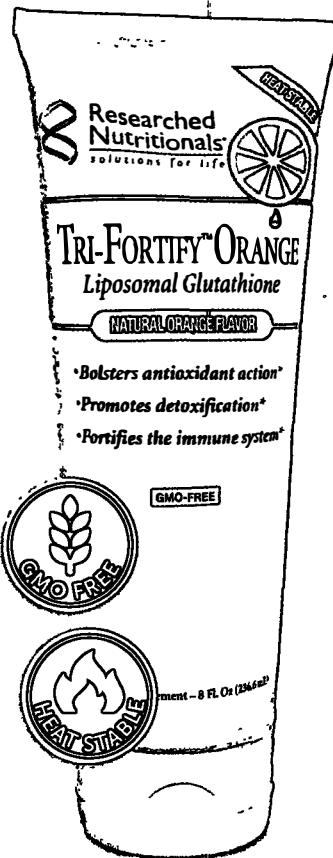
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**Review of Hormone Aberrations in Rheumatoid Arthritis and Systemic Lupus Erythematosus: Testing and Treatment Suggestions** | 45

by Alena Guggenheim, ND

Rheumatoid arthritis and systemic lupus erythematosus are on the rise, with rates 2 to 3 times higher for women than men. With conventional medicine offering only limited help for these conditions, an alternative treatment focusing on adrenal, sex, and adipose hormones may help obtain remission without the use of pharmaceuticals.

**Mitochondria: Overlooking These Small Organelles Can Have Huge Clinical Consequences in Treating Virtually Every Disease** | 50

by Chris D. Meletis, ND, and Kimberly Wilkes

Research on mitochondria has extended far beyond what was originally known about these tiny organelles, including the role that these “body batteries” play in almost all diseases. When mitochondria suffer, the whole body suffers. So what is causing mitochondrial dysfunction?

**DNA Methylation and the Global Genome** | by Kenneth Smith | 57

Epigenetics are chemical changes that affect DNA expression without altering DNA sequence itself. DNA methylation is the best understood part of the epigenome, and changes in methylation are associated with cancer, autism, Alzheimer’s, and numerous other health conditions. With an understanding of epigenetics in mind, diagnosis and treatment may lead medicine toward treating the whole patient.

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by Diego Saporta, MD, FAOAO

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by Dr. John Hahn

Allergies, possibly caused by underexposure to pathogens early in life, stimulate a variety of symptoms that interfere with daily life. Besides avoiding known allergens, a combination of conventional and alternative therapies provides the greatest relief.

**Standing Up for Health** | by Jacob Schor, ND, FABNO | 70

Forget everything you thought you know about exercise and health. As it may turn out, it isn’t working out that is good for you; it is sitting down that is bad for you – and decreases lifespan. But is this a causal relationship, or a symptom of individual predisposition for activity?

**Field Control Therapy: Apparent Documented Reversal of Crohn’s Disease and Prompt Cure of Longstanding Irritable Bowel Syndrome**

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## Letter from the Publisher

► continued from page 10

readings, and a growing number of patients are measuring their blood pressure at home with similar devices. Electronic devices have been upgraded, and rather than the cuff being wrapped around the upper arm, newer devices can be put on the wrist or even index finger. The result is that doctor and patient are recording blood pressures, but it is infrequent that the readings in the office and at home are the same. Invariably the reading at the cardiologist's office is elevated; however, let's not forget the ophthalmologist or dentist who also frequently records higher readings. At the same time, the patient is measuring at home; and lo and behold, the reading is normal or at least lower. Of course, there is the well-documented "white coat syndrome": the outpouring of epinephrine by the adrenal glands during a state of fear acts as a vasoconstrictor and increases the blood pressure. Unfortunately, if the measurement is elevated, another drug may be required to "control" the blood pressure. It may be that a 24-hour monitoring of blood pressure needs to be done to get a better assessment of the average pressure before medication is increased. However, there is another side to the white coat syndrome that is equally concerning: when the patient attempts to decrease the blood pressure measurement by lying supine and meditating quietly. Of course, a relaxed, quiet state will lower the pressure, but is that lower reading an accurate depiction of the blood pressure state throughout the hectic day? Wouldn't it make more sense to take a reading after one has come home from doing errands or has been busy with chores?

My final take on the game of hypertension is my curmudgeonly stance on digital devices. In my unscientific study at the office, invariably, a measurement by me manually auscultating the blood pressure, and a subsequent measurement using the patient's device, do not match. And it is not a consistent pattern. My measurement is frequently higher; however, often it is lower – maybe one-third of the time, they do match. I admit that it is possible that I am not measuring the blood pressure properly. However, there are times when the readings diverge so much, higher or lower, that I insist that the patient invest in a new device. There is nothing to guarantee the accuracy of these devices, and when patients claim that they always get lower (or higher) blood pressure readings at home than the office, I have them do a recording in the office and compare it with my reading. The wrist and finger digital machines I find particularly suspect.

### Rheumatoid Arthritis

A trip to the larger art museum in most cities generally includes a work by Pierre August Renoir, the great 19th-century French impressionist. Renoir was a prolific painter,

known to have completed more than 6000 paintings, but less known is that not a few of these paintings were done while he was crippled with rheumatoid arthritis. Renoir's arthritis progressively worsened, as there were no effective medications at the beginning of the 20th century. In the years before his death in 1919, his hands were completely mangled and gnarled, and he was unable to move his arms except with poorly controlled thrusts. Confined to a wheelchair, he still painted until the control of his arm movements completely failed. Not willing to give up art, which soothed his soul and the pain of his disease, he took up sculpture, directing a worker to place the clay according to his instructions.

Nowadays, it is rare for a patient with rheumatoid arthritis to deteriorate to such a degree. After the development of corticosteroids, chemotherapy agents such as methotrexate became mainstays in RA treatment. The recent development of biologic modifying agents known as disease-modifying antirheumatic drugs (DMARD) has revolutionized rheumatology and the treatment of arthritis. The terrible progression of arthritis has been essentially eliminated; unfortunately, these agents are extremely expensive, and insurance companies frequently balk at ongoing payment. Additionally, DMARDs pose rare but serious risk for major unrelated conditions, including malignancy and death. How can the naturopathic or integrative physician contribute to the care of the rheumatoid arthritis patient?

In this issue, Alena Guggenheim, ND, who has written previously in the *Townsend Letter* about the management of arthritis, discusses hormone alterations in rheumatoid arthritis and systemic lupus erythematosus. Guggenheim reviews the interrelationship of adrenal and gonadal hormones with inflammatory cytokines that increase inflammation in both RA and SLE. She notes that the measurement of a fat-related cytokine, adipokine, is the "best marker to predict the severity of joint destruction"; an elevated adipokine before treatment initiation foretells greater severity of disease. Guggenheim's thesis is that low adrenal and gonadal hormones will exacerbate the RA and SLE process. Her other major concern is that estrogen activity must be closely monitored and addressed. Consumption of xenoestrogens, as found in conventionally grown foods and water from plastic containers, must be curtailed. The measurement of estrogen metabolites allows the practitioner to monitor if untoward estrogen activity is being well controlled.

Jonathan Collin, MD

# Emerson Ecologics Announces First Annual Conference for Integrative Health-Care Practitioners

Emerson Ecologics is excited to announce its first annual conference, "IGNITE: The Business of Better Medicine." The conference will provide integrative health-care practitioners with the necessary business knowledge to develop a thriving and fulfilling practice.

Scheduled for November 13–15, 2015, at the Omni La Costa Resort and Spa in San Diego, California, the conference will be a one-of-a-kind, "get it done" event, where attendees can expect to accomplish key projects and leave with an action plan in hand. Highlights of the event include keynote presentations from Jeffrey S. Bland, PhD, FACN, CNS, and Tieraona Low Dog, MD, as well as hands-on workshops led by industry experts.

The conference workshops are designed to address key business challenges related to clinic operations, sales and marketing, and patient compliance, with a focus on providing valuable and actionable takeaways. In addition, representatives from Emerson's most trusted professional brands will be on site, guaranteeing that attendees walk away with a broad community of supportive peers, partners, and experts.

"Most practitioners, including myself, have struggled to balance their passion for patient care with the stress of building a business," said Dr. Jaclyn Chasse, medical director for Emerson Ecologics. "I am so excited to be working with Emerson to deliver the business knowledge not taught

in medical school, but equally important to creating a successful practice."

The conference will build on the success of Emerson's IGNITE series of practice growth webinars and events. Designed to deliver the personalized business advice that practitioners have come to expect from IGNITE, the event will feature an expanded range of topics and experts, including:

- Mastering Sales & Marketing: Miriam Zacharias, MS, LPSN
- Enhancing Patient Compliance: Dan Kalish, DC
- Leveraging Technology: Peter Osborne, DC, CCN
- Optimizing Clinic Operations: Leandra Fishman, Practice Management Consultant

"Often, practitioners don't realize how closely their clinical success is tied to the success of their business," said Dr. Dan Kalish, founder of the Kalish Institute and Method, a Web-based functional medicine training and mentorship program founded on over 20 years of positive clinical results. "The heart of building a client base and thriving referral network revolves around the relationships you develop with your patients, as well as the communication skills required to provide them with an optimal treatment plan and health outcome."

"At Emerson, we are passionate about advancing integrative medicine, and we know that the clinical and business success of our practitioners is vital to accomplish this," added Chasse. "We are thrilled to launch this transformative conference to help our customers succeed and reach more patients."

For more information or to register for the conference, visit [eelGNITE.com](http://eelGNITE.com)

## About Emerson Ecologics

For more than 30 years, Emerson Ecologics LLC has been providing practitioners a convenient way to select and purchase from over 275 brands of professional-quality nutritional supplements, vitamins, prescription medications, and natural health products. Customers include naturopathic, chiropractic, and medical doctors, licensed acupuncturists, nutritionists, and integrative practitioners, as well as their patients. Emerson Ecologics is also widely recognized for its innovative Emerson Quality Program (EQP) and is committed to helping integrative practitioners succeed as healers as well as business owners. Headquartered in Manchester, NH, with distribution centers in Virginia and California, Emerson Ecologics is GMP registered by NSF International and licensed to distribute pharmaceutical products. For more information, visit [emersonecologics.com](http://emersonecologics.com).

## TAP Integrative Launches an Online Educational Community for Integrative Practitioners

TAP Integrative announces the launch of an online educational community resource dedicated to furthering the evidence-informed and experience-based knowledge between integrative practitioners. TAPintegrative.org is a membership site designed for "on-demand" access to clinically reviewed and science-based clinical practice topics and research, leading clinical experts, and a community of integrative health-care professionals. A nonprofit organization founded and sponsored by Integrative Therapeutics, TAP's mission is truly unique.

"TAP stands for the teaching, advocacy and practice of integrative medicine," said Dr. Lise Alschuler, executive director of TAP. "Our goal is to support the community of practitioners that are committed to the practice of integrative medicine. Since education and practical knowledge are both necessary for continued growth in our practices, it's exciting to see TAP Integrative become a resource that can provide both. Our hope is that TAP soon becomes the go-to trusted resource for deepening and advancing clinical expertise."

TAP's content is presented in multiple formats including video discussions, audio abstracts, blogs, case discussions, graphic overviews, research reviews, and patient education tools. The website is designed so that the practitioner can quickly take away key insights from a clinical topic or can delve deeply into the topic. Collaboration between members also takes place by exchanging best practices in the member forum, or by directly asking the subject experts. TAP offers members a number of unique benefits including access to a drug–nutrient interaction database and, in collaboration with institutional member Southwest College of Naturopathic Medicine, a digital article retrieval service.

"A TAP member can learn from either experts or experienced peers in various fields of practice, with the flexibility to access learning on their own schedule," continues Alschuler. "Membership is available to health-care professionals and students. TAP encourages sharing experiences and will become a tool to improve your daily practice. The ultimate goal and outcome of TAP is truly to improve patient outcomes."

Alschuler shares further insight into the development of TAP Integrative at <https://www.youtube.com/watch?v=YaBrVH4U-xM>.

To learn more about the membership portal, visit [TAPIntegrative.org](http://TAPIntegrative.org).

# National College of Natural Medicine to Offer Undergrad Degrees

The National College of Natural Medicine (NCNM) will begin offering undergraduate programs – a bachelor of science in integrative health sciences and a bachelor of science in nutrition. NCNM received approval to begin both programs in fall 2016 from the Northwest Commission on Colleges and Universities, the regional accreditation agency for postsecondary educational institutions recognized by the US Department of Education. The new undergraduate degrees, offered by the new School of Undergraduate & Part-Time Studies, will join the medical school's rapidly expanding roster of postgraduate programs, which include the Schools of Naturopathic Medicine, Classical Chinese Medicine, and Research & Graduate Studies.

Both undergrad offerings are two-year, pre-med and pre-health degree completion programs, which focus on integrative medicine or nutrition, respectively.

The increasing interest in natural and integrative medicine, as well as the critical need to strengthen the health-care workforce in the US, has heightened the importance of adequately preparing students for professions in the health and wellness fields. As integrative medicine expands into hospitals and clinics throughout the country, it becomes ever more necessary for NCNM and other educational institutions to provide accessible pathways for future students in graduate and doctoral medical programs. These new undergraduate degrees are designed to help them develop the critical thinking and associated skills required for future graduate medical training.

The programs are designed for students who have previously completed two years of college course work, such as community college students who want to complete their undergrad degree, transfer students from a traditional four-year college

or university, or students who have previously withdrawn from a bachelor's program and want to continue.

The new educational offerings will appeal to students interested in careers in integrative medicine, such as naturopathic medicine, Chinese medicine and acupuncture, chiropractic medicine, herbal medicine, nutrition, holistic nursing, and holistic dentistry. These unique undergraduate programs have been developed to meet the demand for access to health-care or research careers.

In speaking about the programmatic changes at the nearly 60-year-old institution, NCNM President David J. Schleich, PhD, said, "It has long been on our agenda to develop preprofessional programs to better prepare students for the academic demands of medical school and graduate programs."

## Degree Program Overview

Both undergrad programs blend traditional healing knowledge with contemporary science and evidence-based medicine. To accomplish these goals, each program consists of three threads that are integrated throughout the curriculum: a core thread (integrative health sciences or nutrition), a hard sciences thread (such as genetics, immunology, or physics), and a social sciences thread (such as ethics, cultural competency, or self-reflection).

The integrative health sciences degree features a variety of complementary and integrative medical topics such as herbal medicine, whole-food nutrition, and mind-body medicine. The nutrition degree focuses on topics such as whole-foods nutrition and the connection between diet and disease. Both programs feature a capstone project in which students are required to draw on all aspects of the

curriculum to develop a final project, write a research paper, or complete an internship.

## NCNM Strategic Goals

Schleich notes that NCNM's growth has been rapid as it actively rolls out new programs. "In just a few short years NCNM has grown from a two-program college into the exemplary medical college it is today, with seven diverse doctoral and master's program offerings within our three distinct schools of medical education. And now we introduce our newest academic enterprise, the School of Undergraduate & Part-Time Studies," he said. "Just in the last few years alone, we've added master's degrees in integrative medicine research, nutrition, global health, and most recently, a new program in integrative mental health. Our enrollment has increased 33% since 2007. With the addition of undergraduate programming, NCNM will continue to attract the best and brightest to build on the legacy first established six decades ago by naturopathic doctors who ensured the future of natural medicine by founding NCNM."

Visit <http://www.ncnm.edu/academic-programs/undergraduate-programs.php> to learn more about NCNM's undergraduate programs.

Founded in Portland, Oregon, in 1956, NCNM is the oldest accredited naturopathic medical school in North America and an educational leader in classical Chinese medicine and CAM research. NCNM offers both postgraduate and undergraduate degree programs: these include four-year graduate medical degrees in naturopathic and classical Chinese medicine; four master of science degrees in integrative medicine research, nutrition, global health, and integrative mental health; and two bachelor of science degrees in nutrition and integrative health sciences. NCNM also provides community education through the NCNM Institutes: Women in Balance, Traditional Roots, and Food as Medicine. NCNM's teaching clinics, including NCNM Clinic, the Beaverton Clinic, and the college's many community clinics, provide low-cost medical care throughout the Portland metropolitan area. NCNM practitioners, residents, and student interns treat approximately 40,000 patient visits per year. Visit [www.ncnm.edu](http://www.ncnm.edu) for more information.



## In Memoriam: Dr. Leo Joseph Bolles 1921–2015

Leo Joseph Bolles, MD, born March 10, 1921, died peacefully in his home on the night of March 15, 2015, surrounded by his friends and family.

Born in Minneapolis, Minnesota, the son of Lee and Gertrude Bolles and brother of Pete and Katherine Bolles, Leo grew up in Montesano, Washington. After a short time in seminary, Leo began his college studies at Grays Harbor College and later transferred to Seattle University. During World War II, Leo enlisted in the Navy, serving on the USS Kennison and rising to the rank of lieutenant junior grade. Upon honorable discharge in 1946, Leo completed his bachelor of science degree at Seattle University, and then continued his education in pursuit of a medical degree at the University of Marquette in Milwaukee, Wisconsin. There he met the love of his life, Margaret Alexa Gengler. With a medical degree and marriage certificate in hand, together they returned to Washington State in 1950. They settled down on Clyde Hill in Bellevue, Washington, and began their life together.

After completing his residency and internship at Virginia Mason Hospital in Seattle in 1953, Dr. Bolles built a successful family practice one patient at a time, with the humble

care and deftness of a true country-style doctor. Leo was an independent and free-thinking soul who faced many challenges practicing orthodox medicine in the battle against such stubborn diseases as cancer, multiple sclerosis, and heart disease. As a result of his tenacious desire to help his patients, he was inexorably led to seek out, develop, and pioneer techniques in the art of medicine that would later come to be known as holistic or preventative medicine.

Dr. Bolles was a voracious reader and lifetime learner; he traveled nationally and internationally seeking out physicians and researchers with unique knowledge in the field of holistic medicine. Over the years, Leo incorporated numerous cutting-edge alternative therapies in his patients' treatments with great success. He was a champion of individual liberty, medical freedom, and the sanctity of the doctor-patient relationship, and fought for these rights at every turn.

Dr. Bolles was a founding member and president of the Northwest Academy of Preventative Medicine, a trustee of the John Bastyr College of Medicine, a member of the American Academy of Medical Preventics, and a member of the Orthomolecular Society. His contribution to the practical advancement of alternative medicine was profound and pioneering, and his impact on the health and wellness of his patients was indelible and widespread.

Throughout his life, Leo Bolles had a great love of the outdoors and in particular a passion for farming. As a teenager, he grew 5 acres of cabbage seed for the Washington

State Department of Agriculture. With the proceeds from this endeavor, he funded his college education. Leo never passed up an opportunity to be outside and put his hands in the soil, split some firewood, or tend a beehive. His appreciation for the natural world led to many memorable excursions with his children: panning for gold in the foothills, climbing Mount Si, hiking Denny Creek, clamming and fishing in Birch Bay, and trout fishing in Eastern Washington. He also enjoyed golfing as another opportunity to enjoy the beautiful Pacific Northwest.

Leo Joseph Bolles was a quiet man, deeply devout; he drew strength from his Catholic faith all through his life. He loved his family deeply and will be sorely missed by all who knew him. Leo was preceded in death by his oldest son, Thomas Lee. He is survived by his wife of almost 67 years, Margaret; children Terry Margaret, Kelly Christopher, Edward Carey, and David Joseph; and their families, including five grandchildren and one great-grandchild.

God has a special place in his heart for you, Leo.

Donations in Leo's memory may be made to either of the following:

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Roman Catholic Chapel  
11824 10th Avenue Southwest  
Seattle, Washington 98146-2776

The Union Gospel Mission  
318 2nd Avenue Extension South  
Seattle, Washington 98104  
206-622-5177



## Shorts

briefed by Jule Klotter  
jule@townsendletter.com

### Gallstones

The gallbladder has two functions: to store liver-produced bile and release it into the small intestine. Without bile, the body cannot break down dietary fats and absorb fat-soluble vitamins. Signs of insufficient bile include indigestion, belching, bloating, cravings for fatty or fried foods, and pain or tension below the ribs on the right side. Gallstones (usually composed of bile components, calcium salts, and cholesterol) can obstruct ducts, limiting the amount of bile released. In some cases, gallstones produce sudden, severe pain after eating. Gallbladder removal (cholecystectomy) is the usual conventional treatment for symptomatic gallstones, but less invasive treatments are available.

Michael Gerber, MD, HMD, lists several treatments for addressing gallbladder stress and insufficient bile, including bile salts, herbs, neural therapy, homeopathy, acupuncture, and liver/gallbladder flush. Mild symptoms may respond to a liver/gallbladder flush, according to patient reports. A liver/gallbladder flush is a folk remedy that involves ingesting olive oil and a citrus juice. Protocols vary. Gerber uses a combination of olive oil, pink grapefruit juice, and Epsom salts. He does not recommend a flush for people in severe gallbladder pain.

For severe pain, Gerber has found castor oil packs, applied over the painful area for 30 to 60 minutes, and massage of the thoracic paraspinal muscles and Bladder 18-19 acupuncture points (at the bottom edge of the scapulae), particularly helpful. He also uses intradermal neural therapy injections (1% procaine) on these and other gallbladder and liver points.

Alan R. Gaby, MD, offers several suggestions for preventing gallstones in a 2009 article for *Alternative Medicine Review*. The first is to identify food allergies and remove offending/reactive foods from the diet. Food allergy/intolerance may contribute to delayed gallbladder emptying, which is known to contribute to

gallstone formation, according to a 1985 study. Gaby cites a study in which gallbladder symptoms were eliminated in "100 percent of 69 patients with gallstones or postcholecystectomy syndrome" after 1 week on an elimination diet. Other dietary changes, such as increasing polyunsaturated or monounsaturated fat, fiber, and vegetable and fruit intake and decreasing refined sugars, have also been linked to fewer gallbladder problems.

Gaby also discusses supplements, such as vitamin C, and a product called Rowachol. Both help prevent gallstone formation. Vitamin C is used by the enzyme that converts cholesterol to bile salts. Rowachol contains six plant monoterpenes that stimulate bile production and inhibit cholesterol crystal formation in bile. It has been marketed for over 50 years and has no reported serious side effects.

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### *Helicobacter Pylori* and Crohn's Disease

Because the bacterium *Helicobacter pylori* can cause peptic ulcers, some researchers hypothesized that it may also contribute to Crohn's and inflammatory bowel disease. In support of this hypothesis, animal models indicate that *H. pylori* can produce bowel inflammation; and a 2006 study found more *H. pylori* in the intestinal mucosa of patients with ulcerative colitis than in the mucosa of healthy controls. However, recent case reports and studies indicate that *H. pylori* may actually protect against Crohn's disease. Antonio Tursi, MD, reported on two patients who developed Crohn's disease 3 to 4 months after receiving triple antibiotic therapy (esomeprazole, amoxicillin, and clarithromycin) to eradicate *H. pylori*. A 2010 meta-analysis, involving 23 studies and 5903 participants, found that *H. pylori* infection was less - not more - prevalent in patients with inflammatory bowel disease (27.1%)



## Shorts

compared with controls (40.9%). Most recently, a 2013 retrospective case control study, led by Zun Xiang, reported an inverse correlation between the presence and severity of Crohn's disease and presence of *H. pylori*.

The 2013 study, involving 477 Chinese patients with GI symptoms, used endoscopy and biopsy to diagnose Crohn's disease (CD) in 229 of the patients. The remaining 248 with normal endoscopy and biopsy results acted as controls. All participants were checked for *H. pylori* by using biopsy sample culture or the C-urea breath test (C-UBT), both of which have higher sensitivity and specificity than the serum *H. pylori*-IgG test, according to the authors. Only 27.1% of the CD patients tested positive for *H. pylori* infection compared with 47.9% in the control group. Zun Xiang and colleagues also divided the CD group into three subgroups: remission (n = 32), moderate CD (n = 88), severe CD (n = 109). *H. pylori* infection rate was highest in patients with the least severe disease; 34.3% of the remission subgroup were *H. pylori* positive compared with 30.7% of the moderate CD group and 22% of the severe CD group.

Zun Xiang et al. point out that *H. pylori* triggers Th1-mediated cell defense, which could account (at least partially) for the protective effect. Although other types of *Helicobacter* may cause inflammatory bowel disease, *H. pylori* appears to be protective. "In conclusion, our results provide evidence for the involvement of *H. pylori* in CD prevalence," the authors write. "These findings should serve as an important reminder to clinicians when considering *H. pylori* eradication in CD patients."

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### NEW!

Ralph W. Moss's UPDATED website!  
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## Helminths and Inflammation

Helminths (parasitic worms that have evolved to live in the intestines or other locations of their animal hosts) can cause disease; but, like commensal bacteria, they may also provide health benefits. In the 1990s, Joel V. Weinstock, MD, and David E. Elliot, MD, first suggested that helminths may be one of the environmental factors that protect against inflammatory bowel disease (IBD) and other immune-mediated illnesses. They noted that people living in industrialized societies, which have less exposure to intestinal helminths, have a higher incidence of IBD. In a 2009 article, Weinstock and Elliot cite epidemiological evidence that helminths may protect against allergies and other immunological diseases. For example, case-control studies in Ethiopia and Vietnam found a lower incidence of asthma in people infected with hookworm. Also, Gabonese children who received antihelminth therapy to eradicate flukes that cause urinary disease (*Schistosoma hematobium*) showed increased risk of house dust mite allergy compared with a control group.

Over eons, helminths have developed methods for subduing their hosts' inflammatory and immune responses in order to promote their own survival and colonization. Intestinal worms call forth regulatory T cells that make IL-10 and TGF- $\beta$ , cytokines that limit immune reactivity. In addition, parasites release compounds that modify lymphocyte, mast cell, NK cell, and macrophage functions, thereby reducing inflammation. *Trichuris suis* (pig whipworm), for example, suppresses TLR4-induced inflammatory responses in human macrophages, according to M. K. Ottow and colleagues.

Weinstock and Elliot hypothesize that helminths' ability to calm the body's immune response may be useful in treating inflammatory bowel disease and other immune-mediated illnesses. As an example, parasite-infected patients with multiple sclerosis in a 2007 study had fewer disease exacerbations and fewer new brain lesions compared with uninfected patients. Although some parasites can incite disease, particularly in immune-compromised people, many worms "hold little pathogenic potential," say Weinstock and Elliot. Several pharmaceutical companies are investigating the use of "pharmaceutical-grade" helminths and testing helminth-derived compounds as possible treatments for inflammatory conditions.

- Correale J, Farez M. Association between parasite infection and immune responses in multiple sclerosis. *Ann Neurol*. 2007;61:97-108. Available at [http://www.coronadobiosciences.com/pdfs/Correale%20and%20FarezAnn\\_MS.American%20Neurological%20Association.2007%2061%2097-108.pdf](http://www.coronadobiosciences.com/pdfs/Correale%20and%20FarezAnn_MS.American%20Neurological%20Association.2007%2061%2097-108.pdf). Accessed April 15, 2015.
- Ottow MK, Klaver EJ, van der Pouw Kraan TCTM, et al. The helminth *Trichuris suis* suppresses TLR4-induced inflammatory responses in human macrophages [abstract]. *Genes Immun*. October/November 2014;15:477-486. Available at <http://www.nature.com/gene/journal/v15/n7/full/gene201438a.html>. Accessed March 25, 2015.
- Winstock JV, Elliott DE. Helminths and the IBD hygiene hypothesis. *Inflamm Bowel Dis*. January 2009;15(1):128-133. Available at [http://opensourcehelminththerapy.org/mediawiki/2/images/0/05/Helminths\\_and\\_the\\_IBD\\_Hygiene\\_Hypothesis.pdf](http://opensourcehelminththerapy.org/mediawiki/2/images/0/05/Helminths_and_the_IBD_Hygiene_Hypothesis.pdf). Accessed April 15, 2015.

## Histamine Intolerance

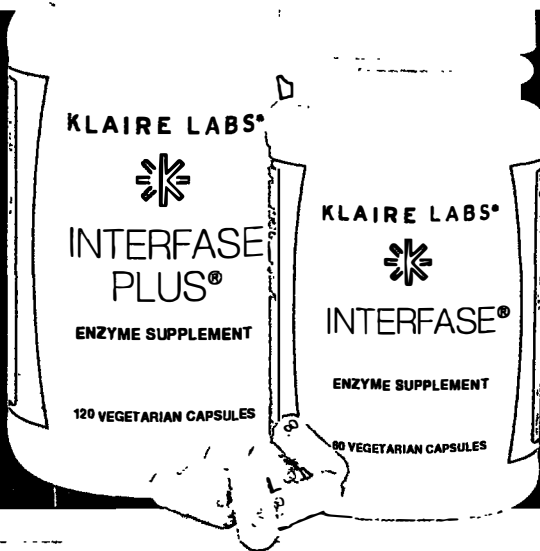
"Histamine intolerance is based on an imbalance between the build up and breakdown of histamine," say Laura Maintz and German colleagues in a 2006 review article. Histamine is produced in mast cells, basophils,

*continued on page 27* ➤

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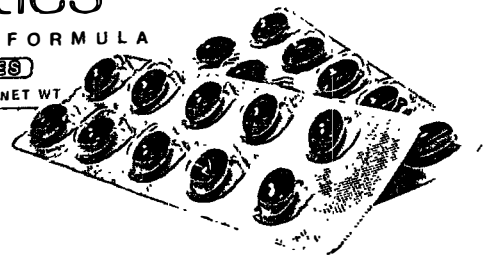
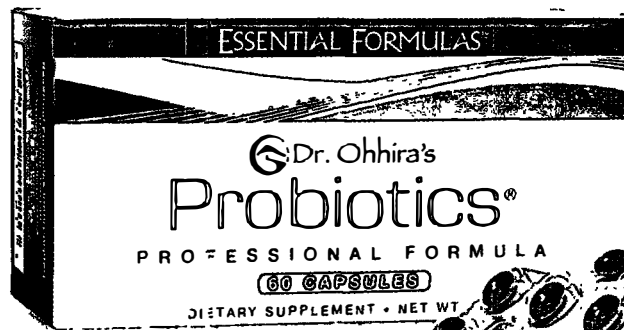
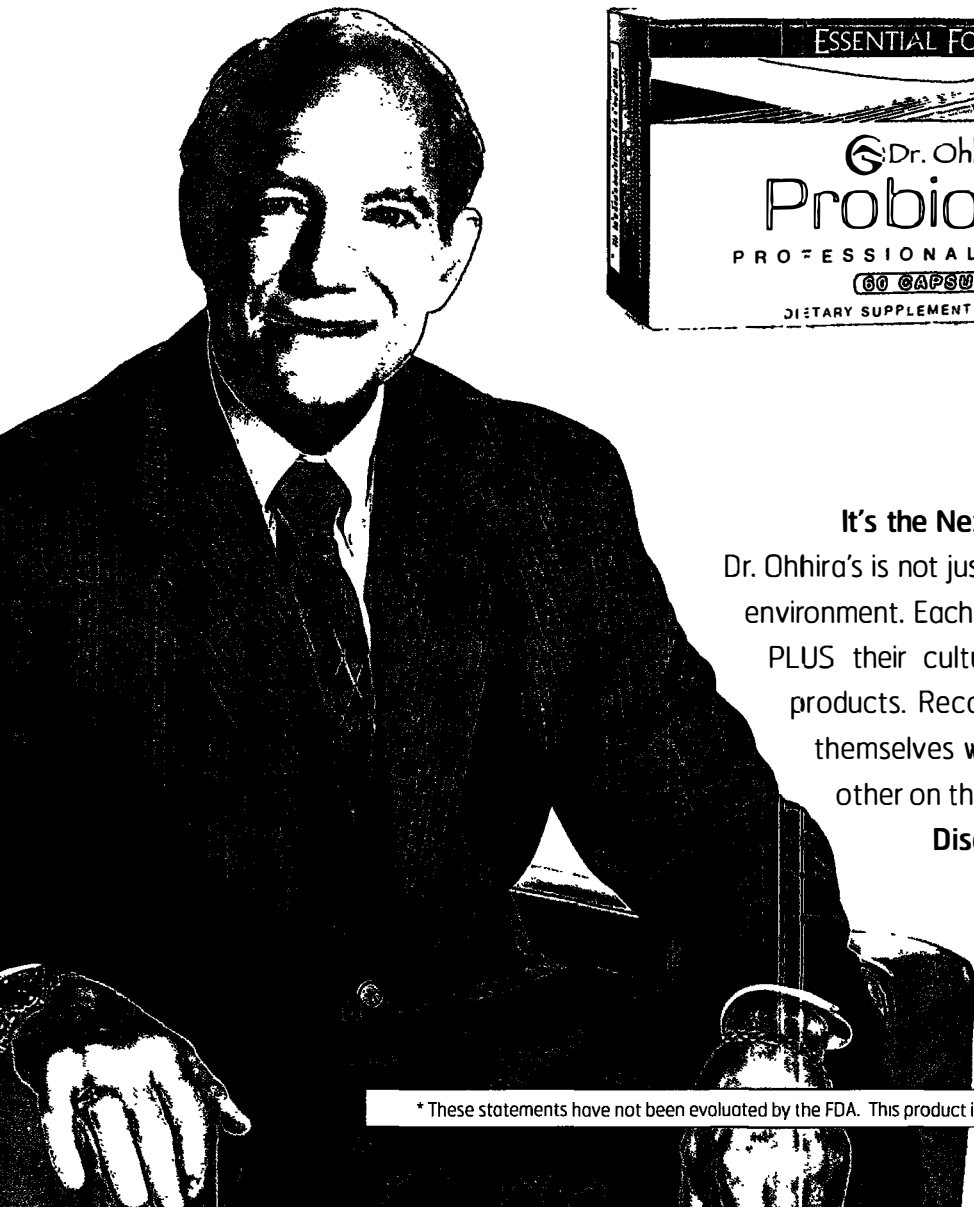
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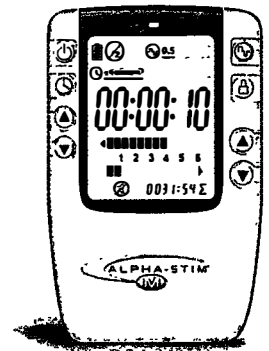




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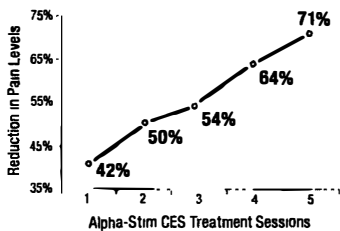
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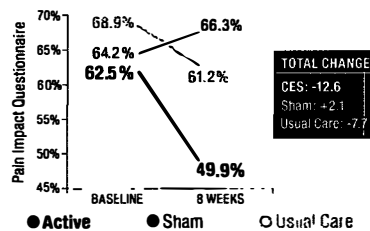
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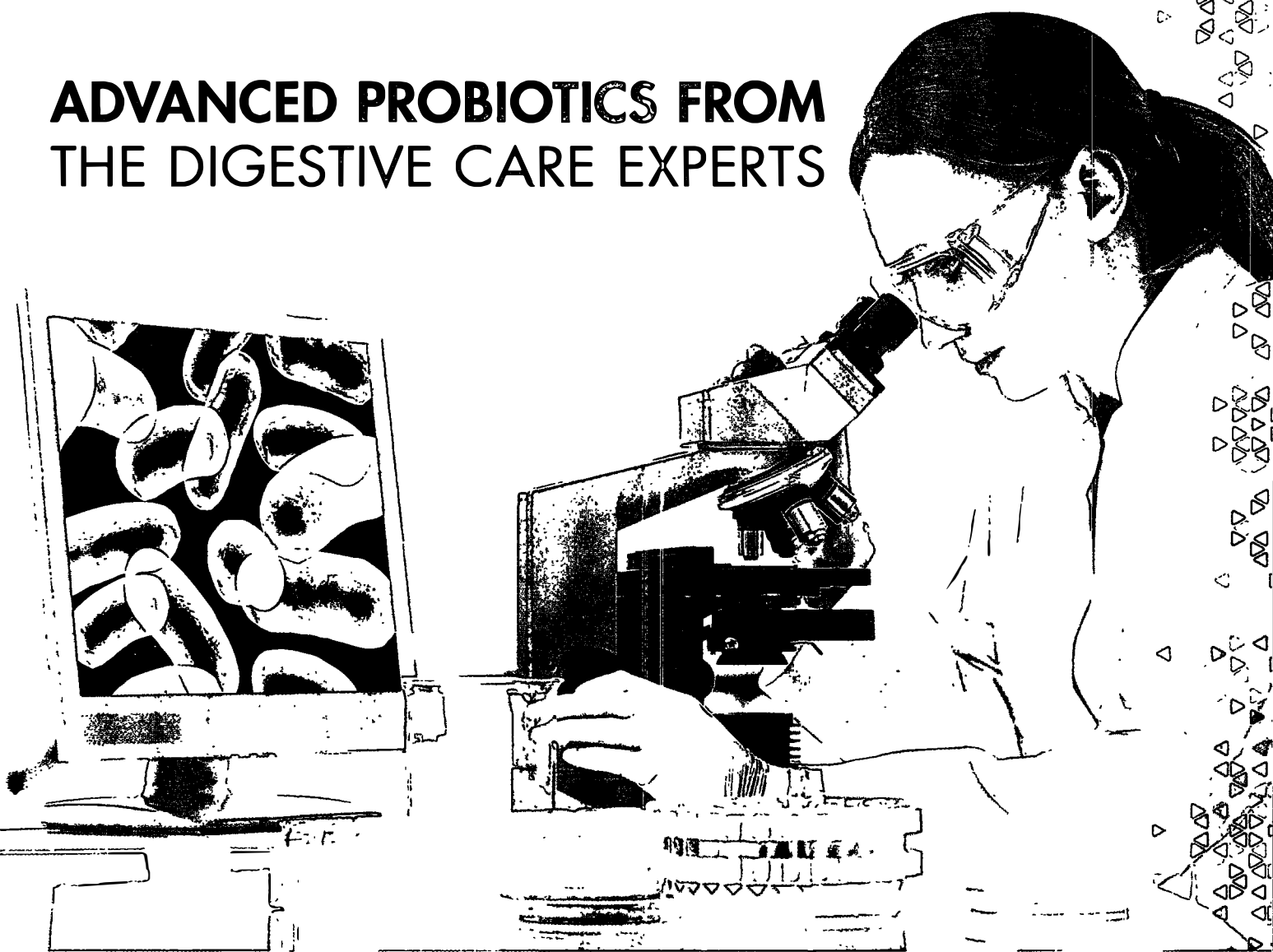
### REFERENCES

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

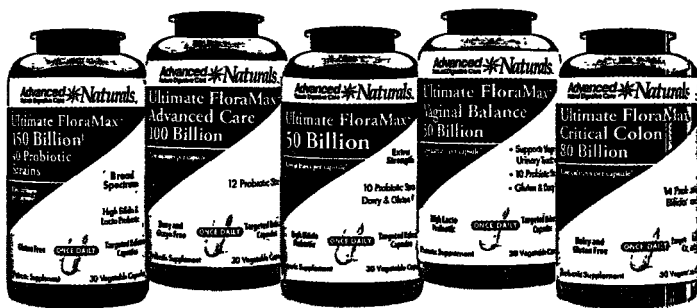
2 Taylor AG, Anderson JG, Riedel SL, et al. Cranial Electrotherapy Stimulation improves symptoms and functional status in individuals with fibromyalgia. *Pain Management Nursing* 2013 Dec; 14(4):327-335

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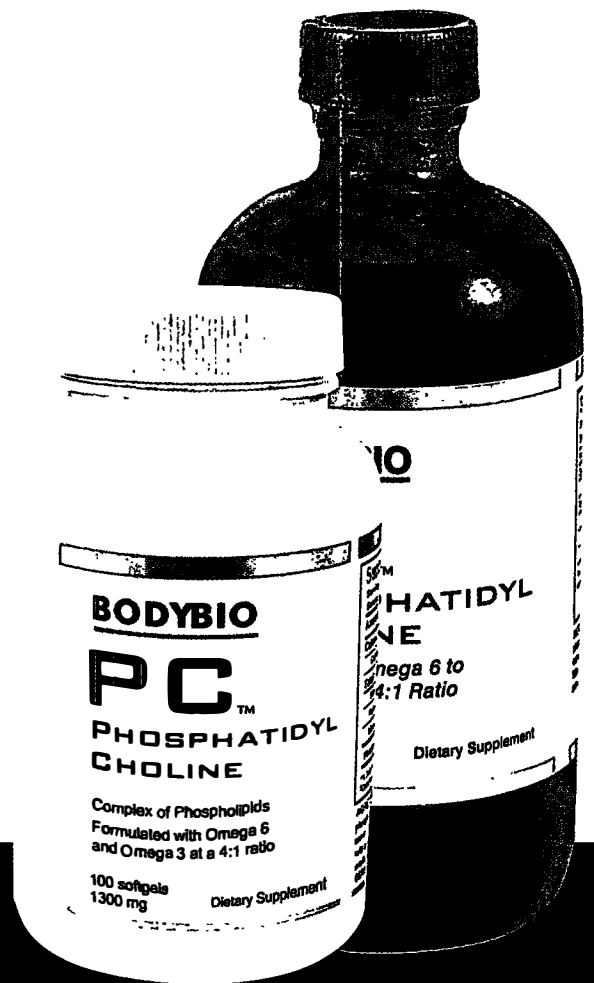
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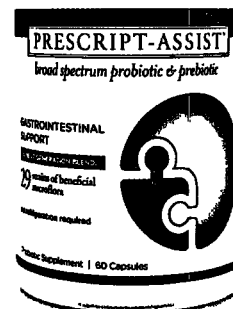
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<sup>1</sup> Pennisi, E. (2011) Body's Hardworking Microbes Get Some Overdue Respect. *Science*, 330 (December 2010), 1619



► continued from page 20

platelets, and some neurons. It stimulates nociceptive (pain sensitive) nerve fibers, vasodilation, gastric acid secretion, smooth muscle contraction, mucus secretion, endothelial permeability, and tachycardia/arrhythmia. Consequently, a buildup of histamine can produce a puzzling diversity of symptoms. Some symptoms – such as sneezing, wheezing, hives, and itching – are characteristic of allergies. But too much histamine can also produce dizziness, nausea, hypotension, abdominal cramps, diarrhea, meteorism (accumulation of intestinal/abdominal gas), and even cyclical headaches and dysmenorrhea in women. High histamine levels have been associated with Crohn's disease, ulcerative colitis, allergic enteropathy, food allergies, colorectal polyps, and carcinomas.

Excessive histamine results from the consumption of too many histamine-rich foods and/or insufficient amounts of the enzyme diamine oxidase (DAO). Normally, DAO breaks down excessive histamine; but, if DAO is not available, headache, rhinitis, flushing, diarrhea, tachycardias or arrhythmias, and other symptoms associated with histamine intolerance arise. Several medications inhibit DAO or stimulate the release of histamine. "All medications, in particular long term treatments, should therefore be taken into account when interpreting histamine intolerance symptoms, as well as the DAO level, where appropriate," advise the review's authors.

When allergy tests are negative for IgE-mediated immune response, Maintz and colleagues suggest that histamine buildup be considered. They recommend using a placebo-controlled histamine provocation test to confirm diagnosis in people who have at least two typical symptoms, a reduced DAO level and/or raised histamine level, and show improvement on a histamine-free diet. Many patients find that maintaining a diary to keep track of symptoms and consumed foods is very helpful.

A histamine-reduced diet is the primary treatment for histamine intolerance. Histamine-rich foods include aged/matured foods such as wine, aged cheese, cured meats, yeast, and sauerkraut. In addition, some low-histamine foods such as citrus fruit, strawberries, pineapple, tomato, spinach, chocolate, egg white, and shellfish can promote the release of stored histamine, thereby producing symptoms,

People with low DAO activity may benefit from vitamin B6 and C supplementation. DAO activity depends on the supply of these vitamins and copper, all of which are cofactors. Vitamin C has the additional benefit of contributing to histamine's breakdown.

Maintz L, Bieber T, Novak N. Histamine intolerance in clinical practice [translation]. *Dtsch Arztebl.* 2006;103(51–52):A3477–A3483. Available at <http://www.aerzteblatt.de/pdf/103/51/a3477e.pdf>. Accessed March 24, 2015.

### Laryngopharyngeal Reflux and Pepsin

Stomach acid is not the only component of gastric fluid that damages epithelial tissue and mucosa during reflux. In the past decade, attention has turned to pepsin (a protein-digesting enzyme produced in the stomach), which can injure laryngeal/esophageal epithelium and produce inflammatory disorders and neoplastic disease. Pepsin remains active even in weak acid environments (up to pH 6.5). Moreover, pepsin is stable for at least 24 hours at pH 7.0 at body temperature and can reactivate in the presence of acid, according to laboratory studies. It becomes totally inactive at pH 8.0. "This is of clinical importance because pepsin, which can be detected in laryngeal epithelia after a reflux event, could be inactive because the mean pH of the laryngopharynx is 6.8," say Nikki Johnston, PhD, and colleagues. "However ... it would potentially remain stable and thus could be reactivated after a subsequent acidic reflux event or once taken up by laryngeal epithelial cells into acidic intracellular compartments."

The most common method for diagnosing laryngopharyngeal reflux (LPR) is simultaneous esophageal and pharyngeal pH monitoring with ambulatory 24-hour double-probe, an expensive procedure with 50% to 80% sensitivity. Researchers have developed a simple pepsin immunoassay to screen for LPR in patients who fail to respond to anti-acid treatment and continue to experience symptoms (e.g., throat burning, bad taste in the mouth, sensation of lump in the throat, heartburn, cough, regurgitation, or eructation). "Gastroesophageal reflux always contains pepsin, but not all reflux occurs below pH 4.0," write John Knight, PhD, and colleagues in a 2005 study. The study compared the assay to pH monitoring in 23 patients with clinical LPR. The participants were asked to cough, clear the sputum from the back of their throat, and spit into a tube containing citric acid (0.1 mol/L;

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► pH 2.5) whenever they experienced LPR symptoms. Using pH monitoring as the control, the pepsin assay was 100% sensitive ("... when the sputum contained measurable pepsin, the patient always experienced LPR by pH monitoring criteria") and 89% specific ("... when a pharyngeal reflux event occurred, measurable pepsin was found 89% of the time"). This "spit-in-a-cup" pepsin assay is less expensive than pH monitoring and noninvasive, making it a useful screening test. The test is in its final stage of development, according to laryngologist Jamie Koufman. Johnston N, Dettmar PW, Bishwokarma B, Lively MO, Koufman JA. Activity/stability of human pepsin: implications for reflux attributed laryngeal disease. *Laryngoscope*. June 2007;117:1036-1039. Available at [www.researchgate.net](http://www.researchgate.net). Accessed March 23, 2015. Knight J, Lively MO, Johnston N, Dettmar PW, Koufman JA. Sensitive pepsin immunoassay for detection of laryngopharyngeal reflux. *Laryngoscope*. August 2005; 115:1473-1478. Available at [www.researchgate.net](http://www.researchgate.net). Accessed March 23, 2015. Koufman J. *The Chronic Cough Enigma*. New York: Katalix Media; 2014:5.

### Vegan Diet and Inflammation

A vegan diet may protect against metabolic illnesses and inflammatory conditions to a greater degree than vegetarian diets, according to a 2014 review article conducted by Marian Glick-Bauer and Ming-Chin Yeh (CUNY School of Public Health, Hunter College, City University of New York). A strict vegan diet consists of whole grains, legumes, vegetables, and fruit. No animal-derived foods – fish, meat, dairy, eggs, or honey – are eaten. Several studies have shown that a vegetarian diet (devoid of meat and poultry) improves cardiometabolic risk factors and lowers the risk of cardiovascular diseases and some cancers when compared with an omnivore diet. The vegan diet appears to have even more health benefits.

Although studies involving vegans are still rare, an increasing number of people are choosing to follow a vegan diet for ethical and/or health reasons. A 2014 study involving Seventh-day Adventists (practitioners of a religion that advocates vegetarianism) found that people who followed a vegan diet had lower incidence of obesity, hypertension, type 2 diabetes, and cardiovascular mortality than those on a lacto-ovo-vegetarian diet (Le and Sabaté 2014). Other studies indicate that a vegan diet reduces inflammation in rheumatoid arthritis and lowers the risk of hypothyroid disease.

In their review, Glick-Bauer and Yeh suggest that the anti-inflammatory benefits of a vegan diet may stem, at least

partially, from the resulting gut microbiota. Several studies have found a difference in gut flora when comparing meat-eaters, vegetarians, and vegans. In one study, for example, Slovenian vegans had a higher ratio of the bacterium *Faecalibacterium prausnitzii* in their guts (Matijašič et al. 2014). *F. prausnitzii*, an abundant butyrate producer, has anti-inflammatory effects. Glick-Bauer and Yeh comment that the gut bacteria which thrive on the abundant fiber content of plant-based diets produce more short-chain fatty acids (acetate, propionate, butyrate). These fatty acids act as signaling molecules that modulate inflammatory response. In addition to the effect on gut microbiota, a vegan diet contains more phytonutrients and antioxidants, avoids some common food allergens/intolerances (such as dairy and eggs), and contains fewer calories.

Despite the abundance of nutrients in plants, a long-term strict vegan diet can result in deficiencies of nutrients found primarily in animal-derived foods such as vitamin B12. Access to vitamin D, calcium, iron, zinc, and long-chain omega-3 fatty acids may also be limited, according to Winston J. Craig. A long-term vegetarian diet has produced hyperhomocysteinemia, protein deficiency, anemia, decreased creatinine content in muscles, and menstrual disruption in physically active women, according to a 2013 Polish review article. Weston A. Price, DDS, found no traditional diet that consisted solely of plant foods in his world travels to compare the health effects of eating traditional whole foods with processed foods. He did, however, come upon groups that advocated vegetarian diets for ethical reasons: "In every instance where the groups involved had been long under this teaching, I found evidence of degeneration in the form of dental caries, and in the new generation in the form of abnormal dental arches to an extent very much higher than in the primitive groups who were not under this influence." Price viewed oral health and structure as a window into the skeletal structure and overall health.

The health benefits of vegan and vegetarian diets may have more to do with their emphasis on nutrient-rich, whole-plant food and avoidance of refined starches, added sugar, and processed foods than on their avoidance of animal-derived foods. As Glick-Bauer and Yeh point out, the Mediterranean diet also improves metabolic conditions such as type 2 diabetes. They conclude, "Thus a patient's personal taste and cultural traditions may need to dictate whether a vegan diet is the ideal choice for medical nutrition therapy."

Craig WJ. Health effects of vegan diets. *Am J Clin Nutr*. 2009;89(suppl):16275-16335. Available at <http://ajcn.nutrition.org/content/89/5/16275.full.pdf+html>. Accessed March 25, 2015. Glick-Bauer M, Yeh M-C. The health advantage of a vegan diet: exploring the gut microbiota connection. *Nutrients* 2014;6(11):4822-4838. Available at [www.mdpi.com/2072-6643/6/11/4822/html](http://www.mdpi.com/2072-6643/6/11/4822/html). Accessed March 25, 2015. Le LT, Sabaté J. Beyond meatless, the health effects of vegan diets: findings from the Adventist cohorts. *Nutrients*. 2014;6(6):2131-2147. Available at <http://www.mdpi.com/2072-6643/6/6/2131/html>. Accessed April 3, 2015. Matijašič BB et al. Association of dietary type with fecal microbiota in vegetarians and omnivores in Slovenia. *Eur J Nutr*. 2014;53:1051-1064. Pilis W, Stec K, Zych M, Pilis, A. Health benefits and risk associated with adopting a vegetarian diet [abstract]. *J Sci Food Agric*. 2013;93:2362-2371. Available at <http://www.ncbi.nlm.nih.gov/pubmed/24964573>. Accessed April 3, 2015. Price WA. *Nutrition and Physical Degeneration*. 6th ed. La Mesa, CA: Price-Pottenger Nutrition Foundation; 1997:279.

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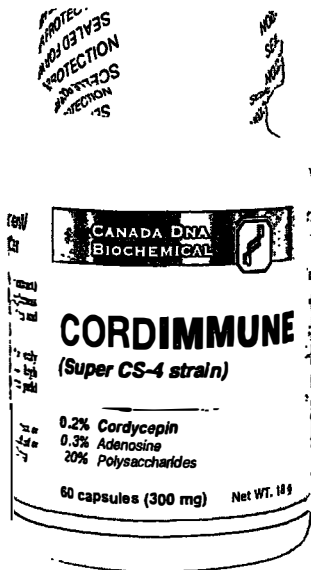
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# Pathways to Healing

by Elaine Zablocki

## Acupuncturist Advocates Balanced Lifestyle, Nonjudgmental Mind

Liz Fukushima has been treating difficult cases with acupuncture and Chinese herbal medicine for nearly 30 years. "I built my practice by letting people know I wanted to treat complex conditions," she recalls. "I told them, 'the more doctors you've flunked out of, the more I want to treat you.'"

Fukushima practices at Life Gate Healing Arts, in Burlington, Vermont. She named her practice after the Life Gate, an important acupuncture point, called *Ming Men* in Chinese. "At the moment of conception, when yin and yang/egg and sperm come together, there is an energy that enters at that point and activates life. That's why I chose Life Gate as the name of my practice."

Fukushima started out taking pre-med courses in college, but decided she wanted a broader undergraduate education. She ended up majoring in religion, with a concentration in Tibetan Buddhism. Then she spent a year in India studying literary and spoken Tibetan.

Soon after she returned, Yeshe Dhonden, the Dalai Lama's personal physician, arrived on a visit to the US. In addition to a series of lectures, he visited a number of acupuncture clinics to treat difficult cases. Fukushima, with her Tibetan language skills and her interest in medicine, was invited to serve as his interpreter for patient consultations. "At that time I was still considering finishing my pre-med requirements, but this experience led me to study acupuncture instead," she says. She trained through a two-year program at the New England School of Acupuncture, and became one of the earliest licensed acupuncturists in Massachusetts.

Fukushima had a special interest in women and gynecological health, so in the early days she treated many women with endometriosis, and developed a protocol for working with infertile couples. Nowadays in vitro fertilization and other forms of assisted reproduction are common, so she often sees patients who want to combine acupuncture and Chinese herbal medicine with assisted reproduction.

From the beginning she worked with people with many different forms of cancer, using acupuncture and Chinese herbs to boost white blood cell counts during chemotherapy.

Today there are expensive medications to boost white blood cells. "Nowadays on many protocols these medications are a standard part of every round of chemotherapy," Fukushima said, "If we only had more individualized treatment, it's possible you could do acupuncture and herbs on the early rounds, and bring out these medications later on. If these methods were fully integrated into treatment, we could lower costs and also lower toxicity."

### Healthy Living: Eat, Breathe, Move, Sleep

In addition to dealing with specific complex illnesses, Fukushima's practice focuses on finding ways to support health. "The more years of clinical practice I have, the more I realize how important it is to eat well and sleep well to support a healthy organism," she says.

After she'd been in clinical practice for two or three years, Fukushima went to Nepal for six weeks. "It was the first time I had been out of the United States for an extended period of time after I had learned to cultivate my medical practitioner eyes," she says. "I watched how human beings there live their lives, and I saw clearly that this human organism is meant to be in motion many hours of the day."

Our society has evolved so that many people spend hours sitting at a desk with their vision fixed at a point 12 inches in front of them. "This is so stressful for the human organism," she says.

"I encourage people to build more movement into their lives, in informal ways: take the stairs, park three blocks away, walk around the block. Every chance you get, move a bit more."

She believes that it is important to teach people to be aware of their breath, and to breathe well.

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# Townsend Letter

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"Your diaphragm is a big muscle, and all the organs in your abdomen could be massaged by this muscle on every breath. Instead, when you just take shallow breaths, everything gets stagnant."

Fukushima doesn't rely on standardized recommendations about the best diet for everyone. Instead she works closely with each patient to discover what foods are most appropriate. "I have an opportunity to get people to really pay attention to what they're eating and how they feel after they've eaten it. I often recommend that people eliminate something for one to three months and then add it back. After that, if it's not good for you, you'll see very clearly how you react to it."

Often she suggests new approaches for people to try. She asked one person with chronic fatigue syndrome to keep a food diary, and noticed that she wasn't eating any protein at breakfast or lunch. When this person increased her protein intake early in the day, many of her symptoms improved.

At the same time, Fukushima notes that the preservatives, food additives, and flavorings in our food supply are very stressful. "I've always believed in eating whole foods," she says. "I encourage people to distinguish between what's a treat and what's a basic food. Biologically we are not prepared to handle the profusion of sweets that constantly surrounds us."

Most of us sometimes experience periods when we don't get enough sleep. "Even if you wake up early, you can take time for relaxation exercises, or focus on your breathing," Fukushima says. "You're resting, and in many cases rest is as valuable as sleep."

The standard advice for people who have trouble sleeping is to turn off the TV and computer around 8:30 at night, but many resist these suggestions. "I had one client with severe hot flashes, what we would call too much fire energy, so she was willing to give this a try. She was also getting acupuncture and taking herbs. Within six weeks her sleep improved, and all that revved-up energy quieted down."

Fukushima encourages people to rethink their choices and priorities in relation to sleep. "At one point I really focused on sleep. I asked every one of my regular clients, no matter how much sleep they were getting, to try sleeping 30 minutes more each night. I said, 'You're not feeling well, you're spending an hour a week and a chunk of money to come see me .... try sleeping a bit more and see what that does.' I can't tell you how many of them felt better within the next month."

### **Enjoy Rest and Nonjudgmental Mind**

Many of our current chronic health problems relate to inflammation. "These inflammatory processes come about because the body doesn't have enough rest," Fukushima says. "It doesn't have rest in the form of sleep. It doesn't have a chance to rest from digesting food. Our world is full of constant entertainment and news, and it's not so easy



**Liz Fukushima**

to let the mind rest. The most powerful way to calm down inflammation is to support good rest."

Fukushima finds that many people in the US have deep-seated moral judgments about their health issues. "They say, 'If I ate better, if I just exercised more, if I wasn't so angry. ...' It's almost a puritanical control thing," she says. "I try to help people understand they don't need to have moralistic judgments about everything they experience."

For example, some people have a tendency to put on weight. This may be related to minute amounts of BPA in the environment. It may be a genetic tendency that runs in the family, a tendency that would actually be useful in times of food shortage. "We don't know why you're 30 pounds overweight, but it doesn't make much sense for you to beat yourself up trying to lose 30 pounds," Fukushima tells her clients. "Why not just lose 10 pounds, eat healthy foods, be active ... and consider that's OK."

She mentions a friend who didn't have any of the signs that predict heart disease ... then it turned out that he had a blocked major artery. "We know many steps that will help prevent heart problems, but they only account for about half the cases of heart disease," she says. "For the other half, we don't have a clue. You can do everything recommended to prevent cancer, but if you do get cancer it's not a moral failure. It's just something that happened."

As a practitioner, Fukushima supports her patients in finding creative ways to increase health, and she also supports them when they are dealing with serious illness. "I say to them, 'How can you find ways to live well, if this is just how it is?' I've seen people adjust to very difficult situations. People can experience a deep interior sense of wellness, even while their body is failing. It is a sense of acceptance: this is just what is happening, this is how it is."

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.



# War on Cancer

by Ralph Moss, PhD

[www.cancerdecisions.com](http://www.cancerdecisions.com)

Scientists at Duke University have come up with an ingenious new treatment for one of the deadliest of all cancers, glioblastoma multiforme (GBM) of the brain. It consists of a dendritic cell (DC) vaccine, which is conditioned not with cancer cells but with a modified form of the ordinary tetanus vaccine.

This "double vaccine" study was the subject of a 16-page report in *Nature* (Mitchell 2015) and many laudatory articles in the news.

"Patients with glioblastoma usually survive for little more than one year. However, in patients who received the immunotherapy, half lived nearly five years or longer from their diagnosis," said John Sampson, MD, of Duke University Medical Center, who oversaw the study, according to NBC News.

Typically, to make a DC vaccine, scientists remove a bit of the tumor, then "pulse" it with white blood cells, to create a plethora of dendritic cells, which are then injected back into the body. This is a standard treatment for prostate cancer (Provenge) and is available experimentally for other cancers in clinical trials or at foreign CAM clinics.

Dendritic cells are also known as "antigen-presenting cells." They hold up examples of a desired target to the killer portion of the immune system. They especially occur in parts of the body that are in contact with the external world, such as the skin, nose, lungs, stomach, and intestines. Although part of the more primitive innate immune system, they also serve as a link to the more evolved adaptive immune system. They are called *dendritic cells* because they resemble the branching structure of dendrites, or nerve cells. (The word *dendron* in Greek means "tree.") But, to avoid confusion, we should point out that they have no particular relationship to the nervous system.

Dendritic cells were first discovered and described in the 19th century by Paul Langerhans, who also discovered the "Isles of Langerhans" that produce insulin in the pancreas. Because of their appearance, he thought that they were nerve cells. It was only a century later that

Ralph Steinman, MD, of Rockefeller University, New York, described the true function of the dendritic cells in immunity. He was awarded the William B. Coley Prize in 1998 (linking his name to that of the American founder of cancer immunotherapy). He won the Nobel Prize in 2011 for "his discovery of the dendritic cell and its role in adaptive immunity." In an odd twist of fate, Steinman died of pancreatic cancer just three days before the Nobel Committee announced the award. The Nobel Prizes cannot be awarded posthumously. But since the committee did not know about his death, it agreed to give the prize (and prize money) to his widow.

Using this combination of DCs and the tetanus vaccine, Duke researchers were able to bring about long-term progression-free survival in 3 out of 6 of the patients who received the tetanus-treated DC. None of the patients who received the ordinary, or "unpulsed," DC survived to the 40-month mark. Obviously, the great weakness of this study is the small number of patients. It will have to be repeated in a much larger group in order to be widely accepted. But there are some tentative conclusions that can be drawn from this, with implications for the field of complementary and alternative medicine (CAM).

Glioblastoma is somewhat different from other cancers. It often contains large amounts of cytomegalovirus (CMV). This is a virus that is present in many individuals, without causing symptoms. It is not clear if CMV causes the cancer or is merely a hitchhiker. In either case, scientists can use CMV as a target, a way of homing in on infected cells. The Duke team has been using anti-CMV antibodies to target these cancer cells, and it has worked somewhat. They extended average survival from 12 to 18 months. Duke scientists decided to add a tetanus shot to the treatment, in order to generally boost the patient's immunity. After receiving standard surgery, radiation, and chemotherapy, the patients also got this combination of DCs and tetanus. The tetanus was the same one that anyone would receive after stepping on a rusty nail.

This general stimulation of the immune system significantly improved the outcome of the treatment. Patients who received the tetanus booster lived more than 26 months on average. One patient has lived 8 years now – after being told that she had about 3 months to live.

“What we think is going on is that this tetanus booster vaccine does such a good job at putting the immune system at high alert ... acting like a siren to the rest of the cells,” said Kristen Batich, MD, of Duke University, lead author on the study. “And so the immune system knows to look for the next incoming danger signal. In this scenario it would be our immunotherapy vaccine that’s specific for the brain tumors in these patients.”

DCs are both very promising and very frustrating. Sometimes they seem to have major positive effects in cancer patients. Steinman reputedly kept himself alive for 5 years with pancreatic cancer using DCs as a major part of his treatment. However, DCs, as usually produced, “have shown limited promise” in advanced cancer, including in GBM (Palucka 2012; Liau 2005; Yu 2004).

The reader may notice that conventional cancer treatment is in some ways edging closer and closer to the holistic philosophy preached and practiced at CAM clinics for decades. Thus, glioblastoma patients in the current trial are receiving a judicious combination of surgery, radiation, chemotherapy, dendritic cell immunotherapy, and now a nonspecific immune stimulation with tetanus vaccine.

We have also seen increased interest in such things as the Novocure electrical device and a ketogenic diet. All of these can help. Thus, on both sides of the CAM divide, we are moving “beyond the magic bullet” (to use Dr. Raymond Chang’s book title) and seeking a synergistic suite of treatments, individualized for the particular patient, that can bring about a better outcome than any single treatment alone.

CAM clinics in Europe and Mexico have been using DCs for over a decade. Not one of these would think of giving DCs alone, without also doing everything in its power to enhance the general immune response. This would include local-regional as well as whole-body heat therapy, and various stimulatory substances, such as medicinal mushrooms, mistletoe products, and low doses of interleukin-2 (IL-2).

There are some advantages of getting involved in a clinical trial, such as the one at Duke. They are less expensive for the patient and often easier to get to. However, if you go to [clinicaltrials.gov](http://clinicaltrials.gov) and enter the words *dendritic cells* and *tetanus*, you come up with only one open study whose status is known, and that is the Duke study. But there are drawbacks. First of all, at this writing, “This study is not yet open for participant recruitment.” But GBM is not a disease that allows for any delays in treatment.

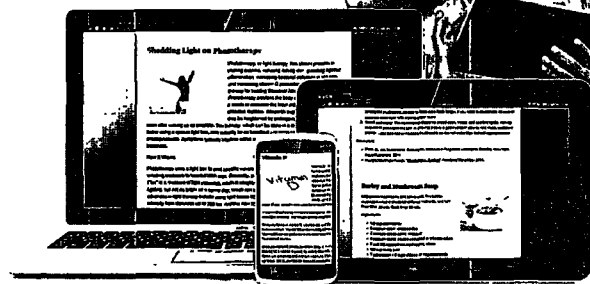


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## War on Cancer

➤ Second, although this is a phase II study, patients will in fact be randomized to receive either the ordinary DCs or the new tetanus-enhanced treatment. This randomization is understandable from a scientific point of view, but it leaves up to half the patients with what almost certainly will be an inadequate treatment. Treatment at a clinic that can give a combination of DCs and immune stimulants might be a better option for many people, especially those who cannot get into desirable clinical trials.

### Exercise and Cancer Survival

A few years ago, I published an article on the value of exercise in survival from brain cancer. Research in the authoritative *Journal of Clinical Oncology* showed that working out on an exercise bike for 30 minutes per day prolonged survival, even in those with aggressive forms of brain cancer such as gliomas (Ruden 2011). The study in question looked at 243 patients who had advanced recurrent malignant brain tumors. Those who exercised briskly and regularly lived on average about 22 months compared with just 13 months for those who were less active. This level of activity was equivalent to walking briskly for 30 minutes 5 days per week. The authors concluded: "Exercise behavior was an independent predictor of survival" (Ruden 2011).

This is no small claim!

"Numerous studies show exercise lowers fatigue and enhances physical function for cancer patients, but we wanted to look at whether exercise fundamentally is associated with the risk of cancer progressing or coming back," said Lee W. Jones, PhD, senior author on the study (Ruden 2011). And indeed it did.

At the time, Jones was an exercise scientist and associate professor at Duke Cancer Institute in Durham, NC. (He is now at Memorial Sloan Kettering Cancer Center, New York.) It would be a good bet for patients to contact a physical therapist who can help them strengthen their muscles and launch an exercise program, where appropriate. The American Physical Therapy Association (APTA.org) is a good first place to begin looking. Health insurance often pays for physical rehabilitation.

A 2013 study at Dana-Farber Cancer Institute, Boston, has extended these findings to another common cancer. The study looked at 237 colon cancer patients who first had a resection of their stage III disease. The authors then measured physical activity 6 or so months after the completion of therapy and 14 months after surgical resection, but before any recurrent disease was detected. The primary end point of the study was these patients' survival time after recurrence (Jeon 2013).

Patients who engaged in more intensive physical activity (measured in what are called metabolic equivalent task, or MET, time per week) showed a statistically significant trend for increased survival after recurrence. There was a

29% reduction of death in this group. Interestingly, survival "was not significantly modified by sex, body mass index (BMI), number of positive lymph nodes, age, baseline performance status, adjuvant chemotherapy regimen, or recurrence-free survival period" (Jeon 2013). In other words, it appears to be a result of the increased level of activity. In 2012, scientists at the National Cancer Institute surveyed the cancer literature, looking for an association between exercise and survival in cancer. They concluded:

There was consistent evidence from 27 observational studies that physical activity is associated with reduced all-cause, breast cancer-specific, and colon cancer-specific mortality. There is currently insufficient evidence regarding the association between physical activity and mortality for survivors of other cancers. Randomized controlled trials of exercise that included biomarker endpoints suggest that exercise may result in beneficial changes in the circulating level of insulin, insulin-related pathways, inflammation, and, possibly, immunity; however, the evidence is still preliminary (Ballard-Barbash 2012).

Exercise is of course very important in diabetes, prediabetes, and metabolic syndrome. So once again we see the link between these conditions and cancer.

It's a cliché to say so, but patients should talk to their physicians before beginning any exercise regimen. That is especially important in this case since, particularly if one already has had heart problems, aerobic exercise might make things worse. Anecdotally, many of us know people who had heart attacks or even died after suddenly starting a vigorous exercise program after being sedentary for a long time. A study by Jones (2014) showed an increase in all-cause mortality or hospitalization at 2 years in some cancer patients who were doing aerobic exercise. But, with that caveat in mind, it is a fair bet that exercise and general physical activity would benefit most people with various kinds of cancer.

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

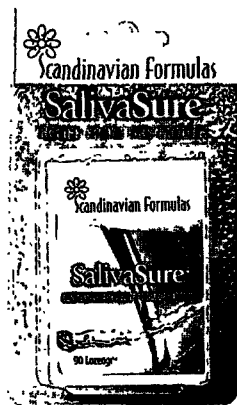


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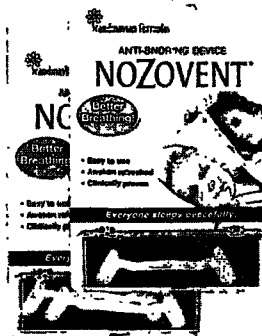
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# Literature Review & Commentary

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

## Low-FODMAPs Diet Improves Symptoms of Irritable Bowel Syndrome

Thirty Australian patients (mean age, 41 years) with irritable bowel syndrome were randomly assigned to consume a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs; less than 0.5 g per meal) or a typical Australian diet for 3 weeks. After a washout period of at least 3 weeks, they consumed the alternate diet for an additional 3 weeks. Daily overall gastrointestinal symptoms were rated using a 0 to 100 mm visual analogue scale (VAS), with higher numbers indicating worse symptoms. The mean VAS score was significantly lower on the low-FODMAPs diet than on the control diet (22.8 vs. 44.9;  $p < 0.001$ ) and the patients' habitual diet. Bloating, pain, and passage of flatus were all reduced on the low-FODMAPs diet.

**Comment:** FODMAPs include fructose, lactose, sorbitol, fructooligosaccharides (fructans, including inulin), and galactooligosaccharides (such as raffinose). Foods restricted on a low-FODMAPs diet include fruits that contain fructose in excess of glucose (e.g., apples, pears), fructan-containing foods (e.g., wheat, onions, leeks, artichokes), sorbitol-containing foods (e.g., stone fruits), raffinose-containing foods (e.g., legumes, lentils, cabbage, and brussels sprouts), and lactose- and fructose-containing foods, if lactose and fructose malabsorption, respectively, are demonstrated. The results of the present study confirm previous research demonstrating that consumption of a low-FODMAPs diet can decrease gastrointestinal symptoms in patients with irritable bowel syndrome.

Halmos EP et al. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology*. 2014;146:67–75.e5.

## Gluten-Free Diet for Irritable Bowel Syndrome

Forty-five patients (mean age, 42.6 years) with diarrhea-predominant irritable bowel syndrome were randomly assigned to consume a gluten-free diet or a gluten-containing diet for 4 weeks. The number of bowel movements per day was significantly less on the gluten-free diet than on the gluten-containing diet ( $p < 0.04$ ). The gluten-free diet had a significantly greater effect on bowel movement frequency in the 11 patients with the HLA-DQ2 or HLA-DQ8 genotype (which are associated with celiac disease) than in the 11 HLA-DQ2/8-negative patients ( $p < 0.02$ ). Small-intestinal permeability was nonsignificantly lower with the gluten-free diet than with the gluten-containing diet ( $p < 0.1$ ) in the group as a whole, and when the analysis was restricted to HLA-DQ2/8-positive patients ( $p < 0.06$ ).

**Comment:** These findings indicate that some patients with diarrhea-predominant irritable bowel syndrome can benefit from a gluten-free diet. Patients who carry genes associated with celiac disease may be more responsive to this diet than others, even though these individuals may not actually have celiac disease. Some of the benefit that results from consuming a gluten-free diet may be due to the elimination of wheat, which is a major source of fructans (one of the FODMAPs – see above). However, the association between diet responsiveness and particular HLA types suggests that autoimmune or allergic mechanisms are involved as well. The increase in intestinal permeability associated with gluten consumption (albeit not statistically significant) suggests that gluten might act in part by increasing the intestinal absorption of antigenic macromolecules.

Vazquez-Roque MI et al. A controlled trial of gluten-free diet in patients with irritable bowel syndrome-diarrhea: effects on bowel frequency and intestinal function. *Gastroenterology* 2013;144:903–911.e3.

### More on Wheat and Irritable Bowel Syndrome

Twenty patients (aged 18–59 years) with irritable bowel syndrome were randomly assigned to receive, in double-blind fashion, products (bread, pasta, biscuits, and crackers) made from ancient wheat (*Triticum turgidum* subsp. *turanicum* [Khorasan wheat]; also known as Kamut) or modern wheat (*Triticum aestivum*) for 6 weeks. After a 6-week washout period during which patients consumed their usual diet, they consumed the alternate wheat for an additional 6 weeks. With the ancient wheat products, significant improvements were seen from baseline in abdominal pain ( $p < 0.0001$ ), bloating ( $p = 0.004$ ), satisfaction with stool consistency ( $p < 0.001$ ) and tiredness ( $p < 0.0001$ ). No significant improvements from baseline were observed with modern wheat products, and the difference in the change between groups was significant according to the Irritable Bowel Syndrome Global Assessment of Improvement Scale and the Irritable Bowel Syndrome Symptom Severity Scale ( $p < 0.05$  for each).

**Comment:** The two studies cited above suggest that consumption of wheat can exacerbate the symptoms of irritable bowel syndrome in susceptible individuals. In contrast, eating Khorasan wheat may improve symptoms. Khorasan wheat is thought to have originated in the Middle East, and to have been introduced into the US by an American airman, who brought the grain here from Egypt. Khorasan wheat is used in the same way as conventional strains of wheat.

Some of the differences in the way these two types of wheat affect symptoms may be due to strain differences in protein structure and other constituents. In addition, during the past 60 years, modern wheat has undergone various genetic modifications (hybridization), in order to improve crop yield. Analysis of modern wheat hybrids has revealed that more than 5% of the proteins in the hybrids are unique, found in neither parent. In one study, 14 new gluten proteins were identified in the hybrids that were not present in either parent. These observations raise the possibility that the apparent increase in the incidence of celiac disease and nonceliac gluten sensitivity in recent decades is due at least in part to genetic modification of wheat.

Sofi F et al. Effect of *Triticum turgidum* subsp. *turanicum* wheat on irritable bowel syndrome: a double-blinded randomised dietary intervention trial. *Br J Nutr*. 2014 Feb 13.

De Lorge M, Salen P. Gluten and wheat intolerance today: are modern wheat strains involved? *Int J Food Sci Nutr*. 2014;65:577–581.

### Fructose and Abdominal Pain in Children

Two hundred twenty-two children (aged 2–19 years; mean age, 10.5

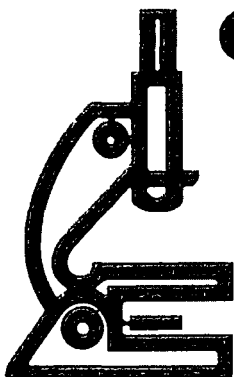
years) with chronic abdominal pain underwent a fructose hydrogen breath test, using 1 g of fructose per kg of body weight (maximum, 25 g). Fifty-five percent of the patients had a positive test (an increase of breath hydrogen of more than 20 parts per million above baseline), and were placed on a low-fructose diet. Seventy-seven percent of those patients reported a resolution of symptoms on the low-fructose diet. Of the 101 patients with a negative fructose hydrogen breath test, 54.4% reported a resolution of symptoms without a low-fructose diet.

**Comment:** Fructose intake has increased substantially during the past 30 years, primarily because of increased consumption of high-fructose corn syrup. The results of the present study suggest that fructose intolerance/malabsorption is common in children with recurrent abdominal pain, and that a low-fructose diet is an effective treatment for many such children.

Escobar MA Jr et al. Fructose intolerance/malabsorption and recurrent abdominal pain in children. *J Pediatr Gastroenterol Nutr*. 2014;58:498–501.

### Probiotic Prevents Infections in Preschool Children

Three hundred thirty-six healthy Mexican children (aged 6 months to 3 years) attending day-care centers were randomly assigned to receive, in double-blind fashion, *Lactobacillus reuteri* DSM 17938 ( $10^8$  colony-forming units per day) or placebo for 3 months, and were then followed for an additional 3 months. Compared with placebo, *L. reuteri* DSM 17938 significantly reduced the frequency and duration of episodes of diarrhea and respiratory tract infections at both 3 and 6 months ( $p < 0.05$ ). Compared with placebo, the number of days with diarrhea in the probiotic group was reduced by 67% during the treatment period ( $p = 0.03$ ) and by 55% during the follow-up period



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## Gaby's Literature Review

>

( $p = 0.01$ ); the number of days with respiratory episodes was reduced by 67% during the treatment period ( $p = 0.01$ ) and by 52% during the follow-up period ( $p = 0.01$ ).

**Comment:** *L. reuteri* DSM 17938 (formerly known as *L. reuteri* strain ATCC 55730) is a probiotic strain originally derived from breast milk. The results of the present study demonstrate that treatment of young children with this probiotic strain can decrease the frequency and duration of episodes of diarrhea and respiratory tract infections. In other studies, this probiotic strain was useful in the treatment of chronic constipation in children and adults and in the treatment of colic in breast-fed infants. *L. reuteri* DSM 17938 is commercially available as Gerber Soothe Colic Drops.

Gutierrez-Castrellon P et al. Diarrhea in preschool children and *Lactobacillus reuteri*: a randomized controlled trial. *Pediatrics*. 2014;133:e904–e909.

### Probiotic for Treatment of Acute Diarrhea

One hundred twenty-seven Turkish children (median age, 12 months; range, 3–60 months) hospitalized with acute gastroenteritis of 12 to 72 hours' duration were randomly assigned to receive, in single-blind fashion, conventional therapy with or without  $10^8$  colony-forming units per day of *Lactobacillus reuteri* DSM 17938 for 5 days. The proportion of children who were free of diarrhea after 24 and 48 hours (50% vs. 5%;  $p < 0.001$ ) and after 72 hours (69% vs. 11%;  $p < 0.001$ ) was significantly greater in probiotic group than in the control group. The mean length of hospital stay was significantly shorter in the probiotic group than in the control group (4.31 vs. 5.46 days;  $p < 0.001$ ).

**Comment:** As discussed in the entry directly above this one, *L. reuteri* DSM 17938 has been found to be effective for the prevention of diarrhea and respiratory tract infections in children, and for treating chronic constipation and infantile colic. The present study demonstrates that this probiotic strain can also decrease the duration of acute diarrhea in hospitalized children.

Dinleyici EC et al. *Lactobacillus reuteri* DSM 17938 effectively reduces the duration of acute diarrhoea in hospitalised children. *Acta Paediatr*. 2014;103:e300–e305.

### Magnesium for Bone Health

In a study of Texas children (aged 4–8 years), magnesium intake and total magnesium absorption (percent absorption was determined by a dual-tracer stable isotope technique) were significantly associated with total

body bone mineral content and bone mineral density. No such associations were observed for calcium intake or total calcium absorption.

**Comment:** Magnesium is a cofactor for alkaline phosphatase, an enzyme involved in bone mineralization. In rats, dietary magnesium deficiency resulted in decreased bone formation and a loss of bone mass and trabecular bone volume. In a study of girls aged 8 to 14 years, magnesium supplementation had a positive effect on accrual of bone mass in the 41% of participants who had suboptimal dietary magnesium intake (less than 220 mg per day).

The magnesium content of typical Western diets is less than the Recommended Dietary Allowance, and is particularly low among girls and young women. Increasing dietary magnesium intake or supplementing with magnesium may help women reach a higher peak bone mass, potentially decreasing the risk of osteoporosis later in life. Good food sources of magnesium include nuts, whole grains, legumes, leafy green vegetables, fish, meat, and dairy products.

Abrams SA et al. Magnesium metabolism in 4-year-old to 8-year-old children. *J Bone Miner Res*. 2014;29:118–122.

### Butyrate for Diverticulosis

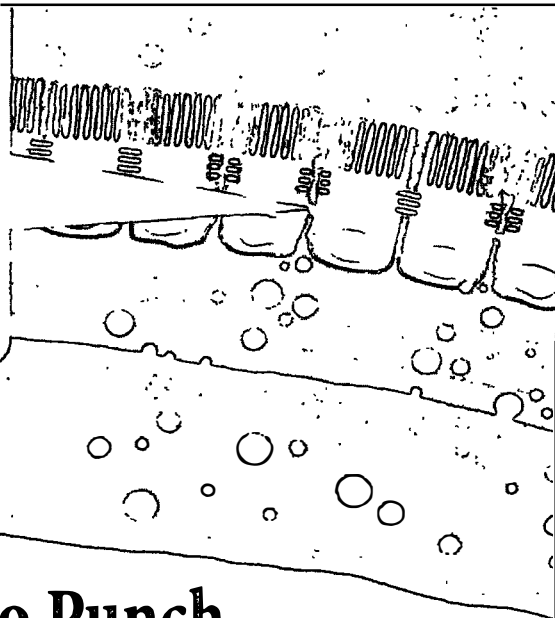
Seventy-three patients (mean age, 64 years) with diverticulosis were randomly assigned to receive, in double-blind fashion, 300 mg per day of microencapsulated sodium butyrate (formulated to be released in the colon) or placebo for 12 months. Among the 52 patients who completed the trial, the proportion of patients who had an episode of diverticulitis (symptomatic diagnosis with acute pain, fever, and leukocytosis) was significantly lower in the butyrate group than in the placebo group (6.7% vs. 31.8%;  $p < 0.05$ ). No side effects were reported.

**Comment:** Butyrate and other short-chain fatty acids (mainly acetate and propionate) are derived from the breakdown of carbohydrates and protein by colonic bacteria. In contrast to most cells in the body, which use primarily glucose and long-chain fatty acids for fuel, butyrate and to a lesser extent other short-chain fatty acids are the preferred fuel for colonocytes (colon cells). Seventy percent of the energy used by colonocytes is derived directly from the colonic lumen, rather than from the circulation. The results of the present study demonstrate that supplying butyrate directly to the colon (by means of a colon-release oral supplement) decreased the number of diverticulitis episodes in patients with diverticulosis. While the specific mechanism of action is not known, butyrate presumably improved the overall health of colonocytes by supplying them with a source of energy.

Krokowicz L et al. Microencapsulated sodium butyrate administered to patients with diverticulosis decreases incidence of diverticulitis – a prospective randomized study. *Int J Colorectal Dis*. 2014;29:387–393.

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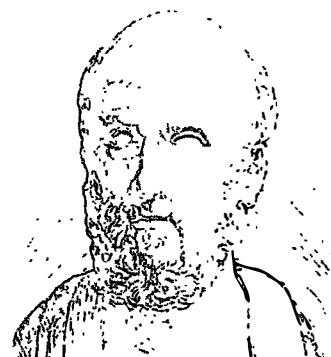
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# Environmental Medicine Update

by Marianne Marchese, ND

[www.drmmarchese.com](http://www.drmmarchese.com)

## The Inflammatory Effects of Carrageenan – A Food Additive

### Introduction

Carrageenans are sulfated polysaccharides obtained from red seaweeds (Rhodophyceae). Carrageenan is widely used as a food additive and has been shown to induce inflammatory responses in animal models and human cells. It is used or has been used as a thickener, stabilizer, or emulsifying agent in many foods, including dairy products, processed meats, soy milk, other cow milk alternatives, and infant formula. Carrageenans are also used in various other products, such as cosmetics, toothpaste, room deodorizers, and pharmaceuticals. Current data suggest an average consumption of 250 mg/day of carrageenan in the US.<sup>1</sup> Studies show that the inflammatory effects of carrageenans can cause ulcerations, polyps, colitis, and colorectal tumors.<sup>2</sup> Newer studies outline the mechanism of action of the inflammatory response to CGN. Food-grade carrageenan is generally recognized as safe (GRAS) by the US Food and Drug Administration (FDA).

### Carrageenan History and Regulation

Carrageenan has been used by the food industry in the US since the 1950s. The FDA approved the use of carrageenan as a food additive in 1961; prior to that it was classified as a GRAS substance in foods. As early as the 1970s, safety concerns were raised in regard to carrageenan. Animal studies using hydrolyzed and unhydrolyzed carrageenan showed that both caused alterations in the cecum. Ulcerations were more severe with the degraded form of carrageenan (poligeenan), which is derived by acid hydrolysis.<sup>3</sup> Food-grade carrageenan is undegraded.<sup>2</sup> In light of this study, the FDA reviewed carrageenan safety again in 1972 and found it safe for use in foods except infant formula, wherein it was determined that the risks outweighed the benefits.<sup>4</sup>

During the late 1970s, processed eucheuma seaweed (PES) was introduced for use as carrageenan. Traditionally refined carrageenan is produced by extracting it from the seaweed and filtering the extract to remove cellulose and

other substances. The production of PES is different in that the other substances are extracted and the remaining seaweed containing carrageenan and cellulose is processed. In 1990, FDA determined that PES (now called Philippine natural grade [PNG] carrageenan) meets its criteria to be classified as carrageenan in the US. In 1994, there were concerns that PNG could be unsafe as a food additive because it is processed with an illegal pesticide, ethylene oxide.<sup>5</sup> Treatment by ethylene oxide results in a chemical residue, ethylene chlorohydrin (ECH), in food. The FDA has determined that the levels of ECH residues in carrageenan do not represent a safety concern.

In 2001 Dr. Joanne Tobacman, a researcher at the University of Illinois at Chicago College of Medicine, published a safety review of carrageenan in *Environmental Health Perspectives*. It was a review of 45 published animal studies and found a link to ulcerations and gastrointestinal inflammation.<sup>2</sup> This study revealed the contamination of food-grade (undegraded) carrageenan by substantial amounts of degraded carrageenan. The review discussed the possibility of production of degraded carrageenan from undegraded carrageenan under reaction conditions similar to those of normal digestion. The concern has focused on the potential for degraded carrageenan to be formed by acid hydrolysis in the stomach and the possibility that this material could promote cancer of the colon. In 1987, degraded carrageenan was classified by the International Agency for Research on Cancer (IARC) as 2B, a possible human carcinogen, based on animal study data. Native, undegraded carrageenan has been classified by IARC as 3, unclassifiable with respect to carcinogenicity in humans.<sup>6</sup> To clarify, native, undegraded carrageenan is a mixture of highly sulfated polygalactosides extracted from seaweeds as used in foods. The cancer-causing degraded carrageenan is prepared from the extract of *Eucheuma spinosum* by partial hydrolysis. Again, there is concern that undegraded, native carrageenan can degrade in the human gut.

In response to Tobacman's article, the FDA did another review and deemed carrageenan safe. It was also determined to be safe at the 57th meeting of the Joint Food and Agriculture Organization of the United Nations/World Health Organization Expert Committee on Food Additives (JECFA) in Rome in June 2001. No one could agree on an acceptable daily intake for humans. Instead, the FAO/WHO Expert Committee on Food Additives (JECFA) rated the acceptable daily intake (ADI) of carrageenan as "not specified."<sup>7</sup> Being convinced of the inflammatory and harmful effects of carrageenan in food, Tobacman in 2008 petitioned the FDA to prohibit the use of carrageenan in food. Her petition cited decades of publicly funded, peer-reviewed studies on carrageenan-induced inflammation in animals and cells. The FDA responded with a letter of denial, without a review.

### Inflammatory Effects

Several studies outline the inflammatory effects of carrageenan and various mechanisms of actions in both animal and human cell studies. In a 2013 study, an in vitro model was established to evaluate the inflammatory effects of  $\kappa$ -CGN. A coculture system comprising human intestinal epithelial-like Caco-2 cells and phorbol myristate acetate (PMA)-stimulated THP-1 macrophage cells was used. The results showed that the secretion levels of TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 from the two cell types were increased significantly by carrageenan.<sup>8</sup> The results also clearly demonstrate that  $\kappa$ -CGN severely damaged the intestinal epithelial Caco-2 cell monolayers in the coculture system.

In 2014, researchers showed that exposure of human colonic epithelial cells in culture and of mouse colonic epithelium in vivo to low concentrations of carrageenan activated the Wnt/ $\beta$ -catenin signaling pathway, leading to increases in nuclear  $\beta$ -catenin, T-cell factor/lymphoid enhancer factor activation, and cyclin D1 expression.<sup>9</sup> The effects were mediated through carrageenan-induced reactive oxygen species (ROS). Carrageenan exposure and ROS production inhibited thioredoxin reductase activity and increased oxidation of nucleoredoxin. The authors concluded that dietary carrageenan could contribute to colon cancer through these mechanisms.<sup>9</sup>

Studies back in 2012 showed the mechanism of the inflammatory effects of dietary carrageenan. In human colonic epithelial cells, carrageenan triggers innate immune pathways of inflammation. The carrageenan-induced inflammatory cascades involve TLR4- and BCL10-dependent activation of NF- $\kappa$ B, leading to increased IL-8 production.<sup>10</sup> It has even been proposed that carrageenan-induced inflammation can cause glucose intolerance, insulin resistance, and impaired insulin. These effects are consistent with the role of TLR4-induced inflammation reported in diabetes and carrageenan stimulation of TLR4-mediated inflammatory cascades.<sup>10</sup>

Older studies showed that another inflammatory mechanism of carrageenan is through its effects on tumor necrosis factor-alpha (TNF- $\alpha$ ). A 2010 study highlighted the effects of carrageenan on TNF- $\alpha$ , demonstrating that exposure to CGN drives TNF- $\alpha$ -stimulated cells toward inflammation rather than toward apoptotic cell death. The

authors even suggest that CGN exposure may compromise the effectiveness of anti-TNF- $\alpha$  therapy.<sup>11</sup>

### Safety

So, is carrageenan in food safe? It depends on whom you ask. Most US regulating agencies state that food-grade carrageenan is safe. A two-part review published in *Critical Reviews in Toxicology* deemed it safe as well.<sup>12,13</sup> Newer studies looking at the mechanism of action of carrageenan clearly show a cellular inflammatory response. Tobacman continues her research and patient case studies demonstrating harmful health effects in the human gut. The Cornucopia Institute is calling for the removal of carrageenan from products and providing consumers with easy-to-use lists of foods with and without carrageenan.<sup>14</sup> Recently, WhiteWave Foods has caved in to the pressures of consumer concerns and announced that it will remove carrageenan from its Horizon and Silk products. Stoneyfield Farm and Horizon have already removed the ingredient.

### Summary

Carrageenan belongs to a group of polysaccharides extracted from certain species of red seaweeds. It is used primarily as a gelling, thickening, and stabilizing agent. The controversial additive is in numerous foods, including dairy products such as ice cream, milk, cottage cheese, whipped cream, and yogurt, as well as many nondairy and cow's-milk alternative products. Studies have shown inflammatory effects in animals and humans and links to inflammatory bowel disease. However, the FDA deems carrageenan a safe food additive, as does the US National Organic Standards Board.

### Notes

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# Anti-Aging Medicine

by Ronald Klatz, MD, DO, and  
Robert Goldman, MD, PhD, DO, FAASP

[www.worldhealth.net](http://www.worldhealth.net)



## Anti-Aging Insights on Inflammation

The body deploys the inflammatory response as a defense mechanism to counter infection. However, unchecked chronic inflammation can be a deleterious process, contributing to conditions from heart disease to irritable bowel syndrome to cognitive decline. Chronic inflammation also reduces the number of vital, healthy years. Vishwa Deep Dixit, from Yale School of Medicine (Connecticut, US), and colleagues identified a compound, known as Nlrp3, as a trigger of aging-related inflammation. The team revealed that this compound causes a loss of function that manifests as insulin resistance, bone loss, frailty, and cognitive decline. The study authors are hopeful that future therapeutics targeted at lowering Nlrp3 might "delay multiple age-related chronic diseases."

Youm Y-H, Grant RW, McCabe LR, et al. Canonical Nlrp3 inflammasome links systemic low-grade inflammation to functional decline in aging. *Cell Metab.* 2013;18 (4):519-532.

### Inflammation and Obesity

The expression of inflammation-associated genes in fat tissue may contribute to obesity. Marjukka Kolehmainen and colleagues from the University of Eastern Finland assessed a group of obese adults with features of the metabolic syndrome who participated in an 18- to 24-week randomized intervention study comparing a Nordic diet (consisting of whole-grain products, vegetables, root vegetables, berries, fruit, low-fat dairy products, rapeseed oil, and three servings of fish per week) with a control diet (low-fiber grain products, butter-based spreads, and limited intake of fish). Participants were asked to maintain their body weight unchanged during the intervention, and no significant weight changes occurred during the study period. Samples of the participants' adipose tissue were taken at the beginning and end of the study, and a transcriptomics analysis was performed in order to study the expression of genes. The team observed differences

in the function of as many as 128 different genes in the adipose tissue of the group consuming the Nordic diet vs. control group. In the Nordic diet group, the expression of several inflammation-associated genes was lower than in the control group. The study authors report: "A healthy Nordic diet reduces inflammatory gene expression in [subcutaneous adipose tissue] compared with a control diet independently of body weight change in individuals with features of the metabolic syndrome."

Kolehmainen M, Ulven SM, Paananen J, et al. Healthy Nordic diet downregulates the expression of genes involved in inflammation in subcutaneous adipose tissue in individuals with features of the metabolic syndrome. *Am J Clin Nutr.* January 2015;101:228-239.

### Inflammation and Sensory Functions

Bioinflammation – the body's response to injury, which may be associated with aging-related concerns from Alzheimer's disease to cancer, may trigger hearing loss.

Michael D. Seidman and colleagues from Henry Ford Hospital (Michigan, US) examined the potential protective mechanism of resveratrol, an antioxidant substance found abundantly in red grapes and red wine, to reduce temporary threshold shifts and decrease cochlear hair cell damage following noise exposure. The team designed a study to identify the potential protective mechanism of resveratrol following noise exposure by measuring its effect on cyclooxygenase-2 (COX-2; key to the inflammatory process) protein expression and formation of reactive oxygen species, which plays an important role in cell signaling and homeostasis. The data revealed that acoustic overstimulation causes a time-dependent upregulation of COX-2 protein expression. And, resveratrol significantly reduces reactive oxygen species formation, inhibits COX-2 expression, and reduces noise-induced hearing loss following noise exposure in rats. Observing that "by giving animals resveratrol, we can reduce the amount of hearing and cognitive decline," the study authors submit that their



findings suggest that resveratrol may exert a protective effect from noise-induced hearing loss by the inhibition of COX-2 expression and reactive oxygen species formation.

Seidman MD, Tang W, Bai VU, et al. Resveratrol decreases noise-induced cyclooxygenase-2 expression in the rat cochlea. *Otolaryngol Head Neck Surg.* 2013 Feb 4.

### Inflammation and Mental Health

Elevated levels of C-reactive protein, a marker of inflammatory disease, may be associated with increased risk of psychological distress and depression. Marie Kim Wium-Andersen and colleagues from Copenhagen University Hospital (Denmark) analyzed CRP levels using data from two general population studies in Copenhagen, which included 73,131 men and women aged 20 to 100 years. Increasing CRP levels were associated with increasing risk for psychological distress and depression in analyses. Other analyses suggest that increasing CRP levels also were associated with increasing risk for hospitalization with depression, according to the study results. The study authors conclude: "Elevated levels of [C-reactive protein] are associated with increased risk for psychological distress and depression in the general population."

Wium-Andersen MK, Orsted DD, Nielsen SF, Nordestgaard BG. Elevated C-reactive protein levels, psychological distress, and depression in 73 131 individuals. *Arch Gen Psychiatry.* Dec. 24, 2012;1-9.

Evidence suggests that certain nutrients and lifestyle choices may serve as effective approaches that may help to curb the chronic inflammatory response.

### Look to Nature to Lower Inflammation

"Feel-good" emotions triggered by enjoying nature's great wonders may lower a person's cytokines. Cytokines are proteins that prompt for increased activity of the immune system, a process necessary to combat infection. However, when the mechanism goes into overdrive, it may contribute to heart disease, type 2 diabetes, autoimmune diseases, mood disorders, and more. Jennifer Stellar from the University of California, Berkeley (US), and colleagues completed two separate experiments, enrolling over 200 young adults. Participants reported on a given day the extent to which they had experienced such positive emotions as amusement, awe, compassion, contentment, joy, love, and pride. Samples of gum and cheek tissue, known as oral mucosal transudate, taken that same day showed that those who experienced more of these positive emotions, especially awe, wonder, and amazement, had the lowest levels of the cytokine interleukin 6, a marker of inflammation. Observing that "awe ... was the strongest predictor of lower levels of pro-inflammatory cytokines. These effects held when controlling for relevant personality and health variables," the study authors submit: "This work suggests a potential biological pathway between positive emotions and health through proinflammatory cytokines."

Stellar JE, John-Henderson N, Anderson CL, Gordon AM, McNeil GD, Keltner D. Positive affect and markers of inflammation: discrete positive emotions predict lower levels of inflammatory cytokines. *Emotion.* 2015 Jan 19.

### Apple Compounds Abate Inflammation

Apple peel is an abundant source of triterpenoids – plant-based compounds thought to influence expression of IP-10, a gene linked to inflammatory disorders including irritable bowel disease. Elke Richling and colleagues from University of Kaiserslautern (Germany) studied the effects of ursanic, oleanic, and lupanic pentacyclic triterpenoids found in apple peel for their anti-inflammatory effects, using colon cancer cells that were exposed to the triterpenoids and then stimulated with pro-inflammatory cytokines. Finding that the apple peel compounds inhibited the expression of IP-10, the study authors submit: "The present study confirms that

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Dr. Nicholas DiNubile, MD

## Anti-Aging Medicine

▶ triterpenoids present in apple peel ... may be implicated in the anti-inflammatory properties of apple constituents, suggesting that these substances might be helpful in the treatment of [irritable bowel disease] as nutrient supplements."

Mueller D, Triebel S, Rudakovski O, Richling E. Influence of triterpenoids present in apple peel on inflammatory gene expression associated with inflammatory bowel disease (IBD). *Food Chem*. 15 August 2013;139(1-4):339-346.

### Inflammation Intervention

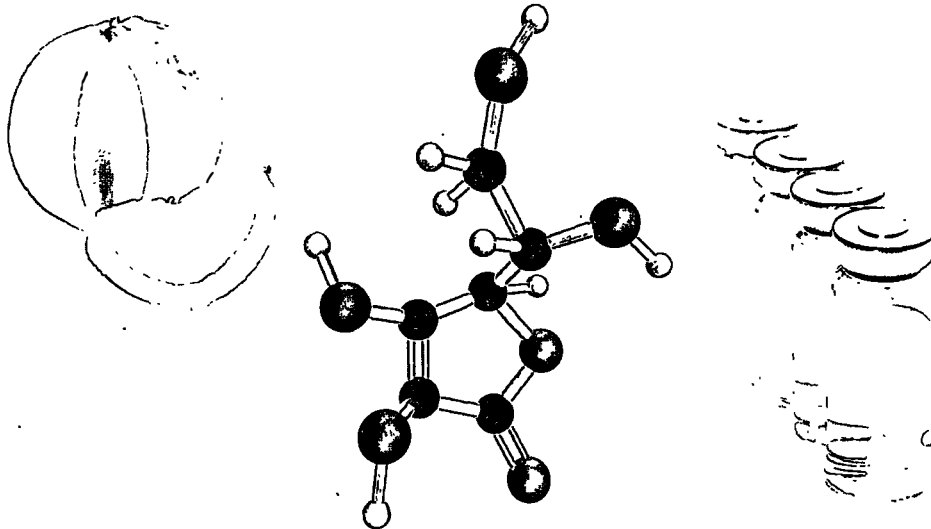
Regular exercise may exert physiological changes that decrease inflammation on a local and systemic level. Nicholas Young and colleagues from Ohio State University (US) completed an in vivo study measuring the regulation and activation of NF-kappa-beta, a protein complex that controls many genes involved in inflammation that is found to be chronically active in many inflammatory diseases, in mice. An inflammatory response was created in mice both before and after exercise through an injection of lipopolysaccharides. The impact of exercise was measured over time following the inflammatory response. There was a strong systemic and local inflammatory response upon

injection of lipopolysaccharides, which was strongest at 2 hours postinjection. NF-kappa-beta activation was seen as a result of the lipopolysaccharides and was detected in lymphatic tissues throughout the mouse. In those groups where mice were exercised pre- and post-LPS injection, the NF-kappa-beta activation was significantly inhibited in whole-body systemic analysis. The effect of exercise on the inhibition of NF-kappa-beta activation was identified as a transient effect, lasting only 24 hours after exercise. Importantly, the role of exercise in inhibiting NF-kappa-beta activation was linked to the suppression of multiple pro-inflammatory cytokines.

Young N et al. Abstract #OP0109. Presentation at EULAR 2014 (European League Against Rheumatism), 12 June 2014.

To stay updated on the latest breakthroughs in natural approaches to manage the body's process of inflammation, visit the World Health Network ([www.worldhealth.net](http://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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# Review of Hormone Aberrations in Rheumatoid Arthritis and Systemic Lupus Erythematosus: Testing and Treatment Suggestions

by Alena Guggenheim, ND

## Clinical Context

Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are common and often debilitating diseases. The prevalence and incidence of autoimmune diseases is increasing, thus pressing the integrative medical community to understand the etiology more deeply in order to improve treatment approaches. The annual incidence of RA is about 40 per 100,000 and the prevalence among women is 9.8 per 1000 and 4.1 per 1000 for men.<sup>1</sup> Women are affected 2 to 3 times more often than men. The prevalence of SLE is 20 to 150 cases per 100,000, again with a strong female predominance of 10:1. SLE prevalence is more common in African American women, with rates of 406/100,000 compared with 164/100,000 in Caucasians.<sup>2</sup> The incidence of SLE does appear to be increasing: rates tripled between a 1950–1979 cohort and a 1980–1992 cohort, although this is complicated by better detection of mild disease.<sup>3</sup>

Conventional treatments often fall short in both these diseases. Biologic medications used in the treatment of RA produce clinically relevant improvement 50% of the time.<sup>4</sup> Mortality in conventionally treated SLE patients shows a threefold increase when compared with the general population.<sup>5</sup> Clinical remission with conventional treatment is rare, and morbidity from treatments is significant. Integrative physicians can formulate effective adjunct treatments for patients with RA and SLE by understanding and therapeutically addressing hormonal aberrations associated with these diseases.

RA onset is highly variable and ranges from insidious, sudden, migratory, and intermittent to unrelenting. It is most often characterized by symmetric swelling, pain, and stiffness in the hands. The most common joints affected are the metacarpal phalangeal joints (MCPs), proximal interphalangeal joints (PIPs), wrists, elbows, knees, midfoot and the metatarsal phalangeal joints (MTPs), although this disease can affect any joint in the body except the sacroiliac

joints, thoracic spine, and lumbar spine. Patients often experience global morning stiffness that lasts >1 hour. In 2010, the American College of Rheumatology updated the diagnostic criteria (Table 1). The new criteria allow for earlier diagnosis, thus allowing physicians to institute disease modifying antirheumatic medications (DMARDs) more quickly.

**Table 1: American College of Rheumatology Rheumatoid Arthritis Diagnostic Criteria**

6 of 10 points
CCP and RF (0–3)
# and size of involved joints (0–5)
>6 weeks' duration <sup>1</sup>
ESR and CRP <sup>1</sup>

The diagnosis of SLE is more complex and can be quite insidious compared with RA, making age of onset difficult to determine, but generally it affects women of childbearing age. SLE is a multisystem, autoimmune inflammatory condition characterized by a fluctuating, chronic course from mild and long-term to rapidly fatal. The hallmark lab finding in SLE is the anti-nuclear antibody (ANA) and anti-dsDNA antibody. Given that the immune system has mounted a response to the very core of the body, it makes sense that many systems can be affected and the symptoms picture is highly variable (Table 2). The American College of Rheumatology Criteria are shown in Table 3 (p. 46).

**Table 2: SLE Systems Affected**

Endocrine/Metabolic	Gastrointestinal
Hematological/Lymphatic/Immunologic	Mucocutaneous
Musculoskeletal	Nervous
Renal/Urologic	Cardiovascular

# Hormone Aberrations

**Table 3: American College of Rheumatology Systemic Lupus Erythematosus Diagnostic Criteria Must Have 4 of 11 Criteria**

Photosensitivity (rash)	
Nonerosive arthritis	Pleurisies or pericarditis
Discoïd rash	Oral/nasopharyngeal ulcers
Malar rash	Neurologic disorder – psychosis or seizures
Hematologic disorder: hemolytic anemia, leukopenia (<4000/mL), lymphopenia (<1500/mL), thrombocytopenia (<100,000/mL)	Renal disorder: proteinuria (>3+ dipstick or >0.5 g/d) or cylindruria (cellular casts)
Positive antinuclear antibody (95%–100%) in the absence of drugs known to cause positive ANA	Immunologic disorder (antibodies to DNA, Smith, cardiolipin, lupus anti-coagulant, or false positive serological test for syphilis)

The etiologies of RA and SLE are a complex interplay between infectious organisms, microbiome/gut immune changes, psychoneuroimmunology factors, environmental toxicity, nutritional deficiencies, dietary factors, genetic and epigenetic changes, and hormones. The focus of this review will be on assessment and treatment of adrenal, gonadal, and adipose hormone aberrations that drive the autoimmune process and inflammation.

## Adrenal and Gonadal Hormones

Untangling the complexity of hypothalamic-pituitary-adrenal axis (HPA) and hypothalamic-pituitary-gonadal axis (HPG) alternations is challenging. Patterns change from the onset of disease and are highly influenced by inflammatory cytokines and glucocorticoid treatment. There are some basic patterns in the HPA axis that predispose an individual to RA and SLE and drive disease activity. Patients often have low serum DHEA-S and low serum, urinary, or salivary cortisol.<sup>6-8</sup> Of these hormones, low DHEA-S is the most strongly correlated with disease activity in RA.<sup>9</sup>

To make matters worse, patients with RA and SLE likely have elevated aromatase activity due to inflammatory cytokine signaling. What little adrenal androgens they manage to make are converted to estrogens. Then, in turn, patients with SLE and RA tend to overly metabolize estrogens into 4- or 16- hydroxysterones. One study found that urinary concentrations of the 2-hydroxylated estrogens were 10 times lower in patients with RA and SLE than in healthy controls and that the ratio of 16-hydroxysterone/2-hydroxysterones was 20 times higher in RA and SLE patients than in controls. B and T cells both have estrogen receptors (ER) on their membranes and respond to E2 by increasing IgG and IgM production. 16-hydroxysterone

also appears to exacerbate a TH2 response.<sup>10,11</sup> 4- and 16-hydroxysterones increase B cell proliferation in autoimmune diseases, and patients with higher levels of these metabolites have increased disease activity scores.<sup>12</sup> To date, there have been no clinical studies on the effect of addressing estrogen metabolism on clinical outcomes.

Exogenous hormones also play a role in risk and disease severity, especially in SLE. The use of estrogen-containing contraceptive agents is associated with a 50% increase in risk of developing SLE.<sup>13</sup> Environmental estrogens present in pesticides, plastics, and detergents also contribute to risk of RA and SLE and increase disease flares.<sup>14,15</sup>

The role of progesterone in RA and SLE is not fully understood and may have positive or negative effects. It has been observed that patients with RA often have symptom improvement during luteal phase and during pregnancy when progesterone levels are very elevated.<sup>16</sup> This may be due to progesterone's immunomodulatory effect: it appears to decrease Th1 and Th17 cytokines.<sup>17</sup>

Elevated prolactin is associated with many autoimmune diseases such as RA, SLE, MS, Hashimoto's thyroiditis, and Sjögren's syndrome. It appears that prolactin increases TNF $\alpha$  secretion from monocytes in RA patients and interferes specifically with B cell tolerance induction.<sup>18,19</sup> The role of prolactin in RA and SLE pathogenesis is not well understood, and more study is needed to prove that elevated prolactin increases disease activity.

## Adipose Hormones

It is important to understand that immune system function depends on metabolic health and that obesity is a predisposing risk factor for RA and SLE. Adipose is not an inert substance; it can make inflammatory cytokines such as TNF $\alpha$ , IL-1 and IL-6, and a class of molecules termed adipokines. Adipokines are proteins made by fat that are highly biologically active. The adipokines that have been best characterized in RA and SLE are adiponectin, leptin, and visfatin, all of which are increased compared with matched controls.

Leptin signals satiety in the hypothalamus but also has receptors on NK cells, T and B cells, and monocytes and can act similarly to inflammatory cytokines on these cells. Increased circulating leptin is associated with many inflammatory diseases such as inflammatory bowel disease, SLE, RA, type 1 diabetes, Behcet's disease, and Graves'. Leptin is higher in women than men, further elucidating the female predominance of SLE and RA.

Adiponectin is an adipokine made by metabolically "healthy" fat. Most research has focused on the antidiabetic and antiarthrogenic activity of this hormone. In SLE and RA, adiponectin is elevated, which may be a compensatory mechanism that is trying to balance the elevated leptin and visfatin, which are increased over matched controls.<sup>20,21</sup> It has been speculated that in the presence of inflammatory disease, higher adiponectin may not be desirable because it may in fact become pro-inflammatory and release

prodegradative enzymes such as matrix metalloproteinases (MMPs) and nitric oxide in chondrocytes.<sup>22</sup>

Of all the adipokines studied in RA, elevated adiponectin is the best predictive marker for joint destruction. If adiponectin is low at the onset of disease, this has high negative predictive value for disease progression.<sup>22</sup>

### Testing and Treatment

With a deeper understanding of the patterns of hormonal dysfunction in rheumatoid arthritis and SLE, we can turn our attention to diagnosis and treatment. There are many options available for hormone testing. Sex and adrenal hormones are best assessed through urine or saliva testing and adipokines via serum. A 24-hour urine test can easily assess estrogen metabolism (2-, 4-, 16-hydroxyestrones), total estrogens, androgens, cortisone, cortisol, and DHEA. The only drawback of a 24-hour urine collection is that it does not assess the diurnal pattern of cortisol release. This can be assessed with either saliva testing or dried urine spot testing for hormones. The dried urine spot testing offers the benefit of estrogen metabolism and diurnal cortisol patterns in one test and can be used to assess hormones in patients treated with sublingual hormone therapy.

### Adrenal Hormones

There are many possible benefits of treating adrenal hormone dysfunction in RA and SLE patients. Quality of life; disease activity; and improving side effects from glucocorticoid treatment such as the increased risk of infection, osteoporosis, and myopathy have all been evaluated, with positive outcomes.<sup>23-29</sup>

Treatment of adrenal hormone imbalances should always start with the basics of establishing strong routines and stress management techniques. Many adrenal herbs are also immunomodulating and should be used cautiously only in stable RA and SLE patients. These include but are not limited to *Withania somnifera*, *Glycyrrhiza glabra*, *Eleutherooccus senticosus*, *panax spp.*, *Cordyceps sinensis*, and *Rhodiola rosea*.

Adrenal hormone replacement therapy is often well tolerated, and a number of different delivery forms are available. If a patient has a cortisol and DHEA deficiency, it is important to provide replacement for both, as DHEA only replacement can cause a worsening cortisol deficiency. One option for patients deficient in both is pregnenolone, dosed between 25 and 100 mg per day. Most female patients will tolerate DHEA dosed under 50 mg without getting symptoms related to overconversion to androgens. Recall that many of these patients are androgen deficient and it is common that DHEA alone can address both hormone deficiencies. If patients develop acne, increased hair growth, or anger issues, 7-keto-DHEA is a good option.

Cortisol deficiency can be addressed with hydrocortisone (Cortef) at subphysiological dosing (< 20 mg total per day) or standardized adrenal glandular. If pregnenolone is used

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for dual replacement, it is important to assess if it is well metabolized with either urine or saliva testing.

### Androgens

Androgen deficiency can be caused by an overexpression of the aromatase enzyme. Aromatase converts DHEA to estrogens rather than testosterone. It is upregulated by inflammatory cytokines such as TNF $\alpha$ , IL-6 and IL-1, and adipokines. The aromatase enzyme can also be inhibited with many integrative interventions. *Turnera diffusa* (damiana) has been used in traditional botanical medicine as an aphrodisiac, and now studies have shown that the constituents pinocembrin and acacetin have strong antiaromatase activity.<sup>30</sup> *Scutellaria spp.* also have antiaromatase activity, and could be a good choice of therapy in patients who have concomitant anxiety.<sup>31</sup>

Dietary polyphenols can inhibit aromatase and decrease inflammatory mediators produced by adipose tissue. Resveratrol, curcumin, and epigallocatechin gallate (EGCG) have been well studied for in vivo antiaromatase activity.<sup>32</sup> If patients are using red wine as a source of resveratrol, it is very important to emphasize moderation because the alcohol will decrease liver metabolism of estrogens. This effect has been studied in red wine, and the strength of aromatase inhibition is stronger than the alcohol effect on the liver processing if intake is limited to 2 glasses per week.<sup>33</sup>

Borrowing from the hormone sensitive cancer research, we have also learned that melatonin can also modulate aromatase activity, highlighting the importance of healthy sleep/wake cycles.<sup>34</sup> Basic sleep hygiene includes going to bed at the same time each night, sleeping in the pitch black, avoiding all screens for 2 hours prior to sleep, and exposure to natural light within 30 minutes of waking.

In the face of overt inflammation, aromatase inhibition alone may not be sufficient to correct the androgen deficiency seen in RA and SLE. Many patients benefit clinically from hormone replacement therapy with testosterone. Testosterone cannot be delivered orally and must be given in a topical preparation (absorption is highly variable), sublingual troche, or implanted trocar. A reasonable starting dose of sublingual troche is 5 mg, titrated up/down based on labs and symptoms.

### Estrogen

First and foremost, patients must be strongly counseled to avoid xenoestrogens. Table 4 provides an abbreviated list of sources and types of xenoestrogens. Encouraging patients to switch to an organic diet and avoiding plastics in food storage is an important first step. One study found that switching to organic foods can drop the level of organophosphate pesticides in the blood by 89% in one week.<sup>35</sup>

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**Table 4: Common Xenoestrogens**

Pesticides atrazine organochlorines	Plastics bisphenol A bisphenol S
Cosmetics phthalates parabens	Estrogen Contraception oral patch etc
Dry cleaning	Water pollution
Dairy products	Meat products

Estrogen metabolism defects can be well managed with dietary changes and nutraceutical interventions. 3,3'-diindolylmethane (DIM) is a compound found in cruciferous vegetables that has been well studied in breast, cervical, and thyroid cancers for its antiestrogenic, positive estrogen metabolism effects. DIM strongly influences estrogen metabolism to help favor 2-hydroxyestrone.<sup>36-39</sup> Patients should be encouraged to eat at least 2 cups of cruciferous vegetables per day, and if the ratio of urine 2:16 OH-estrone is less than 2, DIM should be given. Reasonable dosage range for DIM is 200 to 600 mg per day in divided doses. The ideal diet also includes high-flavonoid foods such as green tea, fruits, and vegetables to encourage healthy estrogen metabolism.<sup>40</sup>

## Prolactin

If prolactin is elevated, *Vitex angus* is a very good option for treatment.<sup>41,42</sup> *Vitex* can have the collateral benefit of increasing luteal phase progesterone levels that may benefit symptoms. Hyperprolactinemia can also be addressed via dopamine agonism. While the prescription medication bromocriptine is an option, tyrosine supplementation or *Mucuna pruriens* can also be effective dopamine agonists.<sup>43-45</sup>

## Adipokines

It is beyond the scope of this review to fully discuss methods to modulate adipokines and improve metabolic health. For patients with RA and SLE, metabolic health can benefit from short-term fasting, exercise, and improvement in sleep cycles. In RA patients, fasting appears to increase T<sub>reg</sub> cells and induce CD4+ lymphocyte hyporeactivity.<sup>46</sup> Adequate sleep can decrease circulating leptin levels.<sup>47</sup> From a dietary perspective, increasing protein levels to 30% of caloric intake and limited carbohydrates can also improve elevated leptin.<sup>48</sup>

All patients should be encouraged to have a minimum 12-hour fast between dinner and breakfast. For motivated patients, a once-weekly longer fast between 14 and 24 hours may be highly beneficial. The metabolic and immune benefits of intermittent fasting are currently being studied in rheumatoid arthritis as well as many other diseases.<sup>49</sup>

Increasing physical activity can also decrease leptin, as well as inflammatory cytokines.<sup>50</sup> There are many options for increasing physical activity. One form of exercise that has been well shown to improve leptin is high-intensity interval training; however, patients with active joint disease may not tolerate this form of exercise training, in which case water-based therapy or pedometer activity tracking can be used.

## Conclusion

To date, no one has researched the clinical impact of simultaneously addressing adrenal, sex, and adipose hormones in RA and SLE. In my experience, treating hormones is absolutely fundamental to obtaining remission without the use of pharmaceuticals and can be that "magic piece" after dietary changes, microbiome modulation, gut healing, and aggressive anti-inflammatory strategies have failed to adequately manage symptoms. Table 5 provides a summary of recommendations. Assessment and appropriate treatment can also minimize side effects and minimize dosage of conventional DMARD therapy. Not only can appropriate hormone treatment affect disease activity, it can also substantially improve quality-of-life measures such as mood and energy, for which your patient will be very grateful.

**Table 5: Summary of Recommendations**

<b>Adrenal Hormones</b>	
Stress management	Establish routines
Adrenal glandulars	DHEA
Hydrocortisone	Caution with adrenal-stimulating herbs
<b>Androgen Support</b>	
Dietary polyphenols	Dietary flavonoids
Melatonin	<i>Turnera diffusa</i>
<i>Scutellaria</i> spp.	DHEA
Testosterone replacement	Sleep hygiene
<b>Estrogen Support</b>	
Avoid xenoestrogens	Dietary flavonoids
Diindolylmethane	Dietary cruciferous vegetables
Weight loss	Luteal phase progesterone replacement
<b>Prolactin Support</b>	
<i>Vitex angus</i>	Tyrosine
<i>Mucuna pruriens</i>	
<b>Adipokine Support</b>	
Short-term fasting	Weight loss
Low-carbohydrate diet	Exercise
Optimal sleep cycles	Protein 30%

## Notes

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# Mitochondria: Overlooking These Small Organelles Can Have Huge Clinical Consequences in Treating Virtually Every Disease

by Chris D. Meletis, ND, and Kimberly Wilkes

The mitochondria are tiny organelles that are often overlooked in the treatment of disease. Yet, mitochondrial dysfunction drives the development of – or worsens the symptoms of – some of the most devastating diseases of modern times, including cancer, cardiovascular disease, Alzheimer's, Parkinson's, autism, and diabetes, as well as many other conditions that don't at first glance seem related to the mitochondria such as autism, bipolar disorder, or osteoarthritis. Ironically, not only are the mitochondria often ignored by many conventional doctors in the treatment of disease, the same patients suffering from mitochondrial-related diseases are given drugs that impair mitochondrial function.

The volumes of research about the mitochondria and mitochondrial dysfunction indicate that what is now known about the mitochondria extends far beyond what we learned in basic biology. An abundance of fascinating research continues to spotlight the role that mitochondrial dysfunction plays in most – if not all – diseases. Mitochondrial dysfunction's role in disease is particularly concerning, given that the mitochondria of the modern human are subjected to some assaults never experienced by people who lived before the early 1900s. Therefore, it's critical to become familiar with these tiny organelles, to learn how their dysfunction can contribute to disease, and to discover the best ways to protect the mitochondria and ensure that they are functioning optimally.

## How Mitochondria Function: A Brief Recap

Before we discuss mitochondrial dysfunction, it is important to review the way in which mitochondria function. It starts with glycolysis, which occurs outside the mitochondria. Glycolysis converts glucose into pyruvate, which is then converted into acetyl-CoA. The citric acid cycle (also known as the Krebs cycle) then takes over inside the mitochondria to convert the acetyl-CoA into the reduced form of nicotinamide adenine dinucleotide (NADH) and the reduced form of flavin adenine dinucleotide (FADH<sub>2</sub>), which are important in a process known as oxidative phosphorylation (OXPHOS).

Through their oxidation and breakdown, NADH and FADH<sub>2</sub> help fuel OXPHOS, which is responsible for producing the energy that powers cells. In OXPHOS, electron donors transfer electrons to electron acceptors by using electron transport chains. Energy is released when an electron is transferred to an acceptor such as oxygen. The mitochondria, using the enzyme ATP synthase, use the energy produced in the electron transport chain to manufacture adenosine triphosphate (ATP) from adenosine diphosphate (ADP). ATP is to our bodies what gasoline is to our cars. We could not function without it and any defects in ATP production often result in fatigue. Metabolic processes that use ATP as an energy source convert it back into its precursors. Therefore, ATP is continually recycled.

The energy produced by OXPHOS causes protons (particles with positive electric charge) to be transported across the inner mitochondrial membrane. This creates a gradient that produces additional energy.

There are five complexes in the electron transport chain:

- Complex I (NADH dehydrogenase) – Complex I is an enzyme that catalyzes the two-electron oxidation of the reduced form of nicotinamide adenine dinucleotide (NADH) by coenzyme Q10 (ubiquinone). During Complex I, ubiquinone also is reduced to ubiquinol, which results in the generation of energy by the creation of a proton gradient.
- During Complex II (succinate dehydrogenase) reactions, succinate is oxidized into fumarate and ubiquinone is reduced. This process does not produce as much energy as Complex I, and is unable to create a proton gradient.
- Complex III (cytochrome c reductase) results in the oxidation of one molecule of ubiquinol and the reduction of two molecules of cytochrome c, a protein responsible for transferring electrons. This reaction very efficiently transfers protons across the mitochondrial membrane, creating a proton gradient, thereby assisting with energy production.
- Complex IV (cytochrome c oxidase) is an enzyme that oversees the last step in the electron transport chain. During this reaction, electrons are transported to oxygen, which is reduced to water, and protons are transported across the mitochondrial membrane.



- Complex V (ATP synthase) is the last enzyme utilized in oxidative phosphorylation. By tapping into the energy reservoir generated by the proton gradient across a membrane, ATP synthase assists with the creation of ATP from ADP and phosphate.

Oxidative phosphorylation is the most efficient ATP producer. For example, for every 1 glucose molecule oxidized, only 2 ATP molecules are generated by glycolysis, whereas the electron transport chain can generate between 30 to 36 ATP molecules.

Oxidative phosphorylation is a critical part of normal metabolism, but it has a dark side as well. The process produces reactive oxygen species (ROS) – for example, superoxide and hydrogen peroxide – which can result in cellular damage and lead to disease and accelerated aging.<sup>1</sup>

### Are GM Foods Harming the Mitochondria?

The mitochondria are subjected to a number of modern-day insults, including toxins. Although there are many toxins that impair mitochondrial function, one of the most prevalent is glyphosate (used in Roundup). Because genetically modified (GM) foods are engineered to be resistant to glyphosate, they're slathered with this herbicide.

This is particularly disturbing given that every year, Americans are eating their body weight in GM foods, according to an analysis by the Environmental Working Group.<sup>2</sup> Additionally, near the Mississippi Delta farmlands, glyphosate and its degradation product aminomethylphosphonic acid (AMPA) were found in 75% or more of air and rain samples in 2007.<sup>3</sup> This indicates that glyphosate is extremely prevalent in agricultural areas.

Glyphosate is especially toxic to the mitochondria when it is combined with surfactants or adjuvants, primarily in the formulation known commercially as Roundup. These surfactants or adjuvants are claimed to be inert, but research paints a different picture. Researchers have shown that adjuvants in glyphosate-based herbicides were as much as 10 times more harmful than glyphosate itself.<sup>4</sup> One group

of researchers found Roundup to be 125 times more toxic than glyphosate alone.<sup>5</sup>

Strong evidence indicates that surfactants or adjuvants disrupt cell membranes and initiate toxic changes to the mitochondria. Studies have shown that adjuvants have been found to exert their toxic effects through interfering with mitochondrial respiration.<sup>3</sup> One study of rat liver mitochondria found that Roundup suppressed mitochondrial Complexes II and III. Treatment of the mitochondria with the herbicide formulation resulted in uncoupling of oxidative phosphorylation, an effect not seen when the mitochondria were treated with glyphosate alone.<sup>6</sup>

Another study investigated the effects of Roundup or glyphosate alone on human buccal epithelial cells of the mouth in order to determine the effects of inhaling the herbicide. Roundup caused cellular membrane damage and mitochondrial dysfunction at levels greater than 40 mg/liter after 20 minutes. Glyphosate alone also was toxic to cellular membranes, but at double the concentration of Roundup used. Both Roundup and glyphosate caused DNA damage, even at lower doses, although Roundup was more toxic than glyphosate alone. Toxicity with Roundup was noted even after short exposure to concentrations 450 times more diluted than that sprayed on agricultural crops.<sup>7</sup>

### Chronic Stress and the Mitochondria

Another modern-day cause of mitochondrial dysfunction is chronic stress. Although our ancient ancestors faced short-term stresses, such as an attack by a saber-tooth tiger, today we deal with chronic, ongoing stressors that take a toll on mitochondrial health.

Researchers have reported that chronic stress results in the production of too much nitric oxide, which could suppress mitochondrial respiratory chain function and trigger oxidative stress.<sup>8</sup> Chronic stress may also cause the mitochondria to produce an overwhelming amount of free radicals, which neurons aren't able to neutralize, causing mitochondrial dysfunction and neuronal cell death.<sup>9</sup>

Chronic stress can deplete the mitochondria's ability to produce energy. The brain is activated by stress, which can produce alterations in the brain's structure and function known as neuronal plasticity. The mitochondria must fuel these changes by producing additional energy. When the mitochondria are working the way they are supposed to, they are able to produce the energy demanded by stress-caused neuronal plasticity, protecting against the development of depression. However, when mitochondrial function is weakened, the brain's energy stores that are used up during stress are not replenished. This compromises neuronal plasticity and may increase the likelihood of developing depression.<sup>10</sup>

### Fructose and Mitochondria

In the US, high-fructose corn syrup was introduced into the food supply in the 1970s. One of the mechanisms by which high-fructose corn syrup may induce type 2 diabetes and obesity is through its ability to cause mitochondrial dysfunction. Rats that were exposed to a high-fructose diet during gestation and lactation had impaired brain mitochondrial function in their old age and decreased mitochondrial phosphorylation efficiency.<sup>11</sup>

Fructose metabolism produces intermediary metabolites that overwhelm mitochondrial capacity in the liver, which can result in the development of hepatic insulin resistance. Additionally, fructose triggers formation of excessive reactive oxygen species, which can overwhelm the mitochondria.<sup>12</sup>

### Some Medications Pose Another Threat

Many medications can cause mitochondrial dysfunction, which has emerged as the mechanism behind many side effects and toxicities of drugs. Some medications can directly affect electron transport chain complexes or damage electron transport chain components. Plus, medications can suppress enzymes necessary for mitochondrial function. In addition, some medications can



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► trigger free radical production, depleting levels of antioxidants such as glutathione. Furthermore, pharmaceuticals can interfere with the absorption of nutrients that the mitochondrial electron transport chain complexes need for proper function.<sup>13</sup>

Many medications for angina, arrhythmia, depression, anxiety, high cholesterol (including statins), cancer, dementia, diabetes, HIV/AIDS, epilepsy, and Parkinson's can cause mitochondrial dysfunction. The antibiotics tetracycline and antimycin A, some barbiturates and anxiety medications, and anesthetics such as bupivacaine, lidocaine, and propofol are all toxic to the mitochondria. Even something as commonplace as aspirin and acetaminophen (Tylenol) can impair mitochondrial functioning.<sup>13</sup>

## Epigenetic Involvement

The mitochondrial damage induced by the factors mentioned above can be transferred to children and grandchildren through epigenetics, heritable changes in gene expression that are not caused by changes in the DNA sequence.<sup>14,15</sup> The epigenetic modification of mitochondrial DNA may be responsible for the pathogenesis of many diseases.<sup>16</sup>

## The Consequences of Mitochondrial Dysfunction

Mitochondrial dysfunction plays a role in the majority of today's most burdensome diseases – including aging itself.

## Aging and the Mitochondria

The mitochondria contain members of gene family referred to as sirtuins, which are involved in longevity. Sirtuins are the conductors of the anti-aging orchestra. These genes control genetic, biochemical, and cellular pathways involved in aging.<sup>17,18</sup> Amplifying the expression of these genes is thought to increase longevity.<sup>19,20</sup>

The mitochondria contain three of the seven mammalian sirtuins, including SIRT3 and SIRT4.<sup>21</sup>

Mitochondrial sirtuins may enhance longevity through mimicking caloric restriction, which protects against age-related disease and dysfunction, including cancer initiation.<sup>22-26</sup>

Beyond the sirtuins, an abundance of scientific evidence shows a strong connection between aging and mitochondrial dysfunction.<sup>27-30</sup> This evidence suggests that as mitochondria are exposed to a cumulative amount of reactive oxygen species and mitochondrial DNA damage, the burden becomes too much to bear, ultimately resulting in decreased lifespan.<sup>26</sup> With age, mitochondrial oxidative phosphorylation becomes less efficient.<sup>31</sup>

## Cancer

Cancer is one of many diseases associated with mitochondrial dysfunction. The risk of developing cancer rises after age 50, which lends support to a potential link between mitochondrial processes involved in longevity and cancer development.<sup>26,32,33</sup> Furthermore, mitochondrial dysfunction in cancer cells is frequently noted in studies and coincides with abnormal cellular metabolism.<sup>34,35</sup> Researchers have found strong support for the likelihood that mitochondrial dysfunction plays an important role in cell transformation and carcinogenesis.<sup>26</sup>

## Autistic Spectrum Disorders (ASD)

Mitochondrial dysfunction is well known to occur in autistic spectrum disorder.<sup>36</sup> The origin of this mitochondrial damage could be partially genetic. However, mitochondrial mutations are found in only 23% of ASD children diagnosed with mitochondrial dysfunction. Therefore, environmental causes such as exposure to heavy metals, exhaust fumes, polychlorinated biphenyls, or pesticides may be more important than genetic factors.<sup>37</sup> The oxidative stress caused by exposure to these toxins may serve as the link between mitochondria dysregulation and ASD.

Endogenous insults such as elevated pro-inflammatory cytokines resulting from an activated immune system could also damage the mitochondria in ASD patients.<sup>38-40</sup>

Other evidence of the presence of mitochondrial dysfunction in ASD patients is the fact that genes involved in the electron transport chain are downregulated (decreased Complex I, III, IV, and V). Genes involved in the citric acid cycle are also downregulated. Furthermore, mitochondrial DNA damage also has been noted in ASD patients.<sup>41-43</sup>

## Mental Disorders

Mitochondrial dysfunction is an underappreciated component of various mental disorders. Bipolar patients experience reduced levels of Complex I of the electron transport chain.<sup>44</sup> Patients suffering from major depression also have abnormalities in Complex I.<sup>45</sup> Similarly, researchers have noted a significant decrease in Complex I activity in schizophrenia patients along with a drop in CoQ10 levels.<sup>46</sup> Mitochondrial abnormalities also have been noted in subjects with obsessive-compulsive disorder.<sup>47</sup>

## Cardiovascular Concerns

Mitochondrial dysfunction is a key player in age-related damage to the heart. The heart has a high metabolic demand and contains a large number of mitochondria. Because ROS is produced in the mitochondria through oxidative phosphorylation, the heart is particularly vulnerable to oxidative damage.<sup>31</sup>

Other evidence for mitochondrial dysfunction's association with cardiovascular disease includes the existence of mitochondrial dysregulation and mtDNA mutations in atherosclerotic plaques.<sup>48-51</sup>

According to one group of researchers, "Development of novel therapeutic approaches for mitochondrial rejuvenation and attenuation of mitochondrial oxidative stress holds promise for reducing cardiovascular mortality in an aging population."<sup>31</sup>

Mitochondrial dysfunction has been associated with the metabolic syndrome (a cluster of risk factors for cardiovascular disease) providing another reason why mitochondrial abnormalities may damage the heart.<sup>52-56</sup>

## Type 2 Diabetes

Diabetes is marked by mitochondrial dysfunction and high oxidative stress levels.<sup>57</sup> Persistently high blood sugar levels harm both mitochondria and mitochondrial DNA.<sup>58</sup> Diabetic patients often experience downregulation of Complex I and/or IV and type 2 diabetes occurs side by side with some diseases related directly to mitochondrial dysfunction such as the genetic diseases Fanconi anemia and Werner syndrome.<sup>59-65</sup>

## Neurodegenerative Diseases

Studies strongly suggest that mitochondria abnormalities may be linked to the development of several neurodegenerative diseases such as Parkinson's disease, Alzheimer's, Friedreich's ataxia, multiple sclerosis, amyotrophic lateral sclerosis, and Huntington's disease.<sup>8</sup> Rat models of Parkinson's disease indicate that reactive oxygen species interfere with mitochondrial processes.<sup>65</sup> Researchers have found that mitochondrial abnormalities caused by amyloid-beta occur early in Alzheimer's disease.<sup>66-72</sup>

## Other Diseases Linked to Mitochondrial Dysfunction

In terms of diseases related to mitochondrial dysfunction, what we've discussed in this article so far is just the tip of the iceberg. For example, mtDNA damage has been noted in osteoarthritis along with downregulated Complexes I, II, and III, and 17 upregulated and 9 downregulated genes.<sup>73-75</sup> Furthermore, in autoimmune diseases antimitochondrial autoantibodies (AMA) can damage the mitochondria.<sup>78</sup> Autoimmune diseases associated with mitochondrial dysfunction include vitiligo, systemic lupus erythematosus, Sjögren's syndrome, rheumatoid arthritis, primary biliary cirrhosis, and psoriasis.<sup>76</sup>

Additionally, researchers have attributed the damage done by obstructive sleep apnea (OSA) to mitochondrial dysfunction. In OSA patients there is a decrease in mtDNA copy number, which is linked to oxidative stress and inflammation.<sup>77</sup>

Other diseases related to mitochondrial dysfunction include

cataracts, fibromyalgia, and non-alcoholic fatty liver disease.<sup>76</sup>

## The Hormonal Link

When supporting optimal hormonal health amongst patients, it is essential to consider the mitochondrial health and function of the target endocrine tissues being treated. Fueling the target mitochondrial cells can dramatically augment therapeutic outcomes. This is because there is an intricate

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interplay between hormones and mitochondria.<sup>77-85</sup> Hormones originate in the mitochondria where cholesterol is converted to pregnenolone, the precursor to all steroid hormones.<sup>78,79</sup> The mitochondrial electron transport chain also plays a role in producing testosterone in the Leydig cells.<sup>80</sup>

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OPTIMAL NUTRITIONAL SUPPORT

# Mitochondria

Furthermore, receptors for estrogens, androgens, and thyroid hormones are located in the mitochondria.<sup>81,82</sup> Estrogens and androgens also are able to shield the mitochondria from damage and estrogen is involved in many aspects of mitochondrial function and biogenesis, including oxidative phosphorylation.<sup>83-86</sup>

## Diagnosing Mitochondrial Dysfunction

Along with clinical observations, an organic acid test is often used to diagnose mitochondrial dysfunction. Organic acids are produced as a result of the breakdown of proteins, carbohydrates, and fats. These acids serve as intermediates in the citric acid (Krebs) cycle.

The presence or elevation of specific organic acids can serve as a marker for mitochondrial abnormalities or indicate exposure to toxins that may harm the mitochondria. For example, 4-hydroxybenzoic acid and 4-hydroxyhippuric acid are metabolites of parabens, toxic compounds found in lotions, cosmetics, other toiletries, and even food.<sup>87,88</sup> Parabens may impair oxidative phosphorylation, resulting in mitochondrial dysfunction.<sup>89</sup> An organic acid test can determine if 4-hydroxybenzoic acid and 4-hydroxyhippuric acid are elevated.

Another example is the organic acid adipic acid (adipate). If the value is elevated it can indicate functional deficiency of carnitine. A deficiency of carnitine can stop long chain fatty acids from entering the mitochondria. This results in insufficient fatty acid oxidation. Organic acid tests also can measure a marker of CoQ10 production.

When interpreting organic acid test results, it is important to be familiar with all the nuances, because some foods and drugs as well as fasting can affect the results.<sup>90</sup>

Functional micronutrient testing also is important, because the pathways critical for ATP production need to be fueled by key nutrients. A deficiency

in these nutrients can compromise mitochondrial health.

## Clinical Considerations in Treating Mitochondrial Dysfunction

Because mitochondrial dysfunction has emerged as a key player in a host of different diseases, it makes sense to include a mitochondrial support component in wellness regimens.

From a lifestyle perspective, a ketogenic diet may enhance mitochondrial health in children with autistic spectrum disorder and epilepsy. A ketogenic diet is a high-fat diet with enough protein for growth but not enough carbohydrates for metabolic needs. This type of diet causes the body to use fat as its main source of fuel. A ketogenic diet has been shown to improve various aspects of mitochondrial function during *in vitro*, *in vivo*, and human studies.<sup>91-95</sup> However, one problem with the ketogenic diet is that it is low in vegetables. The antioxidants in vegetables protect against excess reactive oxygen species generated by mitochondrial dysfunction, hence demanding consideration of supplemental antioxidant protection when consuming a ketogenic diet.

Research indicates moderate exercise also is critical to mitochondrial health. For example, in one mouse model of non-alcoholic steatohepatitis, mitochondrial abnormalities in the liver disappeared after the animals underwent endurance exercise.<sup>96</sup>

## Fueling the Mitochondria

A number of the components required for oxidative phosphorylation need to be frequently replaced. This can be accomplished with supplementation of key nutrients such as L-carnitine, alpha-lipoic acid, coenzyme Q10, creatine monohydrate, and N-acetylcysteine (NAC), which have all been shown to be of benefit.<sup>97</sup>

Mitochondrial bioenergetic enzymes require alpha-lipoic acid, a critical cofactor. In rodent and cell culture studies, alpha-lipoic acid has been found to restore mitochondrial biogenesis, to reduce mitochondrial deformation and intracellular ROS production, and to increase

intracellular ATP synthesis and mitochondrial DNA numbers.<sup>98,99</sup>

One randomized, double-blind clinical trial that used a combination of creatine monohydrate, coenzyme Q10, and alpha-lipoic acid lowered markers of oxidative stress in people with mitochondrial cytopathies while creatine monohydrate used alone in patients with mitochondrial encephalomyopathies enhanced aerobic oxidative function of the mitochondria.<sup>100,101</sup>

L-carnitine also is important to mitochondrial health because it helps transfer long-chain fatty acids from the cytoplasm of the cell to the mitochondria. During carnitine deficiency, there are less fatty acids available for energy production, resulting in symptoms such as myalgia and muscle weakness.<sup>102</sup> It's therefore not surprising that acetyl-L-carnitine (ALC), which is created from acetylation of carnitine in the mitochondria, is a powerful mitochondrial rejuvenator. When paired with alpha-lipoic acid in a nonalcoholic fatty liver mouse model, ALC enhanced the content and size of the mitochondria in the liver.<sup>103</sup> ALC supplementation also promoted the formation of new mitochondria in the livers of old rats, which helped reduce oxidative stress.<sup>104</sup>

Another component of a mitochondrial rejuvenation regimen is the glutathione precursor N-acetylcysteine, researched for its ability to enhance mitochondrial health. In one study of rats with spinal cord injuries, NAC improved mitochondrial bioenergetics and maintained mitochondrial glutathione levels near normal.<sup>105</sup>

Supplementing with citric acid cycle metabolites such as malate, succinate, and alpha-ketoglutarate can also be of benefit.<sup>106</sup>

## Other Mitochondrial Rejuvenators

New studies are showing several other natural agents may have mitochondrial-restoring effects. Evidence is mounting that resveratrol can improve mitochondrial activity. In cells from patients with early onset Parkinson's disease, resveratrol enhanced mitochondrial oxidative

function, which researchers believe is due to a decrease of oxidative stress and increased mitochondrial biogenesis. Resveratrol increased Complex I and citrate synthase activities, basal oxygen consumption, and mitochondrial ATP production.<sup>107</sup>

In other studies, resveratrol prevented mitochondrial dysfunction in a rat model of diabetic cardiomyopathy and increased cell survival after traumatic brain injury, in part by protecting the mitochondria.<sup>108,109</sup>

Surprisingly, glucosamine also emerged as a possible mitochondrial protector when a study published in 2014 showed that glucosamine extends the lifespan of both the nematode *Caenorhabditis elegans* and aging mice in part by enhancing mitochondrial biogenesis.<sup>110</sup>

Other nutrients shown to enhance mitochondrial function include quercetin, green tea, and omega-3 fatty acids.<sup>111–114</sup>

## Conclusion

In treating any health condition and improving overall foundational well-being, we can't forget to look at the proverbial "Energizer bunny" batteries of the trillions of cells that comprise the human frame. Mitochondrial dysfunction is the driving force behind the development or symptom severity in many diseases. Given the widespread involvement the mitochondria have in disease, incorporating nutrients that fuel mitochondrial pathways into any wellness-oriented supplement regimen is key to restoring whole body health. Due to the role hormones play in mitochondrial health – and vice versa – nourishing the mitochondria during hormone replacement therapy also is advised. Bottom line: unfueled cells are destined to underperform.

## Notes

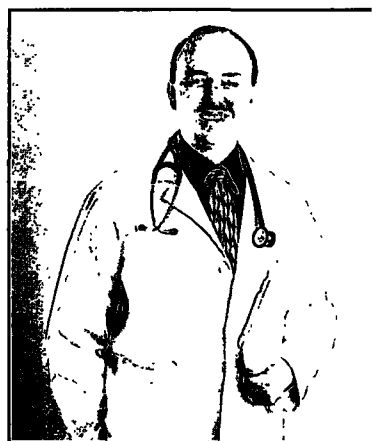
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# DNA Methylation and the Global Genome

by Kenneth Smith

A common scientific viewpoint holds that we are the result of the mechanical sequence and expression of our DNA, as it is DNA that determines the shapes and functions of proteins which build who we are. Put another way, phenotypes, or the observable characteristics of an organism, are the result of genetic determinism.

However, recent discoveries in the burgeoning field of epigenetics are slowly changing this long-held belief. Epigenetic research is not only modifying perspectives on how DNA works but also on health, disease, and evolution. Michael Skinner, a biology professor and founding director of the Center for Reproductive Sciences at Washington State University, says that in the last 20 to 30 years epidemiologists realized that some phenomena simply can't be explained by genetic determinism. For instance, there are hundreds of compounds that do not change DNA sequence but still promote disease. In addition, new findings indicate that the environment has a major effect on biology which genetics can't explain on a molecular level. "Epigenetics provides the link," he says.<sup>1</sup>

## The Epigenome

DNA is composed of four bases: cytosine (C), guanine (G), adenine (A), and thymine (T). The sequence is like a language that when expressed determines the various types of proteins, thereby producing the observable characteristics of

an organism. *Epigenetics* refers to chemical changes that affect gene expression without altering the DNA sequence, resulting in a broader range of phenotypes than found through genetic determinism.<sup>2</sup>

The target of this research is the epigenome, which is composed of methylated DNA, histone proteins, chromatin structure, and noncoding RNA. Research pertaining to the direct influence on DNA by the epigenome is revealing a highly dynamic, complex process of genetic expression. It is becoming increasingly clear that each part of the epigenome influences the other pieces and also regulates the expression of DNA.<sup>3</sup>

DNA methylation is the attachment of methyl (hydrocarbon) groups to DNA. It was once thought that its role was solely to suppress gene expression, and thereby allow for cell differentiation. It is now considered to perform various functions, including cellular memory and stability of cellular processes.<sup>4</sup>

Methyl is composed of one carbon atom bonded to three hydrogen atoms and attaches to DNA at the C base, where it connects with the phosphate backbone of DNA and where the C base links with the G base (CpG). There are approximately 28 million CpG spots along a chromosome.<sup>5</sup> In mammals, there are CpG "islands" (CGI) of higher density. In somatic tissue, most CGI are unmethylated, an important point to which we'll shortly return.<sup>6</sup>

Histones are proteins around which DNA binds. Histone modifications occur due to methylation, acetylation, and phosphorylation. DNA methylation is different from histone methylation, with the effects of the latter being more transient.<sup>7</sup> Histone modifications also mediate DNA transcription.<sup>8</sup> Histones unwind for regions of DNA being transcribed. When methylated, histones do not unwind and genetic expression is silenced.

Several histone proteins cluster into ball-like shapes known as nucleosomes. Each nucleosome has 8 histone molecules with 146 base pairs.<sup>9</sup> DNA winds around these beads and links one nucleosome to another. Tightly packaged nucleosomes protect and bind DNA, and this string of beads forms chromatin, the third part of the epigenome. As nucleosomes fold into chromatin fibers, they form the chromosome.<sup>10</sup> The structure of the chromatin regulates transcription, and DNA methylation affects chromatin stability.<sup>9,11,12</sup>

Noncoding RNA (ncRNA) is perhaps the least understood part of the epigenome. A central consideration of molecular biology is that ncRNA acts as an intermediary between a gene, or DNA sequence, and its encoded protein. Recent research suggests that ncRNA may have layers of information or signals that control chromatin structure and epigenetic memory. Like the other components of the epigenome, it acts



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► as a regulatory influence, playing a significant role in health and disease.<sup>13</sup>

Epigenetic regulation has two basic levels: (1) development and specialization of cells, and (2) inheritance.<sup>14</sup> In both instances, there are cascades of genetic and epigenetic processes that are highly integrated.<sup>15</sup> The direct effects of the epigenome on DNA are variable and dynamic.<sup>16</sup> Skinner, who has investigated epigenetics for over 15 years, says, "There will never be a genetic-only process just as much as there will never be an epigenetic-only process. The two are so highly integrated one cannot function without the other."<sup>1</sup>

### DNA Methylation

To date, DNA methylation is the best characterized component of the epigenome, and therefore serves as a good example to illustrate the mechanics of the entire epigenome.<sup>3</sup> DNA methylation was noted about 60 years ago but only recently was its regulatory activity determined.<sup>17</sup>

There are three primary enzymes, DNA methyltransferases (DNMTs), that generate, maintain, and strip away methylation.<sup>18</sup> Part of the regulatory activity of DNA methylation involves various processes and states. For instance, researchers have categorized the processes of DNA methylation in terms of maintenance, demethylation, remethylation, and de novo methylation. Maintenance methylation is simply DNMTs maintaining methylation patterns necessary for normal cellular functioning. Demethylation is when a CpG site or CGI are stripped of DNA methylation, remethylation occurs when DNA methylation patterns are restored, and de novo methylation is when a new pattern appears. What orchestrates the entire process remains a mystery.

The states of methylation include normal, hypo- (too little), and hyper- (too much) DNA methylation. In a normal state, DNA methylation

typically suppresses gene expression. However, it is now known that if there is too little methylation present, a gene that causes disease may be expressed. Conversely, with too much methylation, a gene that inhibits disease might be aberrantly suppressed.

### DNA Methylation and Disease

Cancer is the most widely studied disease known to be associated with epimutations, where a part or parts of the epigenome don't properly function. Characteristic of cancer, there is often genomewide DNA hypomethylation and CGI hypermethylation, whereas in a healthy state, CGIs are normally unmethylated. The effect is that hypomethylated areas may allow tumor-growing genes to be expressed, and the hypermethylated CGIs inhibit expression of tumor-fighting genes.<sup>18</sup> Other epimutations, such as histone modifications due to methylation, acetylation, and phosphorylation, have also been associated with cancer.

The brain is the most heavily DNA methylated part of the body.<sup>19</sup> Neural development, survival, and connectivity have been linked to DNA methylation and chromatin stability.<sup>13</sup> In many cases wherein epimutations are associated with disease, direct causality has not yet been determined. That said, epimutations have been found in neurological problems such as mood, stress, and memory disorders, neurodevelopmental disorders including autism, schizophrenia, and intellectual disability, and neurodegenerative diseases such as Parkinson's and Alzheimer's.<sup>4,20,21</sup> A direct link between DNMT1 alteration and dementia and hearing loss has been documented.<sup>22</sup> Neuroepigenetics is a new subfield focusing on epigenomic research of nondividing, or slowly dividing, cells.

Other known associations between epimutations and disease include obesity, allergy, cardiovascular, and problems with aging. Metabolism-

related epimutations have also been linked to obesity-related disorders and cancer.<sup>21,23</sup> Skinner holds that, except for infectious and injury-related diseases, "There is not a disease we have that does not have an environmental epigenetic component to it."<sup>1</sup>

### Environment and Epimutations

Many environmental influences are not known to affect the DNA sequence but can modify the epigenome and thereby regulate gene expression.<sup>16</sup> Studies indicate that a variety of environmental conditions influence DNA methylation. Prescription drugs, pesticides, and fertilizer have all been linked to epimutations.<sup>24,25</sup> DNA methylation patterns were found to change rapidly after exposure to black carbon from automobile fumes.<sup>26</sup>

Endocrine disruptors such as bisphenol A (BPA), a human-made carbon-based synthetic compound found in plastics, are associated with reproductive, obesity, and metabolic diseases.<sup>27</sup> A common means of ingestion occurs when they leach into drinking water from plastic containers. In addition, DDT is associated with epimutations associated with several diseases.<sup>28</sup> Although DDT is banned in the US, several countries continue to use it agriculturally, and these contaminated products are imported into the US with limited federal inspection.

Another environmental stressor leading to epimutations is maternal dietary deficiencies in vitamins or other nutrients.<sup>29</sup> Harsh social conditions may also act like exposure to a toxin and affect behavior, memory, and health.<sup>30</sup> Maternal behavior, for instance, can inhibit de novo methylation or inappropriately stimulate demethylation.<sup>12</sup> The consequences may be far ranging in that the next generation may return to the original phenotype (observable characteristic) in the absence of stress, or a new heritable phenotype may emerge as a consequence of environmental stressors.<sup>31,32</sup>



## Imprinting

Genomic imprinting occurs when epigenetic marks are established in the germ line such that sperm or eggs carry information that transfers to the next generation. When a cell replicates during normal development, epigenetic marks are copied along with DNA sequences, and so the marks such as DNA methylation are maintained through cell division and influence the expression of the parents' chromosomes in their offspring.<sup>33</sup>

In the progeny, these marks are erased twice and restored by remethylation during the early stages of development. The first wave of demethylation occurs when a stem cell is ready for tissue differentiation. Since gene expression is not suppressed due to DNA methylation, different phenotypes begin to emerge. The second wave affects germ cells, leading them to become gender specific.<sup>5</sup> The reestablished imprints are maintained in somatic cells, later to be transferred to the next generation.

Both waves can be highly sensitive to environmental toxins or toxic conditions such as stress.<sup>34</sup> Toxins may produce *imprintlike* methylation patterns, epimutations, that act the same as imprints.<sup>16</sup> These aberrant patterns can occur during any stage of life and may lead to adult-onset diseases such as obesity and diabetes. Like normal imprints, epimutations are heritable.

## Heritability

Heritability is a key component of epigenetics. Some diseases, such as obesity and diabetes, might have originated with DDT exposure to a parent or grandparent.<sup>5</sup> That is, the initial exposure to DDT may have caused an epimutation in a would-be parent and this aberrant pattern was later inherited. The epimutation in the offspring then regulated DNA expression in such a way that obesity or a related disorder manifested regardless of diet or exercise.

The range of epimutation disorders is stunning. In addition to the assortment of physical and psychological diseases already mentioned, evidence also indicates that olfactory memory can be affected. Using olfactory molecular sensitivity, prior to conception, parents were conditioned with a fear response to an odor. Avoidance responses based on smell remained active in subsequent generations.<sup>35</sup>

Furthermore, aberrant methylation patterns may affect mate selection and therefore evolution.<sup>14 36</sup> For example, three generations after male rats were treated with a fungicide, female rats continued to prefer male rats who were not exposed.<sup>37</sup> If new phenotypes emerge based on DNA methylation changes, and these patterns continued to be passed down, this could portend an evolutionary change brought about by the environmental circumstances that influenced and shaped the epigenome.<sup>38</sup>

## Transgenerational Inheritance

Transgenerational inheritance is the ability of a phenotype or disease to be transmitted to subsequent generations through the germ line even though the subsequent generations were not exposed to the initial environmental factor or toxicant.<sup>39</sup> Epimutations related to aberrant DNA methylation patterns have been tracked to the F5 generation, or the fifth generation after direct exposure.<sup>5</sup>

In one study, analysis of endocrine disruptors in plastics revealed 197 epimutations in gene promoters of sperm in the third generation after initial exposure to endocrine disruptors and with no exposure to the next generations.<sup>27</sup> Another study found that dioxin, a byproduct of industrial processes, was found to increase the incidence of multiple diseases in the first and third generations of animals after initial exposure. A woman becoming pregnant 20 years after dioxin exposure may therefore run a risk of establishing a transgenerational disease.<sup>40</sup>

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## Treatment

A leading epigenetic researcher who is helping realize the promise of new epigenetic therapies is Stephen Baylin, MD, deputy director of the Sidney Kimmel Cancer Center and head of the cancer biology program at Johns Hopkins University. DNA methylation research has been his dominant focus since the mid-1980s. "Epigenetics is a work in progress," he says. "We're only at the tip of the iceberg as to how to utilize it."<sup>41</sup> The tip of that iceberg, though, is already demonstrating promise.

For instance, there is a defined shift in DNA methylation patterns for some diseases as well as for aging. Methylation patterns are also very stable for indicating states of health and disease, including identifying a specific diet.<sup>42</sup> This stability in states of both health and disease permits new models and therapies that target the epigenome to be developed.

Baylin, for example, is developing assays that will identify patients who might derive benefit from epigenetic therapy, by itself or from giving it before traditional cancer treatments such as chemotherapy and radiation. He states that even though the number responding robustly to the epigenetic therapy alone is only a small subset of patients within the overall population of those with lung cancer, since that disease is the biggest killer worldwide, the number would be quite large. "But we would have to know upfront who those patients are."<sup>41</sup>

Furthermore, aberrant methylation patterns have been shown to silence chemotherapeutic genes, thereby preventing their effectiveness. This situation has been reversed by changing DNA methylations with a diet focusing on antioxidants.<sup>43</sup> Deleterious effects on chromatin due to poor maternal care have also been pharmacologically reversed.<sup>9</sup> In another instance, hypermethylated cancer has been reversed with DNA methyltransferase inhibitors, thereby



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allowing DNA methylation to return to normal levels.<sup>10</sup> And a histone deacetylation inhibitor has shown promise for the treatment of ALS.<sup>41</sup>

Baylin is also investigating how to reformat existing drugs by using a lower dosage in order to create a new paradigm that will “bring epigenetic therapy to a forefront position in cancer management.” As part of this effort, he envisions altering signaling pathways associated with DNA methylation and then understanding how those pathways drive efficacy of a drug.<sup>41</sup>

In other areas of cancer research, Baylin says the low dose approach is gaining momentum. Low doses of a DNMT inhibitor have been found to alter tumorigenesis pathways and upregulate immunomodulatory pathways, and low-dose DNA methylation inhibitors have shown promise for treating leukemia.<sup>44,45</sup>

For maintaining normal DNA methylation or for treatment, vitamin B12 and folate are known to facilitate DNA synthesis. Methionine from green leafy vegetables helps maintain healthy DNA methylation patterns.<sup>43</sup> Other dietary tips include the use of epigallocatechin-3-gallate (EGCG) from green tea, genistein from soybean, isothiocyanates from plant foods, curcumin from turmeric, resveratrol from grapes, and sulforaphane from cruciferous vegetables such as broccoli, cauliflower, and cabbage.<sup>46</sup> However, ingesting high levels of these vitamins, especially folate, may be toxic and do more harm than good. In addition, many plants have chemicals such as



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genistein that at high levels are toxic. It is therefore best to stay within daily recommended levels.<sup>1</sup>

### The Global Genome

In recent years, the amount of epigenetic research has exploded. While most studies have focused on animals, the few human studies available corroborate animal research.<sup>47</sup> With humans, it is usually a matter of following someone who was accidentally exposed to a toxicant and hoping that the heritability trail doesn't get lost.<sup>5</sup>

Even with mounting data indicating associations between various parts of the epigenome and a range of diseases, it will take time for this thinking to filter into mainstream medicine. Skinner says that the articulation of epigenetics may take another three generations before studies such as those for DNA methylation become settled science.<sup>1</sup> Controversy remains since few direct causal relationships between the epigenome and disease have been established. And there may be other epigenetic mechanisms not yet revealed. By all accounts, though, investigators call for further research.

All in all, epigenetic research is illuminating a newly defined regulatory system. Prior thinking indicated that DNA expression was mechanical and chromatin was a structural feature supporting the double helix. The genome and epigenome are now thought to form the global genome wherein DNA expression results from a living, breathing, highly dynamic process and all aspects of the genome, epigenome, and environments of an organism interact.

### A Holistic Application

Perhaps one application of the global genome is modeling holistic medicine by examining the global patient. DNMTs, for instance, represent a portion of one's internal environment, while toxins or toxic conditions represent the external environment. Bench lab and clinical models of exactly how both environments interact and affect states of health might develop more quickly with an understanding of how environment affects the parts and the whole of the epigenome and how the epigenome regulates DNA expression. This understanding might then be extrapolated for application to holistic models.

Such models would deal with the global person rather than trying to look at health and disease without regard for the influences of other parts of the body or the influence of the environment. One benefit of this approach is that medical practitioners might be better able to treat multisystem disorders without having treatment for one condition make treating other conditions more complex. But whatever epigenetic research may yield in the coming years, in the interim it is clear that this endeavor is producing a greater understanding of the effects of environment on health, disease, and inheritance as well as establishing new pathways for more effective therapeutic approaches.

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# Low-Dose Allergen Immunotherapy (LDA) vs. Subcutaneous Injection Immunotherapy: A Comparative Study

by Diego Saporta, MD, FAAOA

## Introduction

Immunotherapy (administered either by injections or sublingually) is a very old treatment modality. Noon and Curtis were already working with these treatments in the early 1900s.<sup>1,2</sup>

Administration of low-dose allergen immunotherapy (LDA) was first described by Dr. Leonard McEwen in England (at the time, it was called EPD, or enzyme potentiated desensitization). He published several papers between 1967 and 1987, including a double-blind, controlled study.<sup>3-9</sup>

The American EPD Society was founded in the US to study the treatment. This society conducted a large multicenter study from 1993 to 2000, involving practitioners from the US and Canada. This, the North American EPD Study, evaluated 10,372 patients. The results showed a "satisfactory" response rate of 76% (20% excellent, 30% very good, and 26% good).<sup>10</sup>

EPD became unavailable in the US in 2001. Soon afterward, Dr. W. A. Shrader developed a similar treatment that he called LDA.<sup>11</sup> LDA is now used by a relatively small number of practitioners (slightly over 100 MDs or NDs) in the US and Canada.<sup>10</sup> While it is expected that the number of practitioners who incorporate LDA into their practices will increase over time as information about this treatment is now being offered in some societies, it is not likely that LDA will ever be used as frequently as conventional immunotherapy, as it lacks the scientific background of conventional immunotherapy and it is not approved by the FDA.<sup>12</sup> As long as LDA remains a non-FDA-approved modality, it will most likely remain a "noncovered" service by traditional insurance companies. While McEwen and Shrader have published about this topic, there is not enough research about this treatment modality.<sup>3-9,13,14</sup> It is improbable that large prospective trials with a placebo group will ever be planned to evaluate efficacy of LDA. All these reasons will likely prevent wide acceptance of this treatment modality.

LDA was incorporated into the author's practice in 2009. As with any new treatment modality, the question was, is it as effective as the one already in use? More

importantly, patients often ask this same question before making a decision.

In contrast with LDA, subcutaneous injection immunotherapy (SCIT) has been used in the author's practice for more than 20 years, and sublingual immunotherapy (SLIT) since 2003. When SLIT was incorporated, demonstrating efficacy and finding that it performed as well as SCIT was an important piece of information at the time of patient counseling.<sup>15</sup> For similar considerations the present study was planned with the objective of finding how LDA performs when compared with SCIT in order to properly advise patients when discussing treatment options. It was very obvious from the first few administrations that LDA was safe and effective, but this information is not enough to determine if its efficacy is similar to usual immunotherapy.

## Methods

Allergy charts from patients either on SCIT or LDA were consecutively collected. Inclusion criteria were:

Patients of either sex, any age, with or without asthma, who had been receiving either treatment for a minimum of 1 year, and had completed the symptom scoring sheet.

Data were entered into spreadsheets, utilizing only pertinent information, including date of test, age, sex, asthma diagnosis, and symptom-scoring sheet information, therefore keeping all personal information confidential. After recording this information, spreadsheets were organized in columns corresponding to each one of the parameters to be analyzed.

The data were sent to a statistician for analysis. A chi-square test was used to determine whether the samples were significantly different from each other, and the ANOVA was then used to compare the average values.

## Symptom Scoring Sheet

A symptom scoring sheet is a useful instrument to evaluate how an allergy patient is doing during treatment. Our symptom scoring sheet includes the following fields:

- a. Twenty-five symptoms that include 4 symptoms of the Total Nasal Symptom Score (TNSS): sneezing, runny nose, nasal obstruction, and nasal itching, and 21

other symptoms that we consider important for the management of the allergic patient. The symptoms are scored on a scale of 1 to 5, where 1 is "mild" and 5 is "very severe." (0 implies that symptom is not present).

- b. Peak Flow (PF) value is the numerical value obtained with a PF meter at the time of scoring. The PF value is very simple to obtain and yet a very useful tool for the evaluation of treatment results. We found that when immunotherapy is successful the PF value increases over time, even in nonasthmatic patients. When the patient is not responding to the treatment, the PF value does not increase or even decreases.<sup>16</sup>
- c. Medications used: A similar 1–5 scoring system is used wherein 5 means that the medication is used daily and 1 that it is used up to 2 times per month. (0 implies that the medication is not being used). The purpose of evaluating medications is not to determine which medication works better but rather how much allergy medication the patient is using at the time of scoring. When treatment is successful, the medication score decreases.

With LDA, scoring is obtained each time treatment is administered. With SCIT, scoring is obtained approximately every 2 to 3 months.

The following parameters are obtained each time the scoring is done:

- a. TNSS: This is the numerical value obtained by adding the scores given to the 4 symptoms described above. Maximal value of the TNSS is 20 (4 symptoms x 5).
- b. Number of symptoms (#S): Total number of symptoms that the patient reports on each evaluation. This number includes all the symptoms present at the time of scoring. Maximal value for #S: 25.
- c. Symptom score (SS): This is the numerical value obtained by adding the scores given to any of the 25 symptoms (therefore SS includes also the value of the TNSS). Maximal value for SS: 125 (25 symptoms x 5).
- d. PF value: Numerical value determined when the patient is asked to use the PF meter.
- e. Number of medications (#M): This is the number of medications that the patient is using at the time of scoring. The following medications are considered for assessment of patient's response to treatment:
  - i. antihistamines
  - ii. decongestants
  - iii. leukotriene receptor blocker
  - iv. intranasal steroids
  - v. short-acting bronchodilators
  - vi. inhaled corticosteroids (or combination inhaler)
 Maximal value for #M: 6.
- f. Medication score (MS): This is the numerical value obtained by adding the scores given to medication use according to the 1–5 scale described above. The maximal value for MS: 30 (6 medications x 5). This implies that all medications are used daily.

## Analysis

Both groups were evaluated before treatment initiation for age, gender, presence of asthma and for the values obtained from the symptom scoring sheet (TNSS, #S, SS, #M, MS, and PF).

The following determinations were planned:

1. a pretreatment evaluation with intergroup comparison.
2. scoring values at 12 months of treatment for each group.
3. intergroup comparison at 12 months.
4. scoring values at 24 months of treatment for each group.
5. intergroup comparison at 24 months.

Results were considered significant when  $p < 0.05$ .

## Results

Each group (SCIT and LDA) had 52 charts. All patients received treatment for 12 months. At 24 months information was available only for 41 patients in the SCIT group and 32 patients in the LDA group. Eighteen patients in the LDA group had received SCIT prior to switching to LDA treatment. Significant results ( $p < 0.05$ ) will be shown in bold.

**Table 1: Demographics**

	M/F	Total	Age $\pm$ SD	$\leq 18$ (%)	$\leq 13$ (%)	$\leq 10$ (%)	Asthma (%)
SCIT	23/29	52	45 $\pm$ 23	14 (26.9)	7 (13.5)	3 (6.0)	29 (55.8)
LDA	29/23	52	35 $\pm$ 20	13 (25.0)	12 (23.1)	11 (21.2)	31 (59.6)
			<b><math>p &lt; 0.05</math></b>	N/S	N/S	<b><math>p &lt; 0.05</math></b>	N/S

M/F: Male/Female

Age (SD): Age average  $\pm$  standard deviation

$\leq 18$  (%): Number of children 18 years of age or younger (percentage from the total sample of 52)

$\leq 13$  (%): Number of children 13 years of age or younger (percentage from the total sample of 52)

$\leq 10$  (%): Number of children 10 years of age or younger (percentage from the total sample of 52)

Asthma (%): Number of patients who have asthma (percentage from the total sample of 52)

p: Probability

N/S: Not Significant

Table 1 shows the demographic information for both groups. ANOVA test shows that:

1. Mean patients age is lower in the LDA group ( $p < 0.05$ ).
2. The number of children 18 years of age or younger is similar in both groups. When the children are subdivided by age there is a tendency for the children in the LDA group to be younger. In the subgroup of children 10 years of age or younger, this difference acquires significance ( $p < 0.05$ ). The presence of more young children in the LDA group probably explains the significant age difference between both groups.
3. Asthma incidence in both groups is similar and has no statistical difference (N/S).

## Pretreatment Evaluation

Evaluation of symptoms, medication use, and PF value was done for both groups before the beginning of treatment.

# LDA vs. Subcutaneous Injection Immunotherapy

**Table 2. Pretreatment Evaluation**

Pretreatment	SCIT	LDA	TS
TNSS	9.4 ± 5.8	9.1 ± 6.2	p = N/S
#S	11.7 ± 5.1	13 ± 5.3	p = N/S
SS	34.4 ± 20.1	38.1 ± 23.9	p = N/S
#M	1.73 ± 1.2	1.05 ± 1.1	p < 0.01
MS	6.15 ± 5.6	3.13 ± 3.8	p = 0.01
PF	354.4 ± 103.9	405.5 ± 154.4	p = N/S

Pretreatment: Scoring before treatment initiation  
 TNSS: Total Nasal Symptom Score  
 #S: Number of Symptoms  
 SS: Symptom Score  
 #M: Number of Medications  
 MS: Medications Score  
 PF: Peak Flow Value  
 All values ± Standard Deviation  
 SCIT: Subcutaneous Injection Immunotherapy  
 LDA: Low Dose Allergen Immunotherapy  
 TS: Test of significance  
 p: Probability  
 N/S: Not significant

Table 2 shows that the LDA group was taking fewer medications and medications were less frequently used than the SCIT group before treatment was started. Otherwise there were no other pretreatment differences between both groups.

## Treatment Results for Each Group at 12 Months

**Table 3: Treatment Results at 12 Months**

12 mo/Pre	TNSS	#S	SS	#M	MS	PF
SCIT	p < 0.001	p < 0.001	p < 0.001	p < 0.01	p < 0.01	p < 0.05
LDA	p < 0.001	p < 0.01	p < 0.001	N/S	p < 0.05	N/S

12 mo/Pre: Results at 12 months, compared with the pretreatment results.  
 TNSS: Total Nasal Symptom Score  
 #S: Number of Symptoms  
 SS: Symptom Score  
 #M: Number of Medications  
 MS: Medications Score  
 PF: Peak Flow Value  
 SCIT: Subcutaneous Injection Immunotherapy  
 LDA: Low Dose Allergen Immunotherapy  
 p: Probability  
 N/S: Not significant

Table 3 shows that both treatment modalities elicit a statistically significant improvement at 12 months of treatment in all parameters except #M and PF for the LDA group.

## Intermodality Comparison at 12 Months

**Table 4: SCIT vs. LDA 12-Month Treatment Results Comparison**

TNSS	#S	SS	#M	MS	PF
p=0.73	p=0.09	p=0.67	p=0.06	p=0.08	p < 0.05
N/S	N/S	N/S	N/S	N/S	Yes SCIT

TNSS: Total Nasal Symptom Score  
 #S: Number of Symptoms

SS: Symptom Score  
 #M: Number of Medications  
 MS: Medications Score  
 PF: Peak Flow Value  
 SCIT: Subcutaneous Injection Immunotherapy  
 LDA: Low Dose Allergen Immunotherapy  
 p: Probability  
 N/S: Not significant

Table 4 shows that there are no differences in treatment results between groups at 12 months except for the PF value that appears to improve more with SCIT.

## Treatment Results for Each Treatment Modality at 24 Months

**Table 5: Treatment Results at 24 Months**

24 mo/Pre	TNSS	#S	SS	#M	MS	PF
SCIT	p < 0.001	p < 0.001	p < 0.001	p < 0.01	p < 0.001	p < 0.05
LDA	p < 0.001	p < 0.05	p < 0.001	p < 0.05	p < 0.05	N/S

24 mo/Pre: Results at 24 months are compared with the pretreatment scores  
 TNSS: Total Nasal Symptom Score  
 #S: Number of Symptoms  
 SS: Symptom Score  
 #M: Number of Medications  
 MS: Medications Score  
 PF: Peak Flow Value  
 SCIT: Subcutaneous Injection Immunotherapy  
 LDA: Low Dose Allergen Immunotherapy  
 p: Probability  
 N/S: Not significant

Table 5 shows that both treatment modalities elicit a statistically significant improvement at 24 months of treatment in all parameters except PF for LDA. The #M used in the LDA group, which did not decrease in a significant way at 12 months (Table 3), attained significance at 24 months.

## Intermodality Comparison at 24 Months

**Table 6: SCIT Vs. LDA 24-Month Treatment Results Comparison**

TNSS	#S	SS	#M	MS	PF
p=0.75	p=0.43	p=0.8	p=0.44	p=0.25	p=0.32
N/S	N/S	N/S	N/S	N/S	N/S

TNSS: Total Nasal Symptom Score  
 #S: Number of Symptoms  
 SS: Symptom Score  
 #M: Number of Medications  
 MS: Medications Score  
 PF: Peak Flow Value  
 SCIT: Subcutaneous Injection Immunotherapy  
 LDA: Low Dose Allergen Immunotherapy  
 p: Probability  
 N/S: Not significant

Table 6 shows that at 24 months, the improvement in all parameters for both modalities is not statistically different. The difference in PF value improvement in favor of the SCIT group at 12 months (Table 4) disappeared at 24 months.

# LDA vs. Subcutaneous Injection Immunotherapy

## Conclusions

SCIT and LDA can be considered equivalent in reference to treatment results, even though LDA appears to require more time to attain the same results, at least in reference to the improvement of the PF value.

## Discussion

This study showed that SCIT appeared to score better in 2 parameters: #M and PF (see Table 3), at least initially. As these differences disappeared over time, it could be hypothesized that if a study was done considering only results at longer treatment times (2 years or more), there would be no differences.

## Bias?

The LDA group included a subgroup of 18 patients who received SCIT prior to initiation of LDA. These were patients who were not doing well on SCIT and opted to change into LDA. During study planning, it was not considered that prior treatment, even if failing, could have had an effect (partial improvement) on certain parameters. This could be the case for the PF value by prior administration of SCIT to these patients. Table 7 shows that when these 18 patients were enrolled in the LDA group their PF value had already improved by an average of 67 points.

LDA group may have favored worse outcomes:

1. Uninsured patients frequently choose LDA for economic reasons. It could be hypothesized that for the same reasons, these patients may not spend as much money on medications as insured patients. This could also contribute to the already discussed finding that the LDA group appeared to use fewer medications than the SCIT group. Potential for improvement (reduction in the number of medications used) is affected if the number used at the beginning of the trial is small. Maybe a larger sample would have overcome this difference.
2. LDA group included patients who were not improving on SCIT (and were switched to LDA). These previously treated patients may constitute a more complicated subgroup to treat. If these patients were left on SCIT it is possible that the final outcome of the group would have been worse. On the other hand, if before changing modalities these patients had partially improved, this would bias the LDA results (as discussed for the PF value).
3. There are potential problems in the way the symptoms are reported in the LDA group: By the nature of LDA, when LDA patients come for treatment they are often

**Table 7: Effect of Prior SCIT on PF Value.**

Prior SCIT (18 pts)	B4 SCIT	B4 LDA	Δ PF
AVG PF value	359	426	67 (N/S)

Prior SCIT (18 pts): Group of 18 patients who received SCIT prior to LDA  
 AVG PF value: Average PF value  
 B4 SCIT: Average PF value before SCIT was initiated (at enrollment)  
 B4 LDA: Average PF value before LDA was initiated (but after having received SCIT)  
 Δ PF: Average change in PF value  
 N/S: Not significant

Even though this is a nonsignificant improvement, it is likely a determining factor that prevents the PF value from attaining a statistically significant improvement in the LDA group (Tables 3 and 5), as more than 30% of the sample had already shown some improvement.

For the same reason it is likely that in the intermodality comparison at 12 months (Table 4), the PF value shows better results in the SCIT group, as the SCIT group included patients with the "full potential range" for improvement whereas the LDA group included more than 30% with "less potential range" for improvement. The fact that this difference disappeared over time (Table 6) suggests that ultimately the results of LDA treatment are as good as those of SCIT.

A similar reasoning could explain why the LDA group was using less medication at the beginning of the treatment (Table 2). In addition there are other considerations that could render the LDA group a biased sample. In other words, for the reasons explained below, the results in the



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## LDA vs. Subcutaneous Injection Immunotherapy

➤ already symptomatic because at the beginning of treatment the effect lasts for only a few weeks. During this period, LDA administration is done once every 2 months.<sup>11</sup> It takes from 1 to 2 years for LDA patients to attain a more permanent improvement, and at that stage the administration of LDA becomes less frequent. With SCIT, once improvement develops it usually persists over time. This clearly tilts the scores of the LDA-treated group towards "worse outcome" because when symptoms were scored in this study, patients were often symptomatic again.

4. Some patients are so symptomatic that the consideration of SCIT is dangerous, as intradermal tests or shots have the chance to elicit severe reactions even with risk of life.<sup>17,18</sup> These difficult-to-treat patients may not attain the same level of improvement as less reactive patients. While this type of patient is not represented in the SCIT group, it can be represented in the LDA group as this is a safer treatment modality without risks for severe reactions and it is offered more liberally to those patients who are very reactive.
5. Patients with glycerin sensitivity may not have good results with conventional immunotherapy. They may not tolerate SCIT because of local arm reactions or they may not tolerate SLIT because of the glycerin used as diluent.<sup>19</sup> These patients are included in the LDA-treated group. If treated with conventional immunotherapy their treatment result scores could potentially tilt the SCIT-group scores towards worse outcome.

For all of the above reasons we think that this report is biased against the LDA-treated group. It is very likely that the results are tilted towards better scores in the SCIT-treated group and worse scores in the LDA-treated group. Despite this bias against LDA results, the outcome comparison of patients treated with SCIT or LDA is clearly the same. Therefore we strongly believe that expected results in patients treated with LDA should be at least as good as the ones expected by administering SCIT.

LDA has changed the way we approach the patients: when a patient has severe skin problems, oral allergy syndrome or other clear food issues, more and more we tend to favor administration of LDA as the most appropriate treatment modality (first line of therapy for these cases). In other words LDA has enabled us to successfully treat patients that either failed treatment or received no treatment before LDA was incorporated in our armamentarium: Despite the flaw in the study design and despite the potential bias against LDA, the results of this study are extremely encouraging and allow us to offer LDA as an effective and safe modality that can, without doubt compare to traditional immunotherapy.

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Dr. Saporta completed his training in 1990 at Columbia Presbyterian Hospital in New York City. He is board certified in otolaryngology and has been a fellow of the American Academy of Otolaryngic Allergy (AAOA) since 2001. His private practice in Elizabeth, New Jersey, is heavily oriented to the management of allergic conditions. Interested in the use of oral vaccines since early in his practice, Dr. Saporta presented a protocol for sublingual immunotherapy at the 64th annual meeting of the AAOA that since then has been successfully used for the management of allergic rhinitis with or without asthma.



# Complementary and Alternative Care for Allergies

by Dr. John Hahn

The concept of allergies was first demonstrated in 1906 by Viennese pediatrician Clemens von Pirquet, who noted that some of his patients were hypersensitive to normally innocuous entities such as dust, pollen, and certain foods.

The word *allergy* comes from the ancient Greek words *allos*, meaning "other," and *ergon*, meaning "work."<sup>1,2</sup>

## Four Types of Hypersensitivity Reactions

In 1963 a new classification scheme was developed by Gel and Coombs that described four types of hypersensitivity reactions, known as type 1 to type 4. With this new classification, the word *allergy* was restricted to type 1 hypersensitivities, also known as immediate hypersensitivities, which are characterized by rapidly developing reactions.<sup>3</sup>

In the late 1960s, immunoglobulin E was discovered by Kimishiq Ishizaka.

## Prevalence and Types of Allergies

According to the Asthma and Allergy Foundation of America, 60,000,000 people suffer from asthma and allergies. Allergies are the most frequently reported chronic condition in children, limiting activities for more than 40% of them. Allergies account for more than 17,000,000 outpatient office visits per year, more than 7,000,000 of them for skin allergies. Food allergies account for 30,000 visits to the emergency department each year.<sup>4</sup> Types of allergies include indoor/outdoor, food and drug, latex, insect, and skin and eye allergies. Allergy prevalence overall has been increasing since the early 1980s across all age, sex, and racial groups.<sup>5</sup>

Some 40 million Americans have allergic rhinitis, seasonal/perennial allergies, hay fever, and nasal allergies.

Approximately 10 million people are allergic to cat dander, the most common pet allergy. Indoor/outdoor allergy triggers are the following: tree, grass, and weed pollen; mold spores; dust mite and cockroach allergens; cat, dog, and rodent dander.<sup>6</sup>

Allergic reactions affect the respiratory system's mucous membranes, with symptoms including red, itchy, and watery eyes, sneezing, congestion and runny nose, and itchy or sore throat with postnasal drip and coughing.

Allergic skin reactions affect 7% of allergy sufferers. Atopic dermatitis, eczema, hives, urticaria, and contact allergies are seen within this group of individuals. Hives and welts can be seen on the skin secondary to allergies.<sup>7</sup>

Poison ivy, poison oak, and sumac are the most common skin allergic triggers; however, skin contact with cockroach and allergens and certain foods or latex can also trigger symptoms of skin allergy.

The signs and symptoms of allergies vary with the organ systems involved; however, the most common signs for dust or pollen are airborne particles that cause symptoms in the area in contact with air such as the eyes, nose, and lungs. Allergic rhinitis, also known as hay fever, causes sneezing, itching, and redness of the eyes. Certain inhaled allergens can lead to asthmatic symptoms such as bronchoconstriction, increased mucus production, dyspnea, coughing, and wheezing.

Gastrointestinal hypersensitivity reactions can cause gas, bloating, constipation and/or diarrhea, itchy skin, and swelling of the skin during hives.

Skin allergies bring about eczema and hives (urticaria).

Insect stings, antibiotics, and certain medicines produce systemic allergic

responses known as anaphylaxis, which have multiorgan effects on the digestive, respiratory, and circulatory systems and can be fatal if not treated appropriately.

The genetic bases of allergic reactions are seen with strong familial tendencies; for example, identical twins may have the same allergic diseases 70% of the time. In nonidentical twins, the same allergy occurs about 40% of the time. The likelihood of developing allergies is inherited and related to irregularity in the immune system, but the specific allergen is not.<sup>12</sup>

"Top Asthma Cities" in the US for 2011 are Richmond, Virginia; Knoxville, Tennessee; Memphis, Tennessee; Chattanooga, Tennessee; Tulsa, Oklahoma; St. Louis, Missouri; Augusta, Georgia; Virginia Beach, Virginia; Philadelphia, Pennsylvania; and Nashville, Tennessee.<sup>11</sup>

## Food and Drug Allergies

Approximately 6% of allergy sufferers have food/drug allergies as their primary antigens. 90% of all food allergies are caused by milk, soy, eggs, wheat, peanuts, and shellfish.

The most common drug allergies are to penicillin-based antibiotics.<sup>8</sup>

## Mortality Due to Allergic Reactions

Four hundred individuals die each year as a result of allergic reactions to penicillin-based drugs. At least 200 deaths are reported per year due to food allergies. At least 100 deaths are attributed to insect bite reactions per year. Approximately 10 deaths per year are attributed to latex allergy reactions

## Social and Economic Costs of Allergic Disease

The annual cost of treating allergies was estimated to be approximately \$56

# Allergies

▶ billion in 2007 (<http://www.cdc.gov/VitalSigns/Asthma/index.html>). The direct costs for treating allergies are \$47.6 billion, \$1.3 billion for office visits and \$11 billion for medications. Of the latter, \$7 billion are used for prescription allergy medications and \$4 billion for over-the-counter allergy medications. Indirect costs of allergies (missed work or school), loss in productivity, death, and so on account for approximately \$2.2 billion a year.

Adult allergies are the fifth leading chronic disease and a major cause for work absenteeism, resulting in nearly 4 million missed or lost work days each year and a total cost of more than \$700 million in lost productivity.<sup>10</sup>

## The Hygiene Hypothesis of Allergic Disease

The Th2 immunological response to harmless antigens has been a hypothesis for the development of allergic symptoms in humans. Bacteria and viruses elicit a Th1-mediated immune response, which downregulates Th2 response. The proposed mechanism of action of the hygiene hypothesis was that insufficient stimulation of the Th1 arm of the immune system leads to an overactive Th2 arm, which then leads to allergic disease.

Individuals living in a sterile environment and not exposed to enough pathogens to keep the immune system busy during early development may acquire an immune system that attacks harmless antigens, and thus normally benign microbial agents such as pollen will trigger an immune response. Epidemiological data support the hygiene hypothesis. Studies have shown that immunological and autoimmune diseases are much less common in the developing world than in the industrialized world where individuals live in a more sterile environment and are not exposed to enough pathogens in their early years to acquaint the immune system to harmless antigens.<sup>13</sup>

## The Pathophysiology of Acute Allergic Response

Type 1 hypersensitivity reactions occur when an allergen is encountered for the first time presented by an antigen-presenting cell (APC). This reaction causes a response in a type of immune cell called a Th2 lymphocyte, which belongs to a subset of T cells that produce a cytokine called interleukin-4 (IL-4).

Th2 cells interact with other lymphocytes called B cells, whose role is the production of antibodies. Coupled with signals provided by IL-4, this interaction stimulates the B cells to produce large amounts of immune globulin E (IgE). IgE circulates in the blood and binds to IgE-specific receptors on the surfaces of other kinds of immune cells called mast cells and basophils, which are involved in the acute inflammatory response.

Activated mast cells and basophils undergo degranulation, and release histamine, cytokines, interleukin, leukotrienes, and prostaglandins. These granules go into the surrounding tissue, causing severe systemic effects such as vasodilation, mucus secretion, nerve stimulation, and smooth muscle contraction.

Rhinorrhea, itchiness, dyspnea, and anaphylaxis occur as a result of these chemical mediators.

Late-phase response to an allergic reaction is due to the migration of neutrophils, lymphocytes, eosinophils, and macrophages into the initial site. Late-phase responses seen in asthma are slightly different from those in other allergic responses, although they are still caused by release of mediators from eosinophils and depend upon the activity of the Th2 cells.

Patients with G F M 1 and P 1 null genotypes have increased IgE and histamine production after diesel exhaust exposure.

Glutathione depletion inhibits Th1-cytokine production and favors the Th-2 response. Certain xenobiotics are known to deplete glutathione, such as alcohol, toluene, benzene, mercury, lead, and diesel exhaust particles.<sup>14</sup>

## Diagnostic Procedures for Allergic Disease

Effective management of allergic disease relies on the physician's

ability to make an accurate diagnosis of the etiology. Skin pricks or allergy blood tests are recommended by the NIH guidelines. Radioallergosorbent test (RAST) uses IgE binding (anti-IgE) antibodies labeled radioactive isotopes to quantify those levels of IgG antibodies in the blood. This test has been superseded by the ImmunoCAP Specific IgE blood test, which uses the newer fluorescent-label technology. According to NIC guidelines, skin prick tests and blood tests are equally cost effective.<sup>15</sup>

Challenge testing involves applying a small amount of suspected allergen introduced to the body either orally through inhalation or other routes. Except for testing food and medication allergies, challenges are rarely performed and closely supervised by the physician.

Elimination/challenge test is most often used with food and medicine which are suspected of being antigens.

Patch testing is used to ascertain the cause in contact allergies or contact dermatitis. Adhesive patch just treated with a number of different allergens or skin sensitizers are applied to the back of the patient. The area is examined 48 hours after application and once again in 2 or 3 days post application to measure skin reactions.

## Management of Allergies

The basic treatment to reduce allergic responses is to avoid known allergens. Decreasing IgE overproduction and regulating histamine release in allergic individuals has demonstrated statistically significant reductions in total nasal symptom scores. Traditional allopathic medications used for the treatment of allergies are antagonistic drugs that are used to block the action of allergic mediators or prevent activation of cells in the deregulation process.

Antihistamines, cortisone, dexamethasone, hydrocortisone, epinephrine, theophylline, cromolyn sodium, and antileukotrienes, such as Singulair or Accolate, are FDA approved for treatment of allergic diseases.

Anticholinergics, decongestants, mast cell stabilizers, and other compounds that impair eosinophil chemotaxis are also commonly used to treat allergy symptoms. These drugs help to alleviate the symptoms

of allergies and are imperative in the recovery of acute anaphylaxis, but play little role in the management of chronic allergic disorders.

Immunotherapy is desensitization (or hyposensitization) by which the patient is gradually facing progressively larger doses of the known allergen in question. Hyposensitization therapy relies on the progressive skewing of IgG antibody production to block excessive IgE production seen in atopy.

Immunotherapy may also involve IV injections of monoclonal anti-IgG antibodies. These antibodies bind to free and B-cell associated IgE, feeling their destruction. This form of immunotherapy is very effective in treating several types of atopy; however, it should not be used for the majority of people with food allergies.

Sublingual immunotherapy is an orally administered therapy which takes advantage of oral immune tolerance to nonpathogenic antigens such as foods and resident bacteria. This therapy currently accounts for 40% of allergy treatment in Europe.<sup>1617</sup>

## Conventional Therapies for Allergies and Asthma

Quick relief inhalers for asthmatic symptoms with expiratory wheezing and shortness of breath are beta agonists such as albuterol and pirbuterol. These medications act within minutes and last several hours. Ipratropium (Atrovent) is mostly used for emphysema and chronic bronchitis, but it's sometimes used to treat asthma attacks.

Oral and intravenous corticosteroids such as prednisone and methyl prednisone are conventional therapies for severe asthma. They can, however, cause serious side effects when used long term, so they should only be used only short term to treat severe asthma symptoms.

Omalizumab (Xolair) is the medication specifically for people who have allergies and severe asthma. This drug functions by altering the immune system. It is delivered to the patient by injection every 2 to 3 weeks.

## Alternative Therapies for Allergies

The use of nettle extract (*Urtica dioica*) has been a traditional form of treatment for various forms of respiratory allergies. Recent research

has shown that nettle extract affects the key receptors and enzymes associated with allergic rhinitis.

The use of citrus bioflavonoids, which include rutin, quercetin, hesperidin, and naringin, has shown clinical results in the treatment of capillary permeability associated with allergic rhinitis. Citrus bioflavonoids increase intracellular vitamin C. These bioflavonoids also have an antiallergy and anti-inflammatory effect by preventing deregulation of mast cells and basophils.<sup>18,19</sup> Oral enzymes such as protease, amylase, lipase, and cellulase are useful in the treatment of food sensitivities since they allow the breakdown of food protein, fats, and carbohydrates to smaller particle form for absorption which is less antigenic.

Enzymes also stimulate immune activity and bolster immune system function by promoting growth of healthy intestinal flora. Enzyme therapy is especially effective at fighting allergies because enzymes can break down protein allergens and work to block the process that causes an allergic reaction.<sup>20</sup>

## Summary

It has been my clinical experience that it is advantageous to utilize a combination of conventional and alternative therapies predicated on the severity of the allergic symptoms.

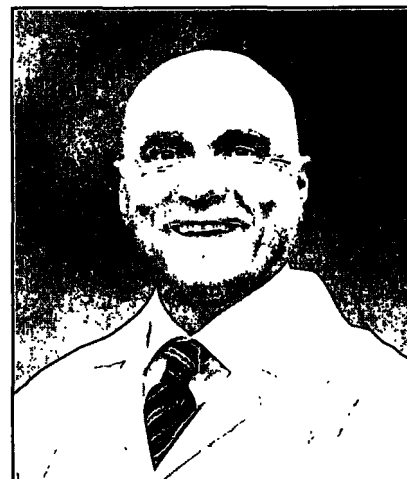
Utilizing simple saline nasal washes to reduce antigen loads and a natural combination of botanical bioflavonoids and enzymes, as mentioned above,

Dr. John Hahn completed his undergraduate studies at Sacramento State University and attended the California College of Podiatric Medicine in San Francisco, where he received his doctor of podiatric medicine degree. He received his degree as a doctor of naturopathic medicine from the National College of Naturopathic Medicine in Portland, Oregon. He is board certified in foot surgery by the American Board of Podiatric Surgery. He has certification in advanced injection and radiowave sclerotherapy, and was certified by the American College for the Advancement in Medicine in IV Chelation Therapy. He has taught as an adjunct instructor at Pioneer Pacific College and Clackamas Community College and was an adjunct professor in the Department of Integrative Medicine at the New York College of Podiatric Medicine. He's an active staff member of the Gresham Station Surgical Center, in Gresham Oregon. Dr. Hahn has several published scientific journal articles and was a contributor to the textbook *Compendium of Podiatric Biomechanics*.

at the beginning of allergy season significantly reduces allergy symptoms when exposed to antigens.

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# Standing Up for Health

by Jacob Schor, ND, FABNO

Chairs, the things we sit in, are like reishi mushrooms – they both have been around forever but were rarely used: only select individuals had the chance to use them. While the medical benefits of reishi mushrooms have been treasured in Chinese medicine for 2 millennia, only the emperor was permitted to take them.<sup>1</sup> Chairs too have had a similar exclusivity. Chairs, although often represented in early Egyptian carvings, on ancient Greek vases, and in early Chinese murals, were thrones: only royalty got to sit.

Chairs became commonplace in the 16th century, at least in well-to-do homes; by the 17th century, even regular people had a chance to sit down. It is only in the last century that a significant portion of us have spent any length of our waking hours sitting down. In the course of human evolution, sitting is an abrupt change in behavior, one to which we are ill adapted.

These thoughts are sitting on my mind today after reading an October 2014 study by Sjögren et al. that reported a statistically significant association between sedentary behavior and telomere length.<sup>2</sup>

Telomeres are the “caps” on the end of each chromosome needed to stabilize the genome. Each time a cell divides, the telomere gets a little shorter, eventually getting so short that the cell dies. Telomere length is a predictor of risk for chronic disease and cancer, fast becoming the ultimate biomarker, a measure of how much lifespan we have left. Preventing telomere shortening is the goal of any intervention promising to improve health.<sup>3</sup> Short telomeres are the hallmark marker of aging.<sup>4</sup>



Klismos chair, with curved backrest and tapering, outcurved legs, on the stele of Xanthippos, Athens, ca. 430–20 BCE.

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Telomere length is a better predictor of heart disease than older biomarkers such as cholesterol. In July 2014, the *British Medical Journal* published a meta-analysis by Haycock et al. that included 24 studies involving 43,725 people. Participants with the shortest versus the longest telomeres had a relative risk for coronary heart disease of 1.54 (95% CI 1.30 to 1.83) in all studies, 1.40 (1.15 to 1.70) in prospective studies, and 1.80 (1.32 to 2.44) in retrospective studies.<sup>5</sup>

Sjögren measured telomeres in blood samples in a group of 49 overweight sedentary people before

and after half of them took part in a 6-month exercise program.

The participants who exercised lost weight, and their lipid numbers improved.

What exercise did not do was lengthen telomeres. In fact, any increase in time spent exercising was associated with a nonsignificant trend toward shorter telomere length. The number of steps taken per day was not associated with any change in telomere length.

This is not what we would have guessed. Exercise is supposed to be good for people. This is such a basic tenet of modern belief that one might be tempted to discount Sjögren's results.

Here's where that history of chairs come in. Most of Sjögren's findings were not statistically significant, they were just trends; but the one strong and clear statistically significant finding was that reduced time spent sitting was significantly associated with increasing telomere length.

Our current faith in the benefits of exercise could be wrong. We may think that increasing exercise will benefit our patients' health, but the real benefit of exercise could be just that it reduces the time spent sitting. Modern sedentary behavior may be the problem, not a deficiency of time at the gym. Exercise's benefit may only be that it gets us to stand up. Exercise itself may even make the situation worse.<sup>6</sup>

For the 2 million years before there were comfortable chairs to sit in, humans expended huge amounts of energy moving about while looking for food. Data suggest that people living in simpler subsistence societies

burn about twice the energy each day as we do.<sup>7</sup>

Repeated cell division is considered the main reason why telomere length decreases, but other causes contribute, in particular chronic exposure to DNA-damaging agents such as ultraviolet, especially oxidative stress and inflammation. Physiologic and psychological stress is also associated with decreased telomere length.<sup>8</sup> Rigorous exercise increases oxidative stress in the body.

Admittedly, regular physical activity reduces risk of some age-related chronic diseases such as cardiovascular disease, cancer, and type 2 diabetes, but the actual reasons why are not yet understood.<sup>9</sup> While we would want to assume that exercise either lengthens telomeres, or at the least prevents shortening, the data have been mixed; studies report that extreme exercise shortens telomeres.<sup>10</sup>

Some studies report positive associations between physical activity and telomere length. Cherkas et al. reported that increased physical activity was associated with increased telomere length equating to a 10-year decrease in biological age between active and inactive subjects.<sup>11</sup> These differences are more pronounced in some studies; for example, ultramarathon runners compared with sedentary individuals have telomeres that suggest a 16-year difference in biological age.<sup>12</sup> Telomere studies have, by and large, been retrospective and so they reveal associations, not cause and effect. The data from these studies might be interpreted to mean not that exercise makes us younger, but that sitting makes us older, or even that people who feel older sit more and don't run marathons.

Studies that compare athletes with sedentary individuals assume that the exercise is responsible for perceived benefits. Perhaps it is the other way around, that being sedentary is what causes the problem; exercise may be beneficial only because the individual sits less.

Back in naturopathic school, we spoke often of the concept of "vital force," or what in Chinese medicine is called *jing*, or "kidney essence": that different people are born with or possess varying levels of some inner vitality. Perhaps we were only referring to telomere length.

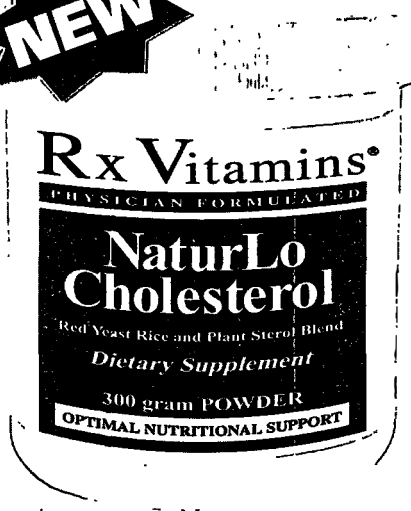
Does running ultramarathons lengthen telomeres; or are only people with long telomeres, or a great deal of vital force, interested in or

capable of running such distances? Our goal may be less to achieve high-intensity exercise levels than to mimic the nonsedentary behavior of our chairless active ancestors.<sup>13,14</sup>

Several studies report an inverted-U relationship between physical activity and telomere length, wherein moderately active individuals exhibit longer telomeres compared with both sedentary and

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OPTIMAL NUTRITIONAL SUPPORT

# Standing Up for Health

► extremely active people. Those who exercised the least or the most had shorter telomeres than individuals in the “middle of the pack” where it comes to energy expenditure, even when effects of age, gender, and body weight were factored out.<sup>15</sup> Moderate but steady activity perhaps should be the goal.

In 2012, van del Ploeg et al. reported an association of “sitting time” with all-cause mortality in a cohort of 222,497 Australians. Sitting for 11 or more hours per day, increased risk of dying by 40%.<sup>16</sup>

Sedentary behavior is also associated with increased cancer risk. An August 2014 meta-analysis, which combined data from 17 prospective studies to include a total of 857,581 participants, reported that sedentary behavior was significantly associated with a 20% increased overall risk of cancer (RR = 1.20, 95% CI = 1.12–1.28). This effect varied between cancer types with endometrial and lung having the largest significant increases in relative risk (RR 1.28 and 1.27 respectively).<sup>17</sup>

In a 2010 meta-analysis, sedentary behavior appeared as a significant etiologic factor for breast cancer. In 73 studies, physically active women had a 25% reduction in breast cancer risk when compared with the least active women. The strongest protection was found for moderate-intensity exercise, both recreational and household activities, sustained over a lifetime.<sup>18</sup>

This author spends a good portion of his workday sitting with patients and then compounds the situation by spending free time reading journals. This is a problem. This current study suggests that exercise, while it may keep us fit, does little to counter the overall effect of such a sedentary life. That quick workout at the gym that we were feeling so proud of may only make things worse.

Thus we need to find ways to not only reduce our own sedentary behaviors but also model this approach for our patients. The lack of an association between daily steps and telomere length is disheartening. Modern American men now average about 5000 steps per day, while men living in Amish farming communities take about 3.5 times that, nearly 18,400 steps per day.<sup>19,20</sup> The measure of possible benefit might not be the energy expenditure as the limited time spent sitting that we should be counting.

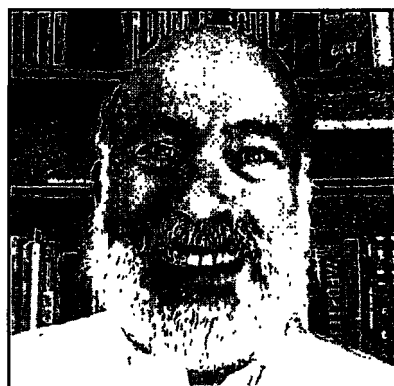
It would have been easy to clip a pedometer to each patient accompanied with a daily step goal. This is still not a bad idea, but if our aim is to reduce time spent sitting, it isn't what we need.

The easiest approach may be to simply stand up while at work. This article was written while I was standing up at my new work desk. Actually I've created three stand-up work-stations for myself: a fancy one purchased online in my home office,

a kitchen counter at home, and a pair of cardboard boxes propped on top of my office desk to elevate my computer to a comfortable height. It took a little getting used to, but it has been an easy enough habit to form.

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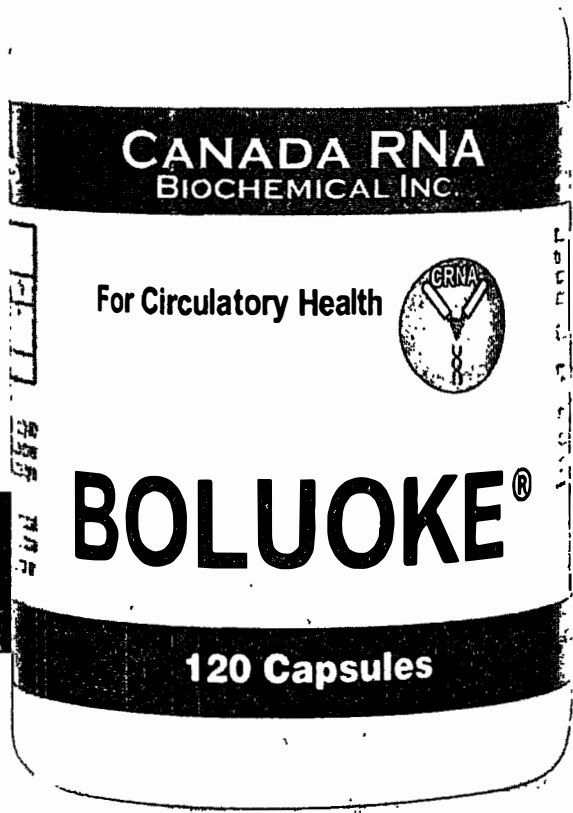
Jacob Schor, ND, FABNO, has practiced as a naturopathic physician in Denver, Colorado, with his wife, Rena Bloom, ND, since they graduated from National College of Naturopathic Medicine in 1991. He was humbled in 2008 when presented with the Vis Award by the American Association of Naturopathic Physicians (AANP). He has had the honor of serving the members of the Oncology Association of Naturopathic Physicians as a board member and currently as president. Dr. Schor began a term on the AANP's board of directors in January 2012. He is a frequent contributor to, and associate editor of, the *Natural Medicine Journal*.

# Simply the Best

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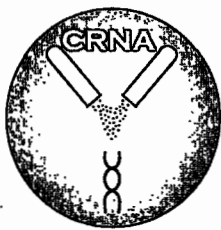
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# Field Control Therapy: Apparent Documented Reversal of Crohn's Disease and Prompt Cure of Longstanding Irritable Bowel Syndrome

by Savely Yurkovsky, MD

This article presents two successful and the only cases of Crohn's disease treated by this author in the last 15 years and also one of the numerous successful cases of irritable bowel syndrome (IBS).

Crohn's disease is a very serious inflammatory intestinal disease of unknown etiology commonly involving the ileum of the small intestine. It is often accompanied with multisystemic debilitating symptoms which are treated in gastroenterology with anti-inflammatory medications, and in case of poor response with high doses of prednisone and even chemotherapy or surgery.

It is considered to be an incurable disease that in particularly severe cases leads to death.

## Case 1

77-year-old man presented for Field Control Therapy (FCT) treatment in 2009 for gastrointestinal symptoms of 25 years' duration and which were officially diagnosed, by capsule endoscopy test in 2005, as due to Crohn's disease. The report read:

**SUMMARY & RECOMMENDATIONS:** Consistent with Crohn's disease, much more so than infectious, neoplastic, or vascular causes. Aphthous ulcer.

His gastrointestinal symptoms consisted of 5 bouts of diarrhea a day, abdominal pains, gas, and bloating. Other multisystemic health problems included bouts of fatigue, severe seasonal allergies, almost constant respiratory infections, Raynaud's disease, memory impairment, emphysema, and urinary urgency, all for many years. Neither conventional nor alternative treatments through his osteopathic doctor have had much success.

## FCT Bioresonance Findings

Gastrointestinal tract: multiple parasitic infections – cryptosporidium, *Blastocystis hominis*, giardia, tapeworms – yeast infections, residues of antibiotics, herbicides, pesticides, and inorganic and organic types of mercury.

In addition to these, two types of mercury, lead, and other toxic metals, as well as urban area environmental pollutants, were detected in multiple organs. His respiratory system, the site of his chronic allergies and never-ending infections, registered viral, fungal, and bacterial infections. In addition, bioresonance testing detected EMFs impairing his brain and other organs, including the immune system. Dozens of organs tested as energetically dysfunctional.

As esoteric as many of these findings might appear, the EPA has officially confirmed that the bodies of average Americans are loaded with at least 100 environmental pollutants, and other official sources deem billions of people as infected with parasites. Also, thousands of scientific references point to electromagnetic fields in our daily environment as being destructive to every organ, literally from brain to toe.

## FCT Treatment

All of the infectious and toxicological agents, as well as malfunctioning internal organs, were addressed exclusively through FCT homeopathic treatment. At times, glandular supplements were used with indications for and dosages determined by bioresonance testing. To address toxic EMFs, proper guidance and memon EMF-protective technology were prescribed, and the patient complied with both.

## Clinical Course

The patient was cured of not only his gastrointestinal symptoms but also all of his multisystemic conditions and even emphysema. In our society, it is common to medically blame every ailment, especially memory

*continued on page 76 >*



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# FCT for Crohn's and IBS

► continued from page 74

and energy problems, on age, starting from middle age onward; yet as he was getting chronologically older, his memory and energy were progressively improving to normal levels on this treatment. Today, at age 83, he receives no drugs and leads an unlimited and vibrant lifestyle.

Yet it took him 3 years, after all of his bowel problems became completely resolved after a year of the treatment, to persuade his gastroenterologist to repeat the test in order to demonstrate the expected disappearance of Crohn's disease. The reason for refusal was: "It is impossible to get rid of Crohn's disease."

When the patient told his gastroenterologist that his chest X-ray showed the reversal of old emphysema and lung scarring, and pulmonary function test became normal too, the reply was just as "logical": "But this is impossible, too." However, after the repeated capsule endoscopy was finally performed, it stated the following:

REASON FOR REFERRAL: History of Crohn's Disease with new-onset diarrhea. Suspicion for small bowel involvement.

SUMMARY & RECOMMENDATIONS: No masses, ulcers or other findings to suggest small bowel involvement of Crohn's Disease.

## Case 2

A young woman in her late 20s was presented to my office in 2002 with the diagnosis of Crohn's disease of 7 years' duration. Her upper GI series, performed only a few weeks prior, reported "duodenitis with probably worsening," and intestinal biopsy, done around the same time, reported "chronic inflammatory ileitis with time interval improvement" (likely due to anti-inflammatory medications and high doses of prednisone). Yet clinically she was showing

anything but "improvement," as her gastrointestinal symptoms consisted of up to 15 bowel movements (or, rather, watery explosions) a day, nausea, maldigestion, and pain, as well as multiple food allergies and severe cravings for sweets and carbohydrates.

The other and multisystemic symptoms included severe fatigue, severe PMS with mood swings, dysmenorrhea, insomnia, generalized arthritic pains, anxiety, and suicidal depression. She was utterly disabled and barely capable of custodial care of herself. Multiple anti-inflammatory and other gastrointestinal drugs, including acid blockers for her duodenitis, high doses of prednisone for months, multiple antibiotics, and nine antidepressants had both failed to aid, and caused intolerable side effects.

Acupuncture and chiropractic provided only mild and transient pain relief. At the time of the visit, she was receiving Asacol and Cipro for her colitis and nutritional supplements for weakness and malabsorption; but due to poor clinical response, she was advised by her gastroenterologist to resort to chemotherapy, which she refused.

She had a few mercury fillings and had received numerous antibiotics since childhood.

## FCT Bioresonance Testing

Throughout her 2½ years of the treatment, the following infectious agents were identified in her GI tract: *H. pylori* bacteria in her duodenum that undoubtedly caused her duodenitis, several worms and smaller parasites, and several species of candidiasis; also, heavy metals – mercury, lead, cadmium – pesticides, benzene, herbicides, and residues of several types of antibiotics, some of which were detected in her GI tract and others throughout the body.

In addition, EMFs were detected in the brain regions that handle

emotions, sleep, and hormonal system. All of these noxious factors affected most of her internal organs, including the entire gastrointestinal system, directly, indirectly, and via their mutual interactions. As a result, as in any serious chronic disease, numerous internal organs, far beyond those which belong to just "disease," tested as severely energetically impaired, including immune, endocrine, detoxifying, excretory, and others. In a nutshell, it was a case of a person in a young-looking skin or shell but with a body filled with the multiple exhausted organs of an aged patient.

## FCT Treatment

The main focus of the treatment was to remove all of the identified toxicological, infectious, and pharmaceutical agents, as well as revitalize all of the energetically malfunctioning organs through mainly homeopathic means according to FCT.

Proper EMF guidance was offered too. On occasion, due to the history of emotionally traumatic childhood that was contributing to her anxiety and depression, classical constitutional homeopathic remedies were used. All of her medications were discontinued soon after FCT treatments commenced.

## Clinical Course

Her Crohn's and practically all of her medical problems became matters of the past, and she was able to return to work. Due to her lost faith in conventional gastroenterology, she did not wish to follow my recommendation to subject to gastroenterological testing in order to document the laboratory reversal of Crohn's disease. At the time she stopped FCT, shortly after her move to the West Coast, she still had some food allergies remaining. Below is her own testimonial of the ordeal.

# FCT for Crohn's and IBS

## Testimonial

I was 21 years old when I developed chronic fevers of 104° with diarrhea and vomiting. I believed that I had food poisoning and that it would pass. Instead, the symptoms became more severe. Unable to tolerate any food, I quickly became emaciated. This persisted for months. I was uninsured at the time and couldn't afford to see a doctor. Finally, too weak to function, I went to the ER, where doctors concluded they didn't know what was wrong with me, gave me Tylenol to reduce the fever, and sent me home after a few days. Soon afterward, the fever returned and I returned to the ER. After many painful and invasive tests, the doctors concluded they believed I had Crohn's disease.

I began taking 16 pills a day. The side effect was that an ulcer began to burn away my esophagus. My

medication was switched to another immunosuppressant. My symptoms never improved. They became worse, now with more added side effects from drugs that required more drugs. The inflammation began to spread, and I was soon diagnosed with fibromyalgia, and rheumatoid arthritis. I was now in chronic pain everywhere and could barely walk.

In my mid-20s, I was given one week to live when my organs shut down. I was scheduled for a blood transfusion. I was saved by emergency medicines such as prednisone, but doctors didn't address my severely low B12 levels that are recorded in my lab work. Once again, I was "patched" up and sent back into the world without a real solution.

By the time I was in my late 20s, I was taking 40 pills of medications a day. I had lost every job because

my health failed me. I was unable to finish my education because of my poor health. And now I was on disability and food stamps. Since none of the medications had been working, and I was considered a medical mystery, the GI doctor now told me the only option left for me was to receive a weekly IV of interferon. When I told him that I was seeking a second opinion, he said that any other doctor would agree with his treatment plan. Luckily, Dr. Yurkovsky was not "any other doctor."

Before trying FCT with Dr. Yurkovsky, I visited an alternative medical doctor who ran helpful tests but still seemed to work within the realm of Western medicine in that he threw a ton of supplements at me, some that were harmful based on my particular condition.

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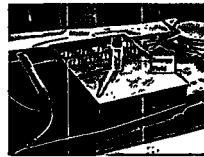
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# FCT and Crohn's Disease

I considered FCT a miracle. Within a few months, the symptoms that had debilitated me for many years, and almost led to my death, disappeared. I was able to tolerate more foods. The inflammation in my bowels had alleviated, and with it the excruciating pain, vomiting, and frequent runs to the bathroom – what had been up to 16 to 20 times a day. I was now digesting food, having normal bowel movements, and waking up naturally energized. The arthritis also went away, and eventually, the fibromyalgia, too. For the first time in years, I was able to walk without pain, and walk for miles!

FCT lifted all the underlying infections that were contributing to inflammatory bowel disease. The only missing element was being aware of food allergies, which a simple blood test determined. Some of my Crohn's symptoms were identical to what I still experience from exposure to yeast or wheat. Twenty years later, my low B12 was explained when, frustrated by frequent burnout that persisted, I got a lab test for intrinsic factor that tested positive for pernicious anemia. When I asked my doctor why, considering the labs from 20 years earlier, I had never been tested, he said because only older patients are known to

have pernicious anemia. Once again, Western medicine sees me as a medical mystery.

I have recently resumed working with Dr. Yurkovsky because he doesn't limit himself in the realms of just medical science, and he doesn't limit his patients by a textbook. He is a pioneer in progressive medicine. He has a systematic approach to awakening and transforming the energy field, thereby creating homeostasis in the body, in a way that no other treatment does. The results speak for themselves.

– Lauralyn Kearney; New York,  
March 12, 2015

## FCT Prompt Cure of Longstanding Irritable Bowel Syndrome

A 69-year-old woman presented to FCT treatment with irritable bowel syndrome of 40 years' duration. Other chronic medical problems: low energy, tremors, insomnia, anxiety, cravings for salt.

## FCT Bioresonance Testing

Over the course of 5½ months, the following noxious agents were identified: yeast and other fungal infections, multiple parasitic infections, residues of antibiotics,

mercury, and Lyme disease. Also, a long list of malfunctioning organs, along with EMFs affecting her brain and abdominal area, were registered too.

## FCT Treatment

As in the previous two cases, the main staple of the treatment was homeopathic, to address FCT's main focus – direct causes of sick organs, and the end result, sick organs themselves. Also, she adhered to EMF reduction guidance and acquisition of effective memon EMF-protective devices.

## Clinical Course

One month into the treatment, she mentioned that her friends complimented her on looking younger and, a little over 5 months into treatment, her irritable bowel syndrome and the rest of her medical problems have ceased to exist.

## Conclusion

Understanding the main categories of the real causes of chronic diseases and the correct means to diagnose and treat these causes must always remain our main goal in the reversal and prevention of these diseases. ♦



Savely Yurkovsky, MD, graduated from Il Moscow State Medical Institute in 1975 with a degree in pediatric medicine. He completed his training in internal medicine and cardiology at Coney Island Hospital of Downstate Medical School, and is board certified in internal medicine. He has been in private practice since 1984 with a special focus on identifying and successfully treating the main causes of chronic diseases via bioenergetic modalities – bioresonance testing and homeopathy, correspondingly, or FCT.

Dr. Yurkovsky has founded a teaching organization, SYY Integrated Health Systems Ltd., dedicated to training in FCT. It has been presented extensively in the US and Europe to medical practitioners since 1999 and demonstrated numerous documented reversals in a variety of chronic diseases.

His book, *The Power of Digital Medicine*, was endorsed for scientific validity by two prominent physicists, MIT Professor George Pugh, PhD, and former chairman of materials science at Stanford University, Professor William Tiller, PhD, and also by Mehmet Oz, MD, from Columbia University Medical School. Its diagnostic and homeopathic aspects were also presented at the annual BTR conference in 2005: Unified Science & Technology for Reducing Biological Threats & Countering Terrorism, affiliated with the Department of Homeland Security and the US Army, as well as at the Department of Psychiatry of Massachusetts General Hospital, Harvard Medical School, and many other professional symposia.

In collaboration with the Department of Gastroenterology of Johns Hopkins University School of Medicine, Dr. Yurkovsky has contributed a chapter on homeopathy to the textbook *Integrative Gastroenterology* (Oxford University Press; 2011) and authored numerous articles on different medical topics. His book in progress explains the inevitability of the current epidemics of autism and numerous

other brain and somatic diseases, and how to solve them.

Contacts for information concerning the ongoing training of health practitioners in FCT can be made through information provided in the FCT ad on page 77.

# Treating for Stealth Viral Infections with Japanese Acupuncture and Herbal Therapy: Butch Levy, MD, LAc

Complex chronic diseases have reached epidemic proportions. The clinical offices of many primary care providers are filled with chronically ill patients struggling with exhaustion, cognitive impairment, sleep disorders, and recurring pain. These illnesses tend to be unresponsive to emergency interventions, surgery, or intensive pharmaceutical treatment, and frequently all our skills and experience still fall short in improving those patients' health and quality of life. In my own practice, a significant number of these conditions are associated with opportunistic viral infections that have gone undiagnosed or have resurfaced.

These covert but potentially aggressive infections include viruses such as flavivirus (West Nile), hepatitis B (HBV) and C (HCV), human papilloma virus (HPV), and many of the herpes viruses, such as cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex (HV-1 and HV-2), and varicella zoster virus. The majority of these infections are considered incurable, although the symptoms are often controllable. Pathogens that are also well-recognized as oncoviruses with the potential to be causative agents in specific cancers include CMV, EBV, HBV, HCV, HH8 (Kaposi's sarcoma-associated herpesvirus), and HPV.

When patients come in with symptoms that suggest these types of infections, I apply Chinese or Japanese medicine in tandem with Western diagnostic tools to broaden the prospective treatments available. Based on the encouraging results I see, I would propose the value of integrative treatment, bridging East and West, for these types of viral infections.

## Diagnostic Concepts

In Western Medicine, immunologists recognize that certain infectious pathogens are able to cloak their identity and remain present in the body. The patient may be relatively symptom free, or not, and possess what appears to represent adequate immune function. Yet under the right conditions, they can be subject to reappearance of these hidden pathogens. What is even more concerning is our inability to detect inner cellular changes that alter normal

homeostatic pathways and potentially create malignant transformation. Just as the recognition that cellular messaging from unfavorable diet and lifestyle can produce inflammation and oxidative stress, these pathogens can create similar issues, but are often unrecognized as the cause of biochemical alterations in the etiology of chronic disease.

Chinese medicine recognized millennia ago that patients could suffer from covert afflictions or "evils," stealth pathogens that would remain in the body. The Chinese system was able to delineate measureable changes in the pulse and in diagnostic areas on the abdomen that alerted the practitioner to the presence of sequestered infection. These diagnostic tools could also be used to detect the progression of illness to deeper levels in the body. For example, one might diagnose EBV and associated symptoms of chronic fatigue, but at what level of illness does it exist? As will be shown, the Chinese approach encompasses greater recognition of progression of disease to deeper levels, suggesting the potential of greater cell injury and with that more serious illness.

The classic herbal text, the *Shanghan Lun* (Treatise On Cold Damage Disorders) by the medical sage Zhang Zhong-Jing, dating from 220 AD, was a manual on the diagnosis and treatment of externally contracted diseases, which today would suggest infections. The text systematically described the invasion of pathogens as they entered the body and the course disease could take unless interrupted, as well as signs, symptoms, and patterns of illness that would emerge as illness spread deeper.

The genius of this treatise was its specific recommendations for both treating ongoing disease and protocol to force the pathogen toward a depth of reduced aggressive potential. Using symptom configurations, abdominal palpation, and pulse patterns, the practitioner was able to discern the level of illness and in concert with the patient's energetic strength, compose an individualized treatment plan. This would include acupuncture and herbal formulas composed of a combination of herbs in an exact

## Butch Levy, MD, LAc

► formulation, designed to match the pattern of presentation in real time.

Applying these strategies in current practice, ongoing treatment requires that with each visit, the exam is repeated and based on changes in response to therapy, the acupuncture and herbs are adjusted accordingly to match the patient's alteration in the pattern of illness, in a chess match of extraordinary proportions. These protocol, developed two millennia ago in Chinese medicine, are still utilized and found to be effective.

### **Integrative Diagnosis, East and West**

In my practice, patients frequently come having already been given a diagnosis by their medical doctor. Typically that information can be a starting point for my own investigation, providing the access point to information based on fundamental Western concepts. I then add another perspective using the Chinese model, conducting two simultaneous but separate examinations, one from each paradigm. This allows for the creation of different perspectives on the same information. Seen from the vantage point of Chinese medicine, I view their condition as a pattern of imbalance, rather than as a fixed diagnosis of disease. Allowing a synergism of both paradigms often provides more than just the sum of two viewpoints, and creates opportunities for therapies that are inclusive of each other rather than exclusive.

The goal then is to view the illness dynamically, recognizing that the patient is continually changing, and is done an injustice by having the label of a disease name placed on them. Certainly it provides an image of signs and symptoms but fails to delineate where they are on the continuum of disease or its severity. Is it just beginning, or full on? Is it winding down or revving up? Labels also imply that everyone is the same, and therefore treatment is the same. As is often expressed in Chinese medicine, "There can be the same treatment for different diseases, and different treatments for the same disease."

**Immunity.** The recognition of immune hyperactivity has revolutionized treatment in fields such as rheumatology. One example is the treatment of collagen vascular diseases. The advancement of pharmaceutical research, in response to this understanding, has created therapies to "shut down" immune overactivity and limit system damage by reducing inflammation. Yet at the opposite polarity, the understanding of an underachieving or vulnerable immune system has generated limited current agreement as to its causes and more importantly resulted in few effective treatment approaches. Situations of immune dysfunction focus primarily on immune compromised patients with a

heightened risk of severe, often overwhelming infection. Otherwise the idea that patients may have some form of immune dysfunction, while acknowledged, offers little therapeutic help to those affected.

**Terrain.** One corollary, which seems relatively underappreciated in allopathic Western medicine, is a focus on the underlying energetic strength of the patient in combating disease. It is not just the illness that determines outcome, but also the inner terrain in which the illness occurs. The Chinese medicine perspective posits that the vital force within, the Qi, determines our energetic strength and functional capacity to respond to threats and changes with the body. The strength of this energy is the essential aspect of our protection and defense against infection. It is recognized that the origin of Qi is the genetic merging of our parents. The Qi can be revitalized from our foods and is inhaled in every breath. It is transformative in the production of fluids and blood, it provides containment, and it is the source of growth and development, as well as physiologic activity and metabolism. Ultimately, the terrain determines outcome, and Chinese medicine can directly influence the Qi for its support.

### **Homeostasis**

**Maintaining global equilibrium.** Eastern medicine reflects a perspective that health can be maintained in a way that offers vibrancy, harmony, and quality to our daily lives. An essential paradigm suggests that each person's health or lack thereof is related to imbalance in the body's global equilibrium. Certainly disease can occur, but the goal is to shift the balance back toward health and recovery whenever possible. This certainly doesn't imply that all we need is balance, and everything will be right. On the contrary, disease often will require Western care, but together a blend of both paradigms can support necessary treatments with a shift toward recovery.

**Intervening before disease begins.** Eastern medicine also developed concepts that recognized the essential need for preventive medicine. If you were to become ill, available urgent care was really not an option, so staying healthy was a necessity. In the ruling court, the physician was only paid if the Emperor remained healthy. Any illness meant a forfeiture of pay. Pursuing that concept of a desire to treat before disease begins is a viable complementary approach to existing Western health practices. This paradigm focuses the practitioner on prevention, rather than just early intervention, and provides tools and protocol to restore homeostasis at a much earlier stage.

## A Systems Perspective

The individual organs represented in the Chinese model are not considered isolated independent systems, as often expressed in Western medicine, but part of a whole, unified and absolutely interdependent. The focus of health requires an interaction of the entire network as a system rather than correcting the dysfunction of a single organ. Consequently the strategy in treatment is to support the interplay within and among the organ systems, with system balance as the fundamental objective, a coordinated effort between mutually dependent structures. Disease disrupts the ebb and flow of the entire organism, as if a sports team were trying to perform with one or two players who are not functioning up to par. When that occurs, the performance of the entire team is impacted.

In Chinese medicine, although one organ may be symptomatic, creating signs of imbalance, therapy requires recognition all of the members of the team and how each might be affecting the others in a potentially supportive or detrimental way. The system is represented with metaphors that relate to the interaction of a large family dynamic. However, the body is not viewed as a chaotic system, but one of great refinement.

Symptoms may be reflected in the function of one organ system, but the cause could be originating from other organ imbalances. The understanding is that the disease is not necessarily a single-organ phenomenon, but could be the downstream or upstream response to an imbalance in another system. In my experience, this phenomenon is surprisingly common. By way of example, core kidney energy in Chinese medicine affects kidney function and the urogenital system, but it is also responsible for the function of the prostate, for reproductive energy, the spine, the lower extremities, and the brain. It is nurtured by the lung and controls the heart while supporting the liver. If the kidney is viewed as a fulcrum point in this model, it may be that weakness or excess in other organ systems are affecting the kidney. Unless they are treated, the kidney will continue to show signs of deterioration, which impacts the other organs.

The implication being that each organ is interconnected to the others, and an imbalance or disease in one is reflected in the function of all to some degree. This creates a whole-person concept of health and illness. People were not considered to have isolated tissue organ complaints. Rather it is essential to evaluate the signaling and interaction among organ systems that would reestablish balance.

## Diagnostic Tools

While Chinese and Japanese practitioners originally studied the same texts, their applications and adaptations are culturally distinct. In the Chinese model, clinical information is derived from talking to the patient, observing

them, looking at the tongue, and taking the pulse. The Chinese practitioner utilizes both herbs and acupuncture, with herbs being the primary focus. The Japanese system, which I have adopted in my practice, developed in two directions. Acupuncture is a tradition usually practiced as a distinct discipline, to the exclusion of herbal treatment. In the early 17th century the Shogun decided that blind people should never be without a profession and were therefore trained as acupuncturists. Even today in Japan, a large percentage of acupuncturists are sightless. Obviously facial and tongue observations were not available. Consequently, Japanese acupuncturists have developed astute palpatory skills.

**Pulse diagnosis.** Probably the most distinct and unique of the fundamental exams in Chinese medicine relates to the pulse system of diagnosis. In contemporary Chinese medicine, taking the pulse involves feeling the radial artery at the wrist. By "listening" with the fingers, one is able to gain information from the flow of fluid through the artery. Pressing with the first three fingers can offer information sensed by each finger individually or by all three as a single unit.

The intention of pulse diagnosis is to first assess three fundamentals: 1) Reflection of depth of disease: is the pulse superficial or deep? 2) The second fundamental: is the pulse weak or strong reflecting the patient's energy? 3) Is the pulse rapid or slow, indicating that the overall system is warm and inflamed, or cold, sluggish, and slow to respond?

At that point, the diagnosis moves into a deeper, more subjective interpretation of the pulse, termed the pulse quality. These qualities are described in the literature as tight (like a guitar string), choppy (reflecting changes in the rhythmic cycle of the pulse from beat to beat), slippery (visualize a rolling pearl in a basin), or hollow (suggesting that when the pulse is pressed, no energy can be detected inside, like pushing on a scallion). There are more than two dozen variations in the waveform of the wrist pulse, reflecting variations in the frequency and amplitude of blood flow as a means of diagnosing body imbalance and dysfunction. Pulse diagnosis can be seen as the ability of the musician to recognize notes and chords, and the melody that their combinations can produce. The practitioner's listening skills may be seen as a reflection of their interpretation of the unique song of life being displayed by their patient.

**Abdominal exam.** The Japanese have developed and refined the art of abdominal palpation. This approach involves palpation of the hara or central abdominal area, the solar plexus, as a way of accessing information from the body's energy source and spiritual center. The Japanese



## Butch Levy, MD, LAc

➤ style of herbal practice is called kampo, and the abdominal examination used to determine the herbal formula is called fukushin. The goal is to palpate the abdomen and correlate it with specific symptoms that form a distinct pattern, called a shoh, and that shoh or pattern directs therapy by indicating a specific herbal formula.

**Palpation.** Touch is an effective way to evaluate the body, to identify the tone of the muscles and tendons and tightness or tension in various areas of the body. Palpation also makes it possible to assess temperature changes from the upper to the lower areas of the body.

**Facial diagnosis.** Color in different areas of the face can indicate organ imbalance. One might observe, for example, a yellow tint reflecting spleen weakness or a blackish facial hue indicating kidney deficiency. Lines in the face may point to emotion, to the emotional personality of the patient, and suggest the involvement of a particular organ system. Facial contours (round, oval, square, or trapezoid) reflect a patient's personality type and can enhance the style of communication they need in order to understand their issues.

**Tongue diagnosis.** Another useful addition in the Chinese model of care comes from tongue diagnosis. Each area of the tongue represents a different organ system, and the color of that area and the contours of the tongue provide clues to pathology in the body. A "geographic tongue" implies intense inflammation. Correct treatment can alleviate the problem, and this will be reflected in the tongue, which will slowly begin to return to normal.

**Diagnostic use of acupuncture points.** Each organ manifests in the outer extremities as well as in the acupuncture meridians. The meridians provide a means of assessing the flow of energy in the body and whether there might be an obstruction or a blockage in energy.

### Treatment Concepts

The Chinese, faced with numerous epidemics over the millennia, have devised evaluation and treatment approaches outlined in classic texts on herbal therapies and acupuncture. Variations based on their methodologies have led to adaptations that are currently useful in the treatment of stealth viral infections.

References made in the Wen Bing text (Warm Disease Theory) state that a cold in the late fall or winter can return to cause illness in the spring. Even hundreds of years ago it was recognized that an infection could incubate for a period of time and then resurface, causing a new illness. The point was not that a cold could later recur. The concern was

that illness had significant potential to return as a deeper level of disease. Treatment for initial infection required a greater emphasis on the prevention of subsequent illness that might go deeper. Consequently, aggressive treatment of acute infection was encouraged. Certainly thousands of years ago, a cold that became pneumonia, a cut that became a cellulitis, or a GI infection that worsened more likely than not could prove fatal.

### Integrative Interventions

When damage to the overall system is eminent, the options left to interrupt the disease and prevent further deterioration are limited. The strongest and fastest means available is often Western drug therapy, which may be the only available option if organ function has weakened and declined to a level that is life threatening. The idea of repair and recovery, at this point, becomes a secondary goal to survival.

From my own observations, Western therapies designed for complex chronic diseases are extremely useful. By affecting a particular metabolic pathway, the downstream production of biochemical molecules will be influenced in a way that changes cellular response, ultimately reducing the symptoms that reflect an imbalance. However, treatment seldom resolves or eliminates the disease.

Although chronic tissue damage may be slowed or stopped, Western medicine has no strategy for repairing or restoring function to the damage that has ensued. Even when the disease process has been inhibited, without the continuation of medication, a return and progression of the disease is a strong possibility. In the situations we encounter with stealth infections, despite a clear diagnosis, the tenacity of the infection often proves difficult, given the level of entrenchment. Chinese medicine encompasses thousands of years of confirmation that the herbal treatments are effective for the patterns they are designed to treat. Please understand that we are not treating a "disease state," but a constellation of symptoms in a patient with a specific energy level. These treatments, when deftly applied, can be hugely successful for the problem.

### Acupuncture

Current interpretation of why acupuncture works is still intelligently theoretical. There is the idea that using needles influences the matrix (fascia and connective tissue), to change the electrical potential within. This then influences local neuro-vascular communication creating a physiological reverberation on a more global scale. Another remarkable aspect of acupuncture occurs in the setting of the Extraordinary Meridians. A useful metaphor from ancient times refers to the establishment of dikes and irrigation canals to control water during times of flood or



drought. The Extraordinary Meridians are used to provide a similar concept. They act as reservoirs that are able to move energy away from areas of excess or bring needed energy to depleted areas.

Using the acupuncture points individually allows for symptom modification, while the Extraordinary points can help up regulate or down regulate systems to better balance the whole. For example a patient with a lurking pathogen causing digestive level issues can be treated with local points for bloating or diarrhea, while the digestive system can be helped by balancing the organs. In addition, if the liver energy, by emotionally overacting, has played a role in the digestive problem, the same approach to that organ can be overlapped as well.

### Herbal Therapies

The Chinese concept of herbal treatment consists of the integration of symptoms, pulse, and tongue diagnosis to arrive at an assessment and treatment with herbal formulas and acupuncture. These formulas are a combination of plant, mineral, and animal substances designed to treat systematic problems as well as organ imbalances.

Many contemporary herbal formulas prescribed are derived from texts that originated two thousand years ago. The Shanghan Lun and the companion text, the Jin Gui Yao Lue (Essential Prescriptions from the Golden Cabinet), provide the framework for interpreting specific symptoms and describe specific herbal formulas for successful treatment. To understand, integrate, and balance the entire person is different than treating symptoms alone. Rather the herbal formulas are based on a construct of illness applied to interpret the depth of disease. The Chinese perspective on infection is also multidimensional. If you understand the path inward that disease can take, then the objective is to reverse that direction and push the infection outward to remove it from the body, whenever possible. This is dynamic movement, however, as the disease can penetrate deeper, causing more severe symptoms or can actually be encouraged in a more superficial direction resulting in the lessening of symptoms. The text also provides valuable information concerning correcting iatrogenic practitioner-induced errors.

The intent of this article is to provide practitioners with a brief overview of the Japanese and Chinese approaches to assessment and treatment for opportunistic stealth viruses, which the Chinese aptly term lurking pathogens – a common, but often unrecognized cause of complex, chronic disease. I view this approach as an important aspect of integrative patient care for certain chronic disorders. Eastern medicine offers additional perspectives to the practitioner for treatment and can be seamlessly

integrated with naturopathic therapy, functional medicine, and Western care. An experienced practitioner of Chinese medicine can aid in shifting the balance of recovery for the patient. Inclusive integrative treatment strategies promote the higher concept that utilizing the best of all models of care can only benefit our patients in restoring health.

### Butch Levy, MD, LAc

Butch Levy is an integrative practitioner, board certified in Family Medicine and NCCAOM certified in acupuncture. Dr. Levy has been in private practice for 37 years, including care from obstetrics and pediatrics to geriatrics and hospice care. In the late 1980's Dr. Levy attended acupuncture school, completing many of the classes, but also apprenticed with and was mentored by Miki Shima to complete his requirements for certification. Dr. Levy's training in Eastern medicine is in the Japanese style of herbal diagnosis using abdominal patterns, fukushin, and his acupuncture style is distinctly toward the Extra Vessel and Divergent Channels. Dr. Levy's current practice integrates allopathic care with Chinese medicine and functional nutritional medicine, bridging east and west with comprehensive, practical approaches to illness. He sees a wide variety of patients, and his focus of interest is toward complex chronic disease, including supportive care for cancer and autoimmunity.

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# Vaccines, Vaccinosis, and Tautodes

by Carvel Tiekert, DVM

While the first word in the title is well known, it is appropriate to start with definitions for the second and third words above. Vaccinosis is a term used within the homeopathic community and is defined as "ill effects of vaccination." During many of our courses and seminars, we have been taught about treating for vaccinosis. Tautode is a term for homeopathic medicines made from vaccines or conventional drugs. (See Yasgur's *A Dictionary of Homeopathic Medical Terminology* for a more complete definition).

I started using vaccine tautodes after reading a book by Jean F. Elmiger, MD. Elmiger was a Swiss internist who was frustrated in the results of his treatment of his patients. He thought that there was a blockage of the appropriately repertorized medicine and theorized that treating them with tautodes would be useful. They were useful, and ultimately he found that as he pursued this approach, it was best to go in reverse order of the vaccines given – in other words, he gave the most recent vaccine's tautode first, and then worked back from there. Elmiger is the originator of a protocol called Sequential Homeopathic Therapy.

Over the past couple of years, I have used tautodes more frequently in the treatment of various problems in dogs and cats, some physiological and many behavioral, with good responses. Tautodes of vaccines are now frequently my first prescription. A number of the patients whom I have treated are appropriate to be included in this discussion. These cases, in my mind, present an irrefutable reason for the use of these medicines, and for that matter a rationale for the use of homeopathy.

**Case 1:** An 18-month-old standard poodle who presented having severe grand mal seizures 1 to 2 times a week. In taking the history, it was determined that these had started within a few weeks of receiving a booster vaccination about 4 months prior to my initial appointment. She was treated with DHPP tautode in a 30C potency, and in the 6 months before I lost her as a patient because of moving, she had only had one petit mal seizure.

**Case 2:** An approximately 9-month-old lab cross rescue that presented with history of separation anxiety, being fearful with strangers (both people and dogs), paced, didn't like eye contact, seemed hypervigilant. The owners were concerned that this dog's fear might have an aggression component, because when people came in the house they were concerned about how the dog would respond. The clients had been working with a behavior specialist with poor response, and had been unwilling to try any drug therapy unless all else failed. After further conversation, I decided to give the rabies vaccine tautode, in a 30C potency. The owners said that within 24 hours, there was a marked change in the dog's behavior and she was much more settled. Within a week, she appeared to be a totally normal dog, and no signs of aggression or fear toward people or animals were apparent. When she came for her next booster, we used the suggestion by Don Hamilton, DVM, of a dose of the medicine the day before vaccination and the day after. She showed no negative effects from the vaccination.

**Case 3:** Daisee (client report):  
Before first dose of Rabvac (tautode):

I think she was about 18 mos when you gave it to her. Aggressive and barky to unknown. Stared and showed teeth. Unresponsive to verbal commands. A tug of war on a leash. Described by trainer as "feral." Incapable of being house-trained even though over a year old. Anxious, on edge to any sound or movement. Barked. Good for a guard dog but then uncontrollable. Hyper – ADD. Could not relax or sit to be petted. Not comfortable with petting as if guard down. Digestive erping in the night or early morning. Destructive in the house and out. Chewed railing on deck, tore pillows, destroyed toys except squeaky ball. Needed constant supervision. Could not be trusted around kids or bikes. Chased and nipped at their feet. Sent to day care but had to be alpha dog or got into trouble competing for alpha dog status. Could not be touched around the mouth or feet.

After first dose:

Lazy and sleepy for a day or two. Then seemed to wake up. Responded to name. Looked at me when I spoke. Not afraid of being touched. Wanted petting. Remembered basic commands like stay and sit. Wanted to please so sat for petting. Played catch with her squeaky ball. Cuddles. More gentle, even kissy. Only four days after [tautode], met new boy and girl (boy autistic) without staring or threatening to bite. However, still afraid of strangers who approached too fast. Daisee wanted control of the meeting process. Could concentrate on me and walking with me. Not perfect but a dramatic improvement. Traveled in car much calmer. Went across country stopping along the way. She was

exceptionally good. Digestive upset seemed to disappear. Bladder control, whoopee! Played with other dogs in a friendly manner without my interference.

Daisee proved that she was no dumb dog. Actually very smart.

After rabies at 4 years old (was given Lyssin at the time of vaccination by veterinarian in Wisconsin, where she now lives):

Aggression began to creep in, bit by bit. Barky and hyper. Edgy and irritable. Snapped at my mother, drawing blood. Leash was a threat again. Pulled and tugged with all her might. Chewed leash to get to UPS man – in effort to protect me? Ignored verbal commands. Started destroying house like window sill – chewed to get at something or someone deemed a threat. Lost interest in ball playing.

After second dose of Rabvac (tautode; client had sent me an e-mail asking for a dose, which I sent to her):

Returned to former self but much more slowly. Took longer for the transition, like 2 weeks instead of less than 1 week initially. Ball-playing returned. Listened to me again. Cuddly and wanted petting. Rolled on back for petting. Got free from house but returned when called. She is a tease. Playful.

This owner is an astute observer and reporter, thanks to her years of experience in dealing with disease in Africa.

**Case 4:** This orange spayed female cat had been successfully treated for episodic explosive behavior with a couple of doses of Phosphorus 30C. The owner called me one day to say that after over a year, the cat had suddenly started the behavior pattern again, and asked whether, since she had another dose of the Phosphorous 30C at home, should she give it, to which I responded that she should. The response was poor, and the owner brought the cat in for a physical since in the cat's history there had been a poorly healed femoral fracture and she wondered if that was aggravating things. There was nothing new from a physical standpoint, and I asked her if anything had happened

recently, to which she responded that the cat had had a rabies vaccination somewhere else about 3 weeks before. I asked her if that was when the sudden change of behavior had started, to which she responded "Yes." I gave her a dose of 30C rabies tautode, and the owner reported that the cat was totally normal 24 hours later.

#### Case 5: (client report)

She got a rabies booster in 2009 when I thought about enrolling her as a pet-therapy cat (one of their requirements). Before the booster, she was quiet but self-confident and enjoyed socializing outside the home environment – she went to cat shows and was even comfortable going to elementary schools and having classes of young children interact with her. After the booster, she seemed to withdraw and become afraid of numerous things, including thunder and strangers. I stopped showing her and never went through with the therapy cat program since her behavior was so different and I knew she wouldn't enjoy it.

You gave her the rabies medicine in September 2013 – she was still shy at that time but not as bad as immediately after the booster, and I had started taking her to cat shows again earlier in 2013 just to see how she'd do after a long absence from them. She tolerated them but was still shy and I had decided to let her "retire" again. After the medicine I tried her in one more show in December and the change was profound – she interacted with the judges and thoroughly enjoyed being in the benching area. She even ended up as Best Household Pet in the show. She still has an occasional "scared" moment, but for the most part, she's back to the cat that I knew before the 2009 booster.

These and other responses that I've seen over the last couple of years make me look at vaccine tautodes as a frequent starting place for the treatment of my patients. Since my practice is very part time, I don't see the patient population that I did in the past. Were I seeing that volume, I suspect that

I would have many more cases to highlight this aspect of vaccinosis.

The question here is not whether vaccines have some valid place in medical practice. I might not have gotten polio and the secondary developmental problems that I ended up with had I been vaccinated, but it wasn't available at the time, so it wasn't an option. I lived in an area that had enough polio that in a radius of less than 100 yards from my home four of us had polio: two of us were just sick for a while, one spent 2 months in an iron lung, and one never got out of an iron lung. We have enough stories about parvovirus infection and distemper within the small-animal veterinary community, let alone rabies, to know that *appropriate* vaccines given at *appropriate* times are useful. So the question is how to reduce vaccinosis. The response to this protocol is obviously very gratifying. At the same time it raises (at least) a couple of interesting questions:

- Does the fact that many vaccines include either mercury or aluminum as preservatives have a bearing? Do the tautodes work in part due to the fact that they are treating the symptoms that can be caused by these two elements?
- Did the fact that Daisee was treated with Lyssin postvaccination affect the treatment with a tautode?

As a side note, when we see the behavioral changes that appear to be related to vaccines, and since they responded to treatment with a homeopathically prepared vaccine (tautode), one has to question the condemnation of Dr. Andrew Wakefield and his position that vaccinations are implicated in the severe increase of autism that seems to be afflicting the children of today. Could/should autistic children perhaps be treated with tautodes – particularly if the disease pattern that they present with fits any of the diseases that they have been vaccinated for?

Anyone interested in a mailable copy of this article to send to others, please contact me at [gordon2838@verizon.net](mailto:gordon2838@verizon.net).

# Insulin Resistance: The Unintended Consequence of Fat Phobia and the Case for Ketosis

by Sara Wood, ND

Insulin resistance (IR) is a condition wherein cellular receptors become less sensitive to insulin, causing an inability for glucose to enter the cell and glucose buildup in the bloodstream.<sup>1</sup> IR leads to a prediabetic elevation of blood glucose and, eventually, to type 2 diabetes (T2D) if there is no intervention. Between 1980 and 2011, the number of US adults diagnosed with diabetes more than *tripled*, leaving 9% of the population with diagnosed type 2 diabetes and more than twice that with insulin resistance.<sup>2</sup> This epidemic is the 7th leading cause of death in the US and costs an estimated \$245 billion a year.<sup>3</sup> Though insulin resistance is present in nonobese individuals and not all obese people exhibit IR, obesity and insulin resistance are almost inextricably linked: excess glucose in circulation is stored as fat, and fat tissue is an endocrine organ that promotes insulin resistance through the release of hormones and cytokines.<sup>4,5</sup> It can be assumed that one without the other is simply a matter of time and, consequently, suggested lifestyle modifications for IR patients focus primarily on weight loss. Additionally, insulin resistance and heart disease are intimately connected. IR is a key component of metabolic syndrome: a cluster of physiologic changes that includes elevated serum triglyceride levels,

hypertension, abdominal obesity, and changes in cholesterol profiles.<sup>6</sup> Recommended strategies for both weight loss and reduction in serum lipids typically include the avoidance of fat, which has led to widespread replacement of dietary fat with carbohydrates, consequent elevations in glucose and insulin, and ironically to further an insulin resistance and diabetes epidemic. In short, treatment for obesity and cardiovascular risk significantly contributes to diabetes, which in turn leads to increased cardiovascular disease and obesity.

## Led Astray

Of all the “nutritional myths” that have been propagated over the past few decades, one of the most harmful has been the idea that dietary fat, and specifically saturated fat, is responsible for weight gain and increased cardiovascular risk. This erroneous idea has driven many people to choose a “low-fat” diet with higher carbohydrate intake and has contributed to the epidemic of blood sugar dysregulation, insulin resistance, and type 2 diabetes.<sup>7,8</sup> In 1977, the initial Dietary Goals for Americans proposed an increase in carbohydrates and a decrease in consumption of saturated fat and cholesterol.<sup>9</sup> These guidelines were based on studies that suggested that diets high in these elements increased the risk of coronary artery disease (an

idea that has since been repeatedly debunked).<sup>10,11</sup> The theory that dietary fat contributes to obesity has evolved because fat contains more calories per gram than either protein or carbohydrates (9 compared with 4); however, this assumption has been discredited several times over.<sup>12-14</sup> Decrease in the consumption of one macronutrient requires caloric compensation from another: a reduction in dietary fat typically results in increased carbohydrate intake. Correlation does not prove causation; however, levels of obesity as well as insulin resistance and type 2 diabetes have increased dramatically since the beginning of the low-fat diet trends, indicating that efforts to improve cardiovascular health and treat obesity have seemingly made things worse.<sup>15</sup> It has repeatedly been shown that the reduction of sugar is more effective at improving insulin sensitivity, weight loss, and cardiovascular risk than avoidance of fat.<sup>16,17</sup> Yet current dietary guidelines still recommend that Americans consume the majority of their calories from carbohydrates and reduce saturated fat to 7% to 10% of total calories.<sup>18</sup> Dietary modifications are difficult for many people to implement, as there are many social, environmental, and emotional associations with food that can be difficult to overcome. In addition to having lifelong habits and biochemical cravings, patients are

confused about conflicting medical information and ill informed by outdated nutritional guidelines.

### **If Fat Doesn't Make People Fat, What Does?**

Insulin controls the admission of glucose into cells for immediate use, and the presence of insulin indicates a fed state, which facilitates the production of glycogen (stored glucose) in the liver and muscle as well as triglycerides in adipose cells.<sup>19</sup> The capacity for glycogen storage is limited to approximately 500 grams (although this varies with muscle mass).<sup>20</sup> When glycogen stores are saturated, excess glucose is stored as triglycerides. Additionally, insulin inhibits the mobilization of fatty acids in adipose tissue. Insulin causes the creation of fat, but prevents the breakdown; therefore the key to fat loss (and the prevention of fat accumulation) is controlling insulin, and insulin production is stimulated by the presence of glucose in the blood. There are several proven ways to lower serum glucose and insulin levels, and though their mechanisms are nuanced and efficacies variable, any effort to control insulin is worthwhile in the prevention or treatment of insulin resistance and diabetes.

### **Spoonful of Sugar**

A common place to start with the reduction of carbohydrates is the removal of "added sugar" (sugar that doesn't occur naturally in a given food) from the diet. This is an idea with merit, as Americans (and the rest of the world) are consuming more sugar than ever before, including a dramatic increase in added sweeteners.<sup>21,22</sup> Added sugar, and especially high-fructose corn syrup (HFCS), has been especially implicated in contributing to obesity, insulin resistance, and type 2 diabetes.<sup>23</sup>

### **Good Carbs vs. Bad Carbs**

Many physicians and diabetic associations are counseling their patients on the benefits of a low glycemic index (GI) or low glycemic

load (GL) diet, wherein rate of digestion, protein, and fiber content of a food cushion the absorption of sugar into the bloodstream and attenuate the glucose and insulin spike.<sup>24-26</sup> The glycemic index is a way to categorize food in relation to its effect on blood sugar and is standardized using glucose as the comparison at a value of 100. This is especially useful in helping patients understand that many foods which they may not consider "sugar," such as grains, potatoes, fruit juices, or baked goods, have a profound impact on blood sugar levels, sometimes equal to or greater than pure glucose. In observational studies, consumption of high-GI foods has been correlated with the incidence of type 2 diabetes and cardiovascular disease.<sup>27</sup> A low glycemic index is typically defined as <70.<sup>28</sup> The glycemic index doesn't take into account the quantity of a food being consumed, although glycemic load does incorporate average serving size. Low-GI and -GL diets change the way that ingested carbohydrates affect blood sugar levels, but they do not necessarily involve a reduction in total carbohydrates.

### **Cut Out the Carbs**

Low-GI diets have a positive effect on blood sugar markers (fasting glucose, insulin, and hemoglobin A1c), serum lipid levels, and weight; however, they are less efficient than low-carbohydrate diets.<sup>29</sup> *Carbohydrate* is a term for one of the three primary macronutrients consumed in food (the other two being protein and fat). Depending on the size of the carbohydrate molecule, it may be classified as a sugar, starch, or cellulose (fiber); and as the glycemic index shows, these do not have equal impact on physiology. The Institute of Medicine currently recommends that adults consume at least 130 grams of carbohydrates/day, although the average consumption is nearly double that.<sup>30</sup> There is no official or regulated definition of "low-carb"; however some consider anything less than the recommended carbohydrate intake (50%–65% of calories or 130 grams/

day) to be low. Another commonly used guideline is the restriction of carbohydrates to 20% of total caloric intake. How "low-carb" is defined does matter, as there is a stepwise improvement in risk of diabetes and heart disease for metabolic syndrome patients that correlates with the reduction in dietary carbohydrates.<sup>31</sup> When it comes to restrictive diets, most regulatory organizations and dietary guidelines favor a low fat diet; however, the low-fat vs. low-carb debate has been well researched, and data overwhelmingly support the benefits of reducing carbohydrates to improve cardiovascular risk markers and reduce excess weight.<sup>32-37</sup>

### **Fat Friendly**

Taking the low-carb diet one step further: if carbohydrates are restricted to a level below the requirements of ongoing metabolic need, the liver releases glucose from its glycogen stores until depleted and then begins to break down fat (from the diet as well as body storage) into ketone bodies which can be used as an alternative source of cellular energy. The three primary ketones produced are B-hydroxybutyrate (BHB), acetoacetate, and acetone, which can be measured in serum, urine, and breath respectively. This is a normal adaptive physiologic response, called ketosis, which has historically enabled humans to survive periods of famine. The human body, and especially the brain, requires either glucose or ketones to produce energy, and we can only store about 24 hours' worth of glucose (glycogen). Without the ability to use fat and protein to produce fuel for brain tissue, our ability to survive even short periods of time without dietary carbohydrates would be severely compromised.

Unfortunately, ketones are perhaps best known in medicine for their role in diabetic ketoacidosis (DKA), a dangerous consequence of uncontrolled diabetes caused by a buildup of ketone bodies in the blood that disrupts the serum acid/base balance. In the presence of insulin,



## Insulin Resistance

ketone production is regulated and toxic levels *do not* occur. During nutritional ketosis, the serum concentration of BHB (the primary ketone in serum) is typically between 0.5 and 3 mM, whereas the serum levels of a ketoacidotic patient can approach 15 to 25 mM.<sup>38</sup> This is a very important distinction to make, as many people confuse the terminology and this mistake has contributed greatly to the condemnation of this diet by many. In small quantities, ketones are not only *not dangerous* but also provide significant benefit to a variety of conditions, including obesity, insulin resistance, diabetes, cancer, and epilepsy.<sup>39-43</sup>

The positive effects of nutritional ketosis have been reported for over 80 years, though the name that most people associate with a low-carb, high-fat diet is Dr. Robert Atkins, who brought the ketogenic diet into the mainstream in the 1970s and continued to be a proponent until his death in 2003.<sup>44</sup> Atkins's popular diet includes an induction phase that is ketogenic, followed by incremental increases in carbohydrates. The level of carbohydrate restriction required to maintain ketosis is individually variable and many people remain in a state of nutritional ketosis beyond the induction phase. The Atkins diet has been immensely popular despite coinciding with the peak of the low-fat craze. Because the fundamentals of a ketogenic diet (high fat and low-carbohydrate) directly contradict the nutritional guidelines, there has been widespread criticism on the safety of ketosis and carbohydrate restriction.<sup>45</sup> To induce nutritional ketosis, not only do carbohydrates need to remain sufficiently low (<50g/day), but *adequate dietary fat is required* to provide alternative energy. The popular (yet unsubstantiated) idea that dietary fat causes weight gain is often one of the biggest obstacles that patients must overcome when adopting this diet.

With each study published debunking the idea that dietary fat causes obesity and heart disease, the case for a low-carbohydrate, high-fat, ketogenic diet is stronger.<sup>46-49</sup> Not all low-carb diets are ketogenic; however, ketogenic diets are all low carb (by definition). Consequently, research that supports the general reduction in carbohydrates further bolsters the case for ketosis. A low-carbohydrate diet reduces insulin resistance, obesity, and cardiovascular risk, and dietary fat (even saturated) does not raise serum lipid levels. The remaining arguments against a ketogenic diet center on the risk of ketones themselves; however, since ketogenic diets have been used for nearly 100 years to treat epilepsy in children, and more recently in adults as well, we do have examples of populations who have safely maintained a state of nutritional ketosis for long periods of time with limited side effects.<sup>50-52</sup> In addition to the general benefits of a low-carb diet, a ketogenic diet offers several supplementary advantages: during the catabolism of triglycerides and fatty acids to create ketone bodies in substitution for glucose, the liver will convert glycerol (the backbone of the triglyceride) and protein into glucose through a process called gluconeogenesis, which requires a significant amount of energy (increased caloric expenditure).<sup>53</sup> Fat and protein (compared with carbohydrates) have a higher satiety effect, and ketone bodies have been shown to directly suppress hunger.<sup>54</sup> So patients on a ketogenic diet increase their metabolic rate and often experience less hunger than on other diets.<sup>55</sup> Lipid profiles do not get worse with the ingestion of high fat (as has long been asserted) on a ketogenic diet; rather total cholesterol and LDL levels actually decrease, serum triglycerides decrease, and HDL levels increase: all improvements in cardiovascular risk markers.<sup>56</sup> Diabetic patients on a ketogenic diet should be closely monitored, as a reduction in medications may be required as insulin levels decrease.<sup>57</sup>

## Call to Action

Hippocrates, the father of Western medicine, once said: "Let food be thy medicine and medicine be thy food." The successful removal of incendiary foods or repletion of essential missing nutrients are among the least expensive, longest lasting, and most empowering treatments for insulin resistance and blood sugar dysregulation. The current epidemic of diabetes is in large part a consequence of the misinformation and institutionalized fear of dietary fats that has been propagated over the past 40 years due to a handful of inaccurate studies.<sup>9</sup> Furthermore, the confusion between the terms *ketosis* and *ketoacidosis* has incorrectly led many physicians and patients to fear the restriction of carbohydrates. There have been many published studies debunking the connection of dietary fat to weight gain and heart disease, and touting the metabolic benefits of a ketogenic diet; however, there is a notorious lag in the time that it takes for ideas supported by research to be implemented into medical practice, making this is an important opportunity for physicians and health-care practitioners to educate patients.<sup>58-61</sup> Additionally, there is tremendous need for revision of current dietary recommendations to reflect what clinical research has proved: dietary fat is not the enemy. It's time to put down the skim milk and embrace the bacon fat.

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Dr. Wood grew up in Colorado and obtained her undergraduate degree in biochemistry from Colorado College. An enthusiasm for science but a passion for people led her to medicine, and a desire to treat the cause of disease, not just the symptoms, led her to naturopathy. After completing her doctorate at the National College of Naturopathic Medicine, Dr. Wood stayed in Oregon and has a private practice focused on endocrine imbalance, digestive dysfunction, immune support, and cardiovascular health.

In addition to her clinical practice, Dr. Wood is a staff physician with Labrix Clinical Services Inc., where she educates physicians and health care providers around the country about hormonal balancing through development of educational materials, contributions to a webinar series, and lectures at local and national conferences. In 2008 she coauthored a book on andropause titled *His Change of Life: Male Menopause and Healthy Aging with Testosterone*.



# Naturopathy: Its Roots in Monastic Medicine

by Prof. [Dr. of Med.] Charles McWilliams

## Preamble

Our histories of medicine discuss Greek medicine at considerable length but pay scant attention to Christian contributions beginning in the Levant and proceeding through the dark ages of Europe. All of the great leaders of Western medicine in earlier and subsequent generations have been influenced by the Greek physicians; for example, Hippocrates, Galen, and Dioscorides. Monastic medicine, the predominant form of health care during the 6th through 12th centuries in Europe and the Levant, and was based on Hippocratic and Galenic theory placed against the backdrop of medieval theology.

All this was the basis of monastic medical practice, which became the forerunner of naturopathy in the US. This short article will serve to show the development of monastic medicine from the ancients to today's New Age medicines and naturopathy.

## Monastic Medicine

Monasticism in Christianity became popular during the time of Constantine. With the government's endorsement of Christianity, many believers found it more difficult to live a godly lifestyle. Christian monasticism grew from the influence of Judaic tradition. The Essenes, a Jewish mystical sect, influenced the development of monasticism. They combined the healing of the body with that of the soul. The word *Essene* has been traced as an Egyptian term

for that of which *Therapeutae* was the Greek word, each of them signifying "healer," designating the character of this sect as professing to be endowed with the miraculous gift of healing.

One of the great contributions of monastic medicine was to preserve the ancient texts of such works from authors such as Hippocrates, Galen, Dioscorides, and Avicenna. Such preservation was the focus of early medical teachings and medical care. The conquest of the Roman Empire by German tribes (Vandals, Visigoths, and Ostrogoths) placed the glory and culture of Rome into the dark ages. The barbarians persisted in cultural destruction for centuries. The monasteries became the repositories of books, sacred texts, and academics. Study was almost exclusively restricted to clergy because the church became the only asylum for it. Thus monastic medicine was born. Greek and Roman medicine, after having played an important part of Roman culture, withdrew into the shadow of the Church. Faith-based medicine combined with physic became a central feature of monastic medicine.

The monks, being the primary caregivers, focused on natural, physical-based medical practices, including well-respected techniques such as general hygiene, bloodletting, dietetics, and herbalism. In the early Middle Ages, religion and the prevalence of illness, plagues, and infectious disease guided the practice, along with folk medicine, herbalism,

and development of medical-surgical care. Since there were poor living conditions, poor hygiene, and no formal schools of medieval medicine, disease was a constant threat in Christendom (Europe) and often controlled people's daily lives. In response to the known epidemics – plague, leprosy, and influenza – the Church began searching for an effective means of medical practice. "Medicine" was then considered a religious necessity for society. In this context, medicine expanded into an important occupation, encompassing a variety of professional and folk practices, ranging from natural, physical-based medicine to religious (monastic) medicine, folk medicine, and herbalism.

One of the important social developments of this time was the introduction of Christian monastic hospitals, which arose as probably the only organized provider of medical care in the early Middle Ages. Serious monastic medicine began to develop in the west when the monastery of Montecassino was founded by St. Benedict of Nursia in 529. From here the Benedictines spread the medical texts and teachings to other monasteries, most notably Fulda in Germany, while Irish missionary monks founded centers in Switzerland (St. Gall and Reichenau) and in Italy (Bobbio). Thus, the monastic medical tradition had its roots deep in the fundamental doctrines of the Christian faith and served a very specific role in the European community.



By the 11th century, women were also given the role of health-care provider and medical practitioner. Among the great healers in 12th-century monastic medicine was Hildegard of Bingen, an ecclesiastical authority known for her visionary capabilities and ideas on natural philosophy as well as for her poetry and musical compositions. She was the author of the original medical text *Liber Simplicis Medicinae*, which contains *Cause et Cure* (Causes and Cures), a section devoted to the understanding of humoral physiology, disease, and herbal treatment. The concepts discussed in *Cause et Cure* incorporate the dominant medical writings constructed by Hippocratic and Galenic tenets of humoral physiology and pathology, as well as medieval theological principles.

Clerical medicine in England, earlier called *monastic medicine*, developed during the late Middle Ages due to King Henry VIII's ordered closing of the monasteries. The more liberal practice of monastic medicine continued to revolve around the belief that medical treatment was inextricably tied to the care of both soul and body.

Thus, the monastic medical system represented a transitional period in the history of medicine during which natural, physical medicine and principles of spiritual healing uniquely coexisted. One of the monastic community's most significant contributions to the field of medical knowledge was its role in copying manuscripts. Physicians were trained primarily through Latin texts and, in a culture where few people could read or write, the monks served as propagators and practitioners of this knowledge.

### Naturopathy

At the dawn of the Renaissance, Christian monastic medicine and hospitals declined in faith and numbers, partly as a result of church-imposed doctrines combined with the reformation and secularization of society. One of the great contributions of clerical medicine was to preserve

"certain cures" and "tried remedies" while applying as a basis of treatment use by electricity, water, and physis, which also led to today's development of nature cure and naturopathy. Rev. John Wesley (1704–1791) was the 18th-century English clergyman who helped to pioneer the transition of monastic medicine to "clerical medicine" in England and applied the use of electricity for the treatment of illness. He is credited as founding the Methodist denomination. Wesley considered it a Christian duty to make medical knowledge and practical treatments accessible to the "Majority of Mankind," a necessary and important aspect also of pastoral duties.

The term *naturopathy* is derived from Greek and Latin, and literally translates as "nature disease." The term was coined in 1895 by John Scheel, a German homeopath practicing the methods of German healer Louis Kuhn and Bavarian monk Father Sebastian Kneipp. Of all the "barefoot Nature" cures that sprang from monastic medicine, the most renowned was that initiated by Kneipp, whose influence survives into this age. Considered by many as the founder of today's naturopathy, he taught Benedict Lust (1872–1945), one of the main founders of naturopathic medicine in the first decade of the 20th century. Lust described the body in spiritual and vitalistic terms with "absolute reliance upon the cosmic forces of man's nature."

Arnold Ehret (1866–1922) was a German health educator and author of several books on diet, detoxification, fruitarianism, fasting, food combining, health, longevity, naturopathy, physical culture, and vitalism. Ehret worked at Lust's Yungborn Sanitarium for 5 years. Ehret continued the naturopathic trend by opening a

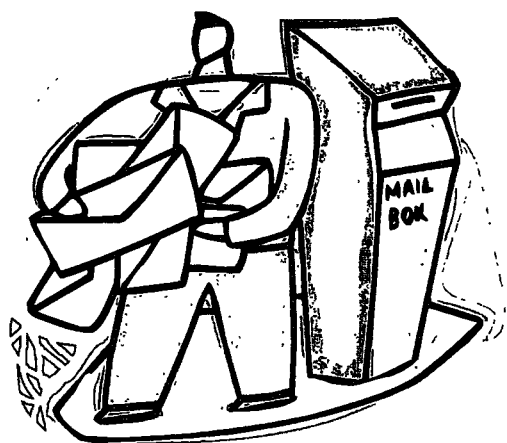
sanitarium in Alhambra, California, before embarking on a nationwide lecture tour. His course on the "Mucusless Diet Healing System" became a book of 25 lessons for his students and later his most famous book.

### Conclusion

Monastic medical practice respected Hippocratic doctrine, that natural causes did contribute to illness and disease, and monks performed nature-based, physical treatments on patients, forms of what we call today *natural medicine* (a system of therapeutics in which only natural, medicinal agents and forces are used for the phenomenon of healing). The design and function of monastic hospitals show that natural medicine practice was overseen and incorporated in an integrated practice that emphasized the importance of the spiritual element in health care combined with dietary reform and extensive use of herbs.

Thus, we could say that what would later lead to the practice of secular naturopathy today was the Christian practice of nature cure, dietary reform, herbalism, and hygiene beginning with the *Therapeutae* (Essenes) and developing through Christianity of Europe. Monastic medicine and naturopathy both have as their goal homeostasis within the body, which may be achieved by the proper and necessary balance between the integrated components of body-mind-spirit. Naturopathic philosophy favors a holistic approach and seeks to find the least invasive measures necessary for symptom improvement or resolution to regain health, thus encouraging minimal use of surgery and unnecessary drugs. Above all, it honors the body's innate wisdom to heal.

Prof. [Dr. of Med.] Charles McWilliams is a physician practicing naturopathy and does missionary service around the world. He is the Grand Master of the Sacred Medical Order of the Knights of Hope (smoch.org). He maintains a large medical practice on Nevis Island, and is a licensed naturopath in Nevis and Ecuador.



# Letters to the Editor

## An Unjust Attack on Greens

I enjoyed the article that Dr. Shaw wrote in the January issue. However, I did research on oxalate and feel that it's unjustly attacking greens, while oxalate is present in meat and other foods. I was just sharing this research information with him. Victoria Boutenko wrote a response about greens and oxalates, especially when spinach got attacked. (See references below for more information.)

I have never found a person who can sit and eat 1 lb of spinach for breakfast, lunch, and dinner. But I know of many meat eaters who get oxalate toxic overload from (loads of) meat: breakfast, lunch, and 16 oz steak dinners. Dr. Shaw did not get into this.

I feel, since my college days, that we should teach or at least make available to students information from both sides; that is, don't teach me evolution and bash creationism. I got into an argument with my professor, a PhD, at Kent State. "This is not a class for religious beliefs at State University." Whoah! Give us both sides. Don't have to go into religion(s).

Many people read the *Townsend Letter* ... I felt that some might benefit from giving up on so much meat and for others not to be afraid of oxalates in spinach and kale.

If Dr. Shaw would like to write another story on the other side of oxalate, that would be great.

If you or Dr. Shaw have any questions, please let me know.

Thanks,  
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## Of Milk and Microbiomes

A couple of comments on the most recent issue:

The first would be on the microbiome article. More and more fascinating information coming out. I was particularly intrigued to see the report on a patient who had received a fecal transplant from an obese person, and then became obese themselves.

The second has to do with the article on milk. I was first introduced to information on A1/A2 milk via an interview with Keith Woodward, the author of *Devil in the Milk*. It particularly intrigued me because, about a year before, I had worked with a 3-year-old child of a young man who would work for me as a kennel person many years ago. I do energy testing, and when we checked his profoundly ADHD child, we found that he was apparently very sensitive to conventional milk. Interestingly, his mother had mucus issues after milk and his sister had some level of attention deficit problems that were aggravated when her father made scrambled eggs to which he added whole milk. I only saw them one time, when they came to visit our gardens, but received an e-mail about a month later saying, "Thank you so much, we have a new child"; by simply getting off of conventional milk (A1), he had made an 80% improvement in ADHD issues. I wish it had resolved them completely, but. ... After that I communicated via e-mail with Keith Woodward and asked him how he felt about ADHD and its relationship to A1 milk. He said he thought that there was a relationship, but it wasn't sufficient that he thought it was appropriate to put in the book.

Another interesting corollary was that I remember at a Jeff Bland seminar many years ago that he presented a paper in which they had seen a direct relationship between the amount of milk consumption and juvenile delinquency. I sent him an e-mail asking if he had that reference, but didn't get a response, so I only have it impacted in my memory.

Carvel Tiekert, DVM

## A Case of MELAS Syndrome Treated with Positive Results

MELAS is the abbreviation for the condition mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes.

MELAS is a progressive neurodegenerative disease, a rare form of dementia caused by mutations in the mitochondrial genome inherited purely from the female parents. MT, TH, MT, TL1, TV are the most common mutations, especially TL1, since it impairs the ability of mitochondria to make proteins, use oxygen, and produce energy. Some of the proteins normally produced are essential to synthesize enzyme complex in mitochondria that help convert oxygen, fats, and single sugars into energy. ATP is not manufactured and results in severe mitochondrial disorders. As result of this process, with disorders in the electron chain transport (ECT) of mitochondria, the MELAS patient builds up a large quantity of lactic acid, a waste product in the body, increasing acidity in the blood, resulting in extreme fatigue.

MELAS syndrome affects many of the body's systems, but particularly the brain (encephalon) and muscles (myopathy). Repeated stroke-like episodes can progressively damage the brain, leading to vision loss, problems with movement, and dementia. Other deep symptoms include muscle weakness, extreme fatigue, headache, loss of appetite. Other damage includes hearing loss, heart and kidney problems, epilepsy, diabetes, and difficulty in walking and moving.

### Prognosis

There is no known treatment for the underlying disease, which is progressive and fatal. However, some supplements have been shown to be helpful, but there have been no consistent reports of success. This includes amino acids, antioxidants, and some vitamins.

CoQ10 has been helpful for some MELAS patients.

Riboflavin has been reported to improve the function of a patient with complex 1 deficiency and the 3250 T→C mutation.

Succinate may be useful in treating uncontrolled convulsions in MELAS patients, but this needs further investigation.

### Clinical Situation

The patient, a 36-year-old woman, Marta, a mother of two children came to my clinic in January 2014, with a diagnosis of MELAS syndrome.

Marta was walking and moving with much difficulty, even from the waiting room to my office. She was in very bad physical condition and psychological distress. Her husband came in with her and helped her to walk and especially to have an open discussion with me. As you see in the above photo, Marta has also has considerable difficulty in moving her finger, difficulty in hearing, and even talking.

She cannot comfortably go for a walk down the street, even slowly for more than one hour, without feeling deep fatigue. Naturally, she cannot perform normal household duties or take care of her two daughters. Marta is suffering from the following symptoms and dysfunctions:

- loss of vision
- cataracts
- hearing loss
- epilepsy
- severe headache
- diabetes
- fatigue



### Initial Treatment

Marta came to my clinic taking a number of drugs to retard some of the degenerative process and control the epileptic crisis.

### What Is My Approach to MELAS Syndrome?

While I have been deeply involved with mitochondrial dysfunction, associated with cancer, I have spent decades studying the role that mitochondria play in health and disease. I had never before had an experience with a MELAS syndrome patient, although I have experience in treating another fatal mitochondrial disease, amyotrophic bilateral sclerosis, with some relative success but accompanied by the incapacity of the patients to pursue the treatment.

Anyhow, my experience was encouraging when Marta first faced me, being a new challenge that life offered me. In such situations, experience and intuition may drive our brain to think about what can be done, even if it can be done. While I have in my clinical pharmacopeia some medication and supplementation that can bypass the blockage in the electron respiratory chain, activating the production of ATP, and decrease acidosis, I asked myself, why not attempt to regenerate the mitochondrial function? Over past decades, approaching 50 years, I was confronted with so many patients with degenerative diseases and for most of them, I resolved their diseases. I told Marta's husband, who himself investigated mitochondria in trying to help his wife, that at least we could attempt to retard the progressive degeneration of her brain and muscles.

I would try one treatment over a period of 30 to 60 days and watch closely how she reacted or not, considering that my past experience in treating mitochondria may help me choose the appropriate treatment but nothing more.

My idea was to use some of the regenerative products that I've used for the past 20 years, even some during the past 40 years, especially for regenerating the whole body, to improve the brain function while activating cellular

## Letters

► respiration. My idea was also to help promote building mitochondrial proteins, a real challenge. However, in the past and up to now, I have reversed mutated P53 and restored it to a normal wild-type function as I described in my past articles published in *Townsend Letter*; therefore, why not try this with mitochondria?

The first medication that came to my mind was the rejuvenating compound called RN13 in ampoule form, to be injected IM, which I often used with success for over 20 years or more, in such cases as kidney dysfunction, geriatric disorders, extreme fatigue, and to increase cellular respiration and vitality in cancer patients as explained in my *Townsend Letter* article of August/Sept 2012.

**RN13** contains the ribonucleic acid from different organs found in the embryo, such as placenta, umbilical cord, pancreas, suprarenal, testes, and so on, as well as amino acids, glutamic acid, vitamins E, B6, and B12, trace elements, biolecithin, and so on.

Posology (dosage): 3 ampoules of 5 ml IM. 3 to 4 times per week.

**Enzyme yeast cells preparation:** each 10 ml dose contains 50 billion biochemically active young yeast cells containing all the vitamins, minerals, amino acids, trace elements, enzymes of the respiratory chain, coenzyme A, NADH, cytochrome, and mitochondrial sequences. It is most important to mention that live yeast cells are high in coenzyme Q10 in a natural, easily assimilable form.

The product, administered orally, reaches the small intestine, enters the blood, and releases all the substances mentioned for immediate healing.

Posology (dosage): 20 ml mixed in a glass of apple juice or carrot/beetroot juice 3 times per day.

**Coenzyme Q10** (100 mg capsules)

Posology: 1 capsule 3 times per day.

**NADH** (5 mg tablet)

Posology: 1 tablet before breakfast.

**Chlorella Growth Factor** (liquid) contains nucleic acids and other DNA ingredients.

Posology: 10 ml 3 times per day.

The patient was also told to improve her regular diet with more vegetables and fruits, whole cereals, tofu, vegetable sprouts, and rice bran, and regular intake of vegetable juices.

### Result

After 2 months of treatment, Marta began to improve and move with more facility, although her husband still accompanied her on consultations.

After 3 months, Marta felt much better, looked healthier, and could walk in the city for 4 hours without feeling tired, which was a major victory.

After 6 months, Marta was completely different compared with the first consultation, felt healthy and especially happy, and the photo below speaks for itself.

### Conclusion

This is more than a victory over a progressive fatal disease that not only affects the whole body, including the brain, but leaves the patient in a distressed condition. The fact that a disease is considered incurable doesn't mean that nothing can be done to help, and that should be the aim of an integrative doctor. Intuition is supposed to be one important quality required in the medical profession, and we cannot always rely on scientific data and proof. I decided to publish this case, especially about the treatment, so that doctors with similar cases may offer some better and longer-lasting improvement for their patients.

While Marta is not cured, she is still taking RN13 and her other medications. At least she can enjoy her normal life and look after her two daughters, but with precaution, since tiredness overtaxes the mitochondria.



January 7, 2015

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## Now Is The Time To Make Yourselves Heard to Safeguard the Freedom of Homeopathy in the US

### Homeopathy Is Now under Review by the FDA

A public hearing on the future of homeopathy in this country took place in the offices of the US Food and Drug Administration in Silver Springs, Maryland, on April 20 and 21. This may have failed to appear on your radar screen, but heads up: *this is important!* This hearing, vital to the continued use and practice of homeopathy in the US, claimed to "obtain information and comments from stakeholders about the current use of human drug and biological products labeled as homeopathic, as well as the Agency's regulatory framework for such products." The FDA was reportedly "seeking participants for the public hearing and written comments from all interested parties, including, but not limited to, consumers, patients, caregivers, health care professionals, patient groups, and industry."

These intentions may sound innocent and open-minded, but many of us in the homeopathic community are alarmed. Current FDA regulations actually date back to legislation passed in 1938, which has allowed homeopathic medicines to be available, sold, and prescribed by practitioners or over the counter since that time. There are those in a variety of camps who would be happy if this permissive legislation were changed or eliminated.

### A Worldwide Movement to Discredit Homeopathy

This recent announcement appears to be part of a worldwide movement in Europe, Australia, and now the US to discredit and eliminate homeopathy as a competitor to conventional pharmaceutical medicine. "Science-based" or "evidence-based" medicine tends to conveniently ignore or downplay the studies that have shown positive results of homeopathic medicine, and it is rare that a pro-homeopathic study is accepted for publication in mainstream journals. We have been aware for decades of a bias against research concerning homeopathy, unless its intent is to disprove the efficacy of homeopathic treatment. While the studies and the reviews of studies on homeopathy are said to be impartial, the best homeopathic results have often been refused publication in prestigious medical journals, and positive conclusions disallowed or eliminated from relevant consideration.

The NIH (National Institutes of Health) reported in its 2007 National Health Interview Survey, a comprehensive analysis of the use of complementary health practices by Americans, that an estimated 3.9 million adults and 910,000 children had used homeopathy in the previous year. This included use of over-the-counter products labeled "homeopathic," as well as visits to a homeopathic practitioner. Out-of-pocket costs for adults were \$2.9 billion for homeopathic medicines and \$170 million for visits to homeopathic practitioners.<sup>1</sup>

It is clear that the money spent by the public on homeopathic care and products has garnered major attention from Big Pharma. It is evident also that consumers' desire to find a viable alternative to pharmaceutical drugs and surgery in homeopathy, herbal medicine, Chinese medicine, chiropractic, and other forms of natural healing has led to what we consider a healthy competition in the health-care marketplace.

### The International Homeopathic Stage

Outside the US, homeopathy has historically been an integral part of national and independent health-care systems, especially in France, Germany, the UK, the Netherlands, Switzerland, the Scandinavian countries, and India. Homeopathy remains extremely popular in France, where all of the practitioners are medical doctors and homeopathic medicines are available in all French pharmacies. In Germany, homeopaths can be medical doctors or *heilpraktikers* (health practitioners). Similarly, in the UK, both medical doctors and registered homeopaths provide homeopathic care. The popularity of homeopathy in the UK and the Netherlands has decreased markedly, over the past 5 years, because of media attacks by the skeptic community, including self-proclaimed "quack-busters," and even, incredibly, stage magicians. To preserve homeopathy in this climate is imperative for its survival.

In the UK, the Queen's physician has traditionally been a homeopath, and is to this day. Homeopathy was well accepted as an integral part of the National Health Service until 2010, when a parliamentary report panning homeopathy decimated the popularity of homeopathic, even among the most respected and experienced practitioners. Though there are still two small homeopathic hospitals, one in London and the other in Glasgow, the popularity of homeopathy has dropped, leading these centers to shift their focus to other complementary and alternative forms of medicine. It is imperative to preserve homeopathy, despite the pejorative political climate, in nations where it has previously flourished.

The homeopathic climate in India, to the contrary, is welcomed by suffering patients from all walks of life: from Bollywood stars to the poorest of the poor; from swanky clinics to the many government-run homeopathic hospitals. According to a 2012 article in the *Times of India*, India boasts more than 200 homeopathic medical colleges, 7000 homeopathic hospitals and dispensaries, and 246,000 registered practitioners, a number that has doubled between 1980 and 2010. Such widespread acceptance should tend to contradict the idea that homeopathy has neither validity nor effectiveness. These homeopathic adherents, along with the



## Guest Editorial

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2.9 million people in the US who either see a homeopath or use over-the-counter homeopathic medicines, obviously believe that they are being helped. Not to mention that homeopathic medicines are safe for newborns, during pregnancy, end-of-life conditions, and highly sensitive individuals who cannot handle prescription medication.

We have studied clinical homeopathy extensively in India with Dr. Rajan Sankaran, and his colleagues in Mumbai, since 1993. These physicians are medical as well as homeopathic doctors. They work in public and private clinics and in hospitals. Due to the nature of India and its health-care system, they see up to 100 or more patients a day; treat patients for serious and life-threatening diseases, unlike most homeopaths in the US; and often work along with and are respected by their conventional medical colleagues. Their results in homeopathy are some of the best in the world, and their cases, mostly videotaped, have been widely published in the homeopathic literature. Furthermore, the standards to present a case at a homeopathic conference or to submit it to publication are rigorous: It must be clear that the prescribed homeopathic medicine has been effective over a period of months or years and that lab values have improved if relevant, and there are often videotaped case records to provide evidence of the results. These clearly effective results should count more, in our opinion, than clinical studies and trials, which, as has been revealed repeatedly, can be manipulated and the results virtually "bought."

### Clinical Research Pro and Con

In Switzerland, we are happy to say, there was a recent study highly favorable to homeopathy: In 2013, The Swiss government released a report on homeopathy that described it as "effective and cost efficient." The results of the Swiss Health Technology Assessment (HTA) report on homeopathy, titled Homeopathy in Healthcare, was a part of the Swiss government's 1998 Complementary Medicine Evaluation Programme (PEK), set up to evaluate homeopathy and other complementary and alternative medicine (CAM) therapies for their "efficacy, appropriateness and cost effectiveness."<sup>2</sup>

Skeptics of homeopathy, both paid professionals and amateurs, have flourished in the current climate of homeopathy bashing. Anything that cannot be explained by current levels of knowledge or research methods is not only fair game for skepticism, but often simply dismissed offhand as impossible and completely ineffective. We should be funding studies to investigate *how* homeopathy works and the mechanism by which it has produced clinical results over the past 200 years. This, unfortunately, is not happening. The results of homeopathy are, even though the mechanism may seem implausible, readily observable clinically. Though researchers have tried, we acknowledge that the mechanism of action explaining how microdoses can affect human and animal health remains elusive. We welcome further research that attempts to explain the mechanisms involved, and believe that the debate will one day be resolved in favor of homeopathy. The clinical effects of homeopathy, however,

can be verified if the research model used takes into account the individualization of treatment using the thousands of homeopathic medicines available, and the fact that homeopathy treats and strengthens the healing and immune responses of the individual who has the disease, rather than focusing on killing organisms, or suppressing bodily processes with drugs.

### We Need to Research How Homeopathy Really Works

The basis of the theory of homeopathic medicine is the principle "like cures like." This means that a substance in nature that can cause a set of symptoms in a healthy person, can improve or cure a person with similar symptoms. The substance is given to the patient in a highly diluted form, so as to eliminate the symptom-causing toxicity of the source material. The medicine is created through a process of serial dilution and shaking, which creates a numerically designated potency, such as 6C, 12C, 30C, depending on the number of dilutions.

Because the dilution factors in homeopathy beyond 12C exceed Avogadro's number, skeptics insist that this eliminates the possibility of any scientifically curative action. However, curative action continues to occur with high potencies. As skeptics say, there is no clear mechanism known that can account for the curative action of homeopathic medicines persisting at astronomical dilutions. Nevertheless, it has been observed routinely in homeopathic practice that potencies with a dilution factor of 12C and above are clinically active. Though the mechanism of action of potentized microdoses remains unknown, "like cures like" functions at any potency.

Skeptics of homeopathy commonly point to the placebo effect as the mechanism for why homeopathic medicines appear to work. Unfortunately, patients don't always respond as though they have been given a placebo when given a homeopathic medicine. A homeopath can prescribe what appears to be a well-indicated homeopathic medicine for a patient without any result. However, when the case is restudied and the correct homeopathic medicine prescribed, the symptoms will dramatically resolve, leaving the patient improved or well. How is this possible? The faith of the patient would not likely be strengthened by one or a series of failed prescriptions, but when given the correct homeopathic prescription, the patient's symptoms that match the homeopathic medicine are considerably reduced or eliminated, leaving the patient improved or cured. Animals and babies, who have no preconceived notions as to what to expect from homeopathic treatment, respond readily to the correct homeopathic medicine, eliminating the possibility that the results in these cases are merely a placebo effect.

### Our Clinical Experience over Three Decades As Homeopathic Doctors

After more than 30 years of the study, practice, and teaching of homeopathy, we do not consider the results of homeopathic treatment to be fantasy or delusional thinking, as skeptics may suggest. There are solid results in a wide variety of physical, mental, and emotional problems, including ulcerative colitis, asthma, allergies, eczema, autism spectrum disorders, PANDAS, ADHD, ODD, anxiety and depression,

vaginitis, menstrual disorders, prostatitis, cystitis, migraine headaches, otitis media, bronchitis, and many others. We and other qualified homeopaths have offered the public and our colleagues the results of our clinical work in the form of video cases, seminars, books and articles, and clinical presentations at homeopathic and naturopathic conferences and seminars. Our articles have appeared in the *Townsend Letter* since the early 1990s, and we consistently try to "tell it like it is" in reporting the actual results of our clinical practice.

It is the professional standard in homeopathy to present cured cases with the symptoms that the patient expressed initially, observations by the practitioner, and a series of follow-up visits, where the patient expresses the changes they have experienced since being treated. Most homeopathic seminars and teaching follow this format. Because each case is individual, the focus is how the original symptoms matched the homeopathic medicine used for treatment, and what changed, physically, mentally, and emotionally, as the result of the treatment. The cases are only presented after the health changes of the patient are stably better, after at least a year, and sometimes after several years of successful treatment for chronic illnesses. Not all of our cases are successful, as with any medical treatment, but most show positive results from treatment that were not present before the patient began the course of treatment. We take our work very seriously. We take time to understand our patients' needs and find the best homeopathic medicine to improve their health and well-being. The course of treatment in chronic cases begins with an extensive interview and physical exam as required. The initial interview normally lasts for 90 minutes.

Follow-up visits are usually scheduled at intervals of 4 to 8 weeks, depending on need. Once the patient has clearly responded to the homeopathic medicine, visits are spaced according to when the patient could potentially begin to relapse or need a change in the potency or frequency of the medicine. In acute cases, the initial visit is usually 15 to 30 minutes, and is monitored by follow-up visits at much briefer intervals until the illness resolves. When we find that our treatment is not effective, we refer our patients as needed for conventional examination, tests, and treatment.

### Our Recommendations to the FDA to Evaluate Homeopathy

When the FDA takes a look at modern homeopathy, its safety and efficacy, we hope that the agency will take into account that homeopathic medicines have been considered safe since legislation authorizing the use of homeopathic medicines that were listed in the Homeopathic Pharmacopeia of the United States in 1906 and again in 1938. The FDA has not been regulating homeopathic medicines as to safety or effectiveness.

According to the NIH National Center for Complementary and Integrative Health, a 2007 systematic review found that highly diluted homeopathic remedies, taken under the supervision of trained professionals, are generally safe and unlikely to cause severe adverse reactions. However, their guidelines also say, "There is little evidence to support homeopathy as an effective treatment for any specific condition." We disagree with that assumption, given the paucity of research on homeopathy and the bias that exists

among conventional medical journals against research on homeopathic medicine, as well as a severe lack of funding for homeopathic research in educational institutions that could potentially generate good quality research on homeopathic medicine.

The research methods used so far in research on homeopathic medicine are ill suited to the task. Homeopathic treatment is individualized to the *person with the illness*, not the *disease* itself. There needs to be a research design that focuses on how well the homeopathic treatment has addressed the total health of the person, physically, mentally, and emotionally before and after treatment, by comparing reported and observable symptoms that have changed. These symptoms can vary in type, specific quality, frequency, intensity, duration, mental and emotional effects on the patient, and a variety of other factors. These differences in reported symptoms are what a homeopath uses to find the best medicine for the patient. In order to assess the clinical effects of homeopathic medicine, it is necessary to create a research model that is compatible with the individualization of treatment that is at the core of homeopathy. Trials of over-the-counter homeopathic preparations with single or multiple homeopathic remedies for a specific acute health condition with easily defined symptoms and parameters for improvement could possibly be tested in more conventional ways, as there is less individualization of treatment in that context.

We hope that the FDA will give due consideration and sincerely reflect on all sides of the issues surrounding the use and regulation of homeopathic medicine. We want to make sure that homeopathy, whether practiced by practitioners or purchased over the counter, will remain readily available to those who wish to use this medical system. If additional research is needed, we hope that it can be done in an environment of unbiased investigation, taking into account the significant differences in concepts and practice between homeopathic and conventional medical theory and practice.

### What You Can Do to Help Preserve Homeopathic Freedom in the US

The comment period by stakeholders and interested parties lasts until the end of June, so there is still time to make your voice heard. For information on the hearings, obtaining transcripts, and how to make written comments before the deadline, go to: <http://www.fda.gov/Drugs/NewsEvents/ucm430539.htm>.

To see the original Federal Register announcement of the hearings, go to the URL above and click on the "Federal Register" link.

Judyth Reichenberg-Ullman, ND, MSW  
Robert Ullman, ND

### Notes

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## A Repackaged Discussion of Allergies

review by Katherine Duff

**No More Allergies**, by Gary Null, PhD

Skyhorse Publishing

307 West 36th Street, 11th Floor, New York, New York 10018

© 2014; \$24.95; hardback; 348 pp.

*No More Allergies* by Gary Null, PhD, was originally published in 1992. Though not mentioned as either an updated version or reissue, *No More Allergies* was republished with a few changes in 2014.

In 1992 the book introduced the concept of allergies as encompassing much more than the standard allergens such as grasses and animal dander. The author described the many possible sources of an allergic reaction, including chemicals in our everyday environment, foods, and even our own hormones. These allergies can start developing in childhood or adulthood. The individual's body can react with either an overly aggressive immune system or underactive immune system, which results in different symptoms.

It was a new concept at the time that allergic responses could cause symptoms in any part of the body – not just the respiratory system. Joint pain, fatigue, and cognitive dysfunction are just a few of the symptoms related to the immune system's overreacting or underreacting. To make the connection between the exposures and the symptoms, there are a variety of methods to identify the cause that the author describes. Elimination of a certain food for four days and then eating only that food on the fifth day should reveal if it is a problem. Blood testing for IgE levels can identify inhalant allergies and blood testing for IgG levels can help to reveal food allergies. For the more difficult to ascertain, keeping a journal in which one notes the onset of a symptom and where one is and what one is doing could help make connections.

Null emphasizes the role of environmental physicians in treating allergies. He describes their work as holistic and open to nutritional and herbal remedies. They recognize biochemical individuality.

Individuals will react differently to the same substance. An environmental physician will conduct a much more extensive history that includes inquiring about chemicals that the person could be exposed to through work, home, and hobbies. Further testing can reveal problematic substances which will guide the physician in neutralization immunotherapy.

For rebuilding a properly functioning immune system, Null offers suggestions for supplements and advice for identifying other contributing factors such as yeast overgrowth, viruses, and parasites. He also includes a discussion about sources of chemical exposures in the home and workplace. Finally, he proposes a "no more allergies diet" through over 80 pages of recipes that do not contain the primary allergens corn, wheat, dairy, sugar, and beef.

Also included in this book is a chapter of bibliographies of studies and articles that support the concept of environmental medicine. The almost 60 pages of references are dated from 1864 to 1990, which while supportive, are not current. And this brings us to the problem of rereleasing a book that was penned over a decade ago. It is simply not up to date. I was reminded of this while reading about sources of electromagnetic radiation with no mention of Wi-Fi or cell towers. The author notes there are 60,000 chemicals in commercial use, but that was in 1992 – now there are 80,000. There is no mention of Lyme disease, an emerging consideration in people with sensitivities. Gluten was mentioned only briefly, and the recipes did not take that sensitivity into consideration, even though many people are now on a gluten-free diet.

Research into environmental sensitivities has continued over the last 20 years and treatments have also been updated; for example, treating inflammation, or the use of the antioxidant glutathione as a current treatment, are not mentioned in this book.

Since only a few changes have been made to the book since the 1992 version, I cannot recommend it to readers seeking to resolve health issues as a result of environmental sensitivities. For those who do wish to read *No More Allergies*, searching the used-book sales for the 1992 version should suffice.

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# Healing with Homeopathy

by Judyth Reichenberg-Ullman, ND, DHANP, LCSW,  
and Robert Ullman, ND

[www.healthyhomeopathy.com](http://www.healthyhomeopathy.com)

## Homeopathy for Surviving a Volcanic Eruption

### What Are the Odds?

You might say that we are crazy to live at the foot of the most active volcano in Chile, right on the Ring of Fire. And you might be right. When we fell in love with and decided to steward this stunning piece of property in Pucón, Chile, 10 years ago, we did investigate the volcano risk pretty thoroughly before signing the dotted lines. The word that we have always used to best describe our southern piece of heaven is *elemental*. Our volcano, Volcán Villarrica ("rich mountain" in English, but the indigenous Mapuche name is *Rucapillán*, "House of the Spirit") lies just in front of our door, 12 kilometers (7½ miles) up the Volcano Road. Historically, this volcano erupts as often as every 20 years, but the previous eruption was in 1984 (the year that we met). Until 5 days ago, that is, when she really blew. Villarrica has a pattern of sending lava trails down fairly predictable crevices, rather than spewing ash far and wide like Mount St. Helen's. Nevertheless, the eruption earlier this year was world class.

In 2005, having checked into the eruption history, we figured that our odds were good to avoid an eruption; and, even if we did experience one, our land, high on a hill, would likely not suffer damage. Little did we imagine that our recent column on homeopathy for climbing a volcano (April 2015) would be soon followed by one on homeopathy for a volcanic eruption!

We have a pattern of missing Mother Nature's giant hiccoughs down here. In 2010, returning from a challenging week in the Brazilian Amazon, we were flying over the expanse of Brazil just when the big Chile earthquake hit. We met the LAN Chile flight attendant at the gate only to hear from her, in Spanish, "There has been a massive earthquake in Chile and the world is ending." No joke – that is what she told us.

In March we were scheduled to fly back to our Chilean home from Quito, Ecuador, where we attended a wonderful Dances of Universal Peace retreat and hiked/rode horseback in Cotopaxi National Park. You must really

be questioning our sanity now because Cotopaxi is 19,300 feet high, and also one of the most active volcanoes in South America. Some consider it to be the world's highest active volcano, but the last eruption was in 1940, before either of us was born. There we hiked up to 14,674 feet, and did indeed experience altitude sickness (*soroche*) for which we took, successfully, homeopathic *Erythroxyton* (coca) and a local herbal tea called *Sunfo*.

A week later, we arrived at the Quito airport at the crack of dawn (our taxi picked us up at 4 a.m.) only to be told that our flight was being delayed nearly an entire day due to mechanical problems. After the initial bristling, we were reminded of a story that we had just heard at our retreat. Papa Ramdas was a famous Indian saint who from 1884 to 1963 lived a simple, humble life. He wanted nothing for himself, was completely surrendered to God in the form of *Ram* (*Ramdas* means "servant of God"), and chanted "Sri Ram Jai Ram Jai Jai Ram" day and night. This is now one of the most popular kirtan chants. One night he arrived at a train station in the traditional garb of a wandering saint carrying a begging bowl. He was promptly arrested by the police for vagrancy and escorted to a local jail cell. The following morning, the highly chagrined local authority apologized profusely, explaining that they had no idea that they had inadvertently incarcerated one of India's most beloved saints. "No problem," responded Papa Ramdas. "I had no place to sleep and you offered me a bed. I had no food, and you offered me something to eat. And now you are taking me back to the train station. How mysterious are the ways of Ram!" As the day unfolded in Quito, that was our mantra. Little did we know it was only the beginning of Ram's mischief!

### A Sudden, Fiery Blaze of Fury

The group who missed the flight was taken by taxi to a five-star Carlton hotel and fed a fabulous buffet breakfast and lunch – much savored after the retreat's rather ordinary

## Healing with Homeopathy

culinary fare. We met new friends, and Bob got to give a Bowen/Matrix treatment to a gentleman headed down to Patagonia to hike who was suffering from severe back pain. We had a few hours to spare, so we headed to the first UNESCO World Heritage site, Plaza San Francisco, to visit the celebrated La Compañía church. A block away, we happened upon the weekly changing of the presidential palace guard and found ourselves, among many others, waving at Rafael Correa, economist and very popular president of the Republic of Ecuador. We did eventually land in Santiago, Chile, at 5:30 the following morning, half a day late. Having checked our packs for a flight a few hours later to southern Chile, we hoped to enjoy a preflight breakfast. On arriving at the restaurant, we were transfixed by the fiery images on the screen. About 4 hours before, our very own volcano had erupted with a spectacular, unforgettable show of force. And we had missed it! We immediately called our caretaker, who assured us that humans, animals, and property were all safe and well. President Michelle Bachelet appeared on the screen and declared Pucón to be in a state of emergency/red alert. We were in shock!

On the plane to Temuco (the closest large airport to Pucón), we conversed with a member of the Channel 13 news team, who pumped Judyth for information about the environs of the volcano and offered to transport us home to Pucón in exchange for a news scoop. We were amazed to see no police or army on the road stopping us. It turned out that they didn't arrive until the following day. Nelson, our caretaker, who was born and raised in the area and observed the whole spectacle from our rooftop deck, with the volcano front and center, immediately became "our man in Pucón." He spent the afternoon guiding and being interviewed by the TV team, and has the 6 minutes of video interview to prove it!

### Panic Sets In Then Subsides

It took a few hours for the gravity of the situation to sink in. Chile is accustomed to volcanic eruptions and earthquakes. The president of Chile, volcanologists, seismologists, police, army, and newspeople arrived on the scene. The problem was that the eruption sent a fiery wall several thousand feet vertical, lava poured down the usual cracks, destroying two bridges, then the mass of volcanic material landed right down where it originated, capping the crater. Locals had always told us that it was a really good sign whenever smoke was emitted from the crater (often over the previous 10 years). But now the sulfurous gas and molten lava were trapped inside, making likely a second eruption. It would be only a matter of time. That sent the locals into panic mode. The powers that be urged evacuation for residents living near the volcano (we were just outside the zone), and most of our neighbors complied. We evacuated, with our two golden retrievers, late Tuesday

night to stay with friends half an hour away, but returned the following morning, determined to stay. We hear that some of those who hastily fled in fear suffered auto collisions, and that a general pandemonium ensued. After a day, the great majority of the tourists and many locals had evacuated (about 3500 according to news reports), the eeriness of all the restaurants' and supermarkets' being closed passed, and, the rhythm of life as we knew it pretty much returned. We felt greatly supported by our caretaker family, who vowed to stay to protect our land, along with our guardian German shepherd, five cats, sheep, and chickens. And, after a night of our own escape, we returned to where we felt the most safe: home. Only very briefly did we consider catching a flight back to the US.

To add a bit more perspective, several years ago we visited the town of Chaitén, in Patagonia, while on a kayak trip in Pumalin Park. There, in late April of 2008, the Michinmahuida volcano, long dormant, erupted for the first time in 9500 years! Nearby Chaitén (population 4200) was covered with a thick blanket of ash, much of which still remains 7 years later. That was our greatest fear, but this ash-spewing tendency has not been the nature of Villarrica. Nevertheless, that was the worst-case scenario in our minds, since we had also been close enough to Mount St. Helen's, when she erupted, to hear the thunderous roar (Bob on the Oregon coast, and Judyth on the Olympic Peninsula of Washington). Two years ago, when close friends came down to celebrate Judyth's 65th birthday, we vacationed in Bariloche and Villa La Angostura, Argentina, still affected by the eruption of the Puyehue-Cordón Caulle volcano, also in Southern Chile, 8 months earlier. We were impressed by the giant earth movers parked amidst 6-foot-high hills of volcanic ash by the side of the road. So it took a couple of days to convince ourselves that our volcano has never behaved in this way, and to calm ourselves. Knowing that those of us still here would stay close in touch and help out when needed, and that our loved ones back home trusted that we could make wise decisions to remain safe, we were reassured.

### All Is Well

The best advice that we can give, in this and any other emergency (or nonemergency) situation is to remind ourselves, "All is well." This was the mantra of the beloved spiritual teacher Robert Adams (see his story in our book *Mystics, Masters, Saints and Sages: Stories of Enlightenment*) as well as the first words of Dr. Eben Alexander, respected neurosurgeon and author of *Proof of Heaven*, during his *60 Minutes* interview that we happened to see on Facebook. These words convey a fundamental natural order of the universe, despite what appears to be chaos. Overriding whatever natural disaster, crisis, tragedy, dire diagnosis, or other seemingly horrific set of events, there lies an underlying perfection. We may not be able to experience or appreciate it at the time, but it is a timeless, placeless, universal principle that affects and protects each and every one of us. In the moment of chaos, that calm and

peaceful presence may not always be easily accessible, but there is no more profound message that we can offer.

### Homeopathic Medicines for the Effects of a Volcanic Eruption

These remedies come to mind:

*Aconitum napellus* (monkshood): This is the first remedy to think of for fear and panic in a natural or other disaster, whether it is an earthquake, landslide, attack, riots, or other shocking event. It is said to be the most acute of all homeopathic medicines. The feeling is sheer terror; of a sudden, intense threat that will lead to immediate death. There is a tremendous anxiety, restlessness, and nervous excitability. The individual doesn't know where to go or what to do, but this state can pass as quickly as it arose. There is great impatience, excitability, hurriedness, heart palpitations, thirst, and dryness of the skin; a sympathetic nervous system/ fight-or-flight response.

*Arsenicum album* (arsenic): The symptoms are similar to those of *Aconite*, but less sudden. There is tremendous anxiety and restlessness and a strong desire for company. The person fears death, disease, being poisoned or contaminated, and being alone. The sense of anguish is similar to that of *Aconite*. There is increased thirst for sips of water, fear of robbers, fastidiousness, and feeling extremely cold.

*Arnica montana* (leopard's bane): This is the number one remedy for injuries of all kinds, trauma, contusion, bruising, bleeding, and shock. The individual may insist that (s)he feels fine and is not in need of any assistance.

*Ignatia* (St. John's Wort): The predominant medicine for grief and loss. This would be the remedy for devastation over losing property or loved ones in an eruption. The person wails, weeps uncontrollably, sobs, and sighs.

*Sulphur* (sulfur): There are many homeopathic medicines that are products of volcanic eruptions, but this is the most common. We would consider this first for skin conditions following an eruption, particularly itching or rashes worsened by heat and hot baths or showers.

*Hecla Lava* (lava of Mount Hecla, an Icelandic volcano): This is the best-known homeopathic medicine made from a volcano. It is a silicate of calcium, magnesium, and aluminum, and also contains iron oxide. It is best known for exostoses (growths) of the bones. We are mentioning it more as an example of a volcano-derived medicine than as one to use acutely following a volcanic eruption.

*Vog*: This is a form of air pollution resulting from the mixture of sulfur dioxide and other gases emitted from an erupting volcano reacting with oxygen and moisture in the presence of sunlight. It comes from a combination of "smog" and "fog." The expression is used commonly in the Hawaiian Islands, especially the Big Island, where the Kilauea volcano, erupting since 1983, emits 2000 to 4000 tons of sulfur dioxide daily. We received this medicine from Michael Traub, ND, a colleague of ours who has used it successfully to treat respiratory complaints resulting from prolonged exposure to Kona and other trade winds that

## Healing with Homeopathy

blow the vog to the southwest. Certainly other volcanic substances could be prepared from volcanoes worldwide.

If the predictions of future earthquakes and volcanic eruptions, especially in the Ring of Fire, prevail, then this information will hopefully prove to be of practical benefit to you and to those near and dear. Be sure to keep a homeopathic medicine kit on hand for when the need arises.

Judith Reichenberg-Ullman and Robert Ullman are licensed naturopathic physicians, board certified in homeopathy. Their most recent book is *The Savvy Traveler's Guide to Homeopathy and Natural Medicine: Tips to Stay Healthy Wherever You Go!* (also available as an app for android and Apple cell phones). Their previous books include *Homeopathic Self-Care*, *The Homeopathic Treatment of Depression, Anxiety and Bipolar Disorder*, *Whole Woman Homeopathy*, *Ritalin-Free Kids*, *Rage-Free Kids*, *A Drug-Free Approach to Asperger Syndrome and Autism*, *The Patient's Guide to Homeopathic Medicine*, and *Mystics, Masters, Saints and Sages: Stories of Enlightenment*. New editions of *Ritalin-Free*, *Whole Woman Homeopathy*, and *Homeopathic Self-Care* are now available as Kindle and iBook versions, as well as mini iBooks of all of the books. The doctors live on Whidbey Island, Washington, and in Pucón, Chile, and practice at the Northwest Center for Homeopathic Medicine in Edmonds, Washington. They treat patients by phone and videoconference as well as in person. They can be reached 425-774-5599, [drreichenberg@gmail.com](mailto:drreichenberg@gmail.com), or [drbobullman@gmail.com](mailto:drbobullman@gmail.com); their website is [www.healthyhomeopathy.com](http://www.healthyhomeopathy.com).

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# Monthly Miracles

by Michael Gerber, MD, HMD

contact@gerbermedical.com

## Nevada Homeopathic and Integrative Medical Association 2014 Conference: Part 3

### Marty Hinz, MD: Amino Acid Therapies: A New Approach

Dr. Hinz, a native of Minnesota, graduated from the University of Minnesota School of Medicine in 1983. He has been the director of emergency medical services at a number of Minnesota hospitals as well as the medical director of the Morgan Park Clinic from 1994 to the present and president of Clinical Research, NeuroResearch Clinics in Duluth, Minnesota, from 1999 to the present. His main interest has been amino acid research and testing, and he has published extensively and lectures tirelessly around the US.

I first attended one of Dr. Hinz's lectures in 2001 in Minneapolis. His main emphasis at that time was on weight loss promoted by the amino acids 5-HTP, tyrosine, and L-dopa. His early protocol worked well. Subsequently, he has broadened his scope of therapeutics to almost all neuropsychiatric conditions relating to the neurotransmitters serotonin, dopamine, norepinephrine, and epinephrine, primarily with a new intriguing emphasis on Parkinson's disease (Figure 1).

### Fascinating Neuroscience Evidence

Dr. Hinz has examined over 1000 databases and helped supervise 2.8 million patient days of documented treatment from data gleaned from 1200 clinics. Although not for the fainthearted, learning Dr. Hinz's approach to managing disease is very rewarding. He is the most prolific PowerPoint composer I have ever seen. His seminars, which he presents around the country every couple of months, are necessary to attend to get an initial insight into his protocols and background science. He uses urinary serotonin and dopamine laboratory values from the DBI Laboratory to determine the sufficiency of amino acid dosing and what type of amino acid protocol should be used. Many data are presented to show that baseline levels of amino acids are not helpful for the initial therapeutic diagnosis or treatment. "Baseline testing is not reproducible from day to day."

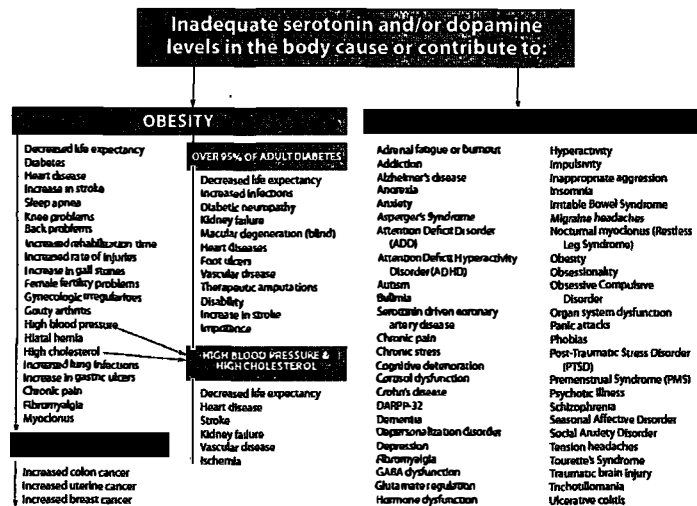
### All Manner of Psychiatric Drugs Deplete Neurotransmitters

Hinz provides data that that all SSRIs, SNRIs, tricyclic antidepressants, amphetamines, and migraine headache drugs and many environmental toxins and foods deplete neurotransmitters. This insight alone is worth the price of admission. If you don't have a reservoir of neurotransmitters, the drugs soon may become ineffective or tachyphylactic and cause a greater excretion of neurotransmitters via monoamine oxidase and catechol-O-methyltransferase, creating a deficiency of neurotransmitters in the presynaptic neuron. Of interest, he notes that the width of the synapse is 1 millionth of a centimeter and that the average neurotransmitter binding time to a postsynaptic receptor last 1 thousandth of a second.

### Three Legs of the Stool

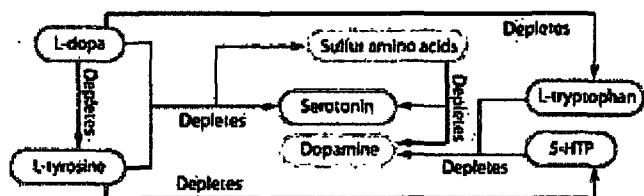
By examining several complicated feedback loops of neurogenic amino acids and sulfur-containing amino acids, Hinz makes his case for replacing these amino acids in a defined pattern that normalizes important neurotransmitter

Figure 1



levels (Figure 2). Organic cation transporter type 2 (OCT2) occurs on a microscopic level at the entire cerebral interface with cerebrospinal fluid, on the surface of every neuron and the liver, intestines, and importantly kidney. Through passive transport, diffusion, and active transport, they deliver serotonin and dopamine to the body in a competitive inhibition manner. For example, if you give 5-HTP to manufacture serotonin, it inhibits the conversion of tyrosine to dopamine, norepinephrine, and epinephrine; and vice versa: giving only tyrosine will impede serotonin formation. They must be given together to rebuild balanced neurotransmitter levels. He assesses this by serial urinary serotonin and dopamine levels. The third leg of the stool is cysteine, a sulfur-containing amino acid. Other sulfur compounds will do, but they are much more expensive in the amounts required to rebuild thiol metabolism which is damaged in neurologic diseases.

Figure 2



### Parkinson's Treatment and Dopamine Dominance

Most patients are treated via Hinz's three-phase system. When the urinary neurotransmitters are initially measured, they are in the high range because the kidneys are eliminating serotonin and dopamine. On replenishment with a balance of 5-HTP and tyrosine, the levels go lower as the body can now absorb them and is holding on to them. In the phase 3 measurement, the levels come again into the midrange; and most of the common anxiety, depression, insomnia, bipolar disease, migraine headaches, and multitude of other diseases respond quite well.

However, another patient type has emerged: the dopamine-dominant patient. These are Parkinson's patients, restless leg patients, and ones with addictive problems. This is another ball of wax. Hinz gives L-dopa from the *Mucuna pruriens* bean from South America with a 40% L-dopa content. L-dopa used to be used in Parkinson's but had to be mixed with carbidopa to control the nausea. Now he uses 5-HTP to control the nausea of L-dopa with tyrosine, cysteine, vitamin B6, calcium, and vitamin C. The doses of L-dopa needed to control Parkinson's can be quite astronomical, 10,000 to 40,000 mg per day or more to overcome the neurotoxic damage to postsynaptic neurons. There are more than 1179 known neurotoxins. The dose of L-dopa is ascertained by doing pill stops, taking the increasing doses 5 days on then 2 days off. If the symptoms get worse, patients increase the dosage; if symptoms get better, they reduce it. Needless to say, the practitioner must

take Hinz's seminars and tune in to his frequent online updates and call him for interpretation of his urinary test results and unique responses from patients (marty@hinz.md.com; 877-626-2220).

### Carbidopa Increases Parkinson's Death Rate by Blocking B6 Irreversibly

In a paper (containing 90 scientific references) published in *Clinical Pharmacology*, Hinz, Alvin Stein, and Ted Cole note that the only indication for carbidopa and benserazide is the management of L-dopa-induced nausea.<sup>1</sup> Both drugs irreversibly bind to and permanently deactivate pyridoxal-5'-phosphate (PLP), the active form of vitamin B6. "PLP is required for more functions and chemical reactions than any other vitamin or mineral. Over 300 enzymes and proteins require PLP to function properly. The five PLP-dependent enzymes – glutamate decarboxylase, arginine decarboxylase, histamine decarboxylase, aromatic L-amino acid decarboxylase, and sulfoalanine decarboxylase are unrivaled in the variety of reactions they catalyze." Carbidopa may induce life-threatening events, including myocardial infarction, neuroleptic malignant syndrome, agranulocytosis, hemolytic and nonhemolytic anemia, gastrointestinal bleeding, thrombocytopenia, hypokalemia, and 90 other syndromes. "Irreversible L-dopa dyskinesias do not exist; they are a function of carbidopa which has a profound ability to induce previously undocumented histamine dyskinesias."

The death rate in Parkinson's patients has increased by 328.7% between 1976 and 2011, when carbidopa was first introduced. This is an amazing revelation and should change the face of the Parkinson's patient lot.

### Notes

1. Hinz M, Stein A, Cole T. Parkinson's disease: carbidopa, nausea, and dyskinesia. *Clin Pharmacol.* November 2014;2014(6):189-194.

## Lyme Disease and Co-Infections: Unraveling the Mysteries

# SPECIAL ISSUE

July, 2015

**Townsend Letter**



# Optimizing Metabolism

by Ingrid Kohlstadt MD, MPH  
www.INGRIDients.com

## The 'Nutrition Takes Guts' Approach Facilitates Health Care Reimbursement

### Introduction

In my experience, patient interest is seldom a barrier to accessing nutritional medicine services. A more formidable challenge is reimbursement for both physician visits and the diagnostic tests that they order. There is no single checkbox on billing forms. Instead, a nutritional assessment requires many screening diagnostic billing codes. An assessment of the gastrointestinal tract can inform nutritional decision-making and can be matched with medical billing codes.

The assessment that I've developed for this purpose is called "Nutrition Takes Guts." Here I present my approach in the order of location along the gastrointestinal tract.

### Screen for Loss of Taste and Smell

Sense of smell and taste diminish at variable rates with age, and their loss has recently been shown to predict life expectancy. Loss of smell can be easily assessed with a physical exam, while patients may be more likely to notice and tell their doctor about a diminished sense of taste. Both are important for diet and recognizing thirst.

While only some underlying causes such as sinusitis, colds, and zinc deficiency can be treated, diagnosing loss of smell and taste is clinically useful even in the absence of treatment. Awareness can be lifesaving when accompanied by practical precautions such as upgrading the kitchen smoke detector, looking at expiration dates of refrigerated foods rather than relying on the "whiff test," drinking water on a schedule, and flavoring with spices instead of sweeteners.

Spices are especially important because they aid digestion, are nutritious (in contrast with artificial sweeteners), and add flavor with fewer calories. Therefore, I recommend that those who can't smell use spices such as chipotle, cocoa, and vanilla to season their food.

For more on treating chemosensory disorders, consider neurologist Alan R. Hirsch's academic text *Nutrition and Sensation* (CRC Press; April 2015). Dr. Hirsch coauthored a chapter on this topic in *Advancing Medicine with Food and Nutrients* (2013), which I edited.

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### Examine for Dental Issues, Especially Among the Elderly

Imagine a meal prepared from a 3-D printer. Such food is quickly becoming available for several applications, including for elderly people suffering from dysphagia (difficulty swallowing). 3-D foods look appetizingly like the real food, but dissolve in the mouth as if they were puree. While most elderly patients with dental and swallowing issues don't need 3-D printed steak, they do need their doctor to examine them for dental problems, which affect overall health. Dental pain makes it harder to meet protein requirements. And a red, swollen tongue is an often overlooked sign of vitamin B12 deficiency.

Gum disease predicts vascular disease and heart attacks, although the association is not fully understood. David Kennedy, DDS, authored a chapter in *Advancing Medicine with Food and Nutrients* on periodontal disease, aptly subtitled "Treatable, Nutrition-Related, and with Systemic Repercussions."

### Apply the Stomach Acid Test

During a meal, the stomach's pH drops to 1, nearly the pH range of battery acid, in order to increase nutrient absorption and foodborne pathogen resistance. Physiologically expensive, stomach acid production wanes during aging and is thought to be why protein requirements increase for the elderly despite a slowing metabolism. Low vitamin B12, anemia, and characteristic nail bed changes point to a decline in stomach acid. Physicians can help patients evaluate the merits of antacids; learn to eat low-sodium fermented vegetables such as sauerkraut, kimchi, and pickled garlic; include vinegar, coffee, and bitters as digestive aids in their diet; and skip the raw bar.

A challenge to clinicians is managing medical conditions, including gastroesophageal reflux, peptic ulcers, and *Helicobacter pylori* infection, in which therapies increase stomach pH (lower stomach acid production). Authors of these respective chapters in *Advancing Medicine with Food and Nutrients* share their clinical strategies.

### Alkalinize the Small Intestine through Diet

Blood has a pH range of 7.34 to 7.45, which is precisely maintained by the kidneys and lungs. A diet high in refined carbohydrates, meat, and salt generates biologic acids that must be quickly neutralized by the body's metabolism so as to protect the pH of blood. As kidney and lung function decline with age, an acid-producing diet metabolism doesn't get balanced as well. The body taps bone calcium reserves and refrains from repairing proteins such as muscle to keep blood at the necessary pH. The loss of bone and muscle tends to be insidious until compounded by minor illness and bed rest because exercise is needed for strong bones. Boosting fruit and vegetable intake and a daily supplement of lime juice, which is biochemically alkalinizing even though it is acidic by pH, or citrate have been shown to protect muscle and bone.

My colleague Susan E. Brown, PhD, offers excellent resources on this topic through the Center for Better Bones and its website, [www.betterbones.com](http://www.betterbones.com).

### Restore the Large Intestine's Microbiome through Diet

The gut's microbial workforce, colonic bacteria, diminishes with age, with the elderly having fewer than half the microbes than people half their age. Ongoing research suggests that bulking up stool can help bulk up muscle. Clinical recommendations include hydration, prebiotics (dietary fiber), and probiotics from dietary sources such as cultured dairy. A diet rich in vitamin C and magnesium and magnesium sulfate baths (Epsom salts) may help regularity, especially for symptoms following antibiotic use. I'll be writing more on this topic as compelling studies emerge.

In summary, nutritional medicine intervenes all along the gastrointestinal tract and can often satisfy a broader set of billing codes.

Ingrid Kohlstadt, MD, MPH, FACPM, FACN  
Faculty Associate, Johns Hopkins Bloomberg School of Public Health  
Executive Director, NutriBee National Nutrition Competition Inc.  
Editor, *Advancing Medicine with Food and Nutrients* (CRC Press; 2013)

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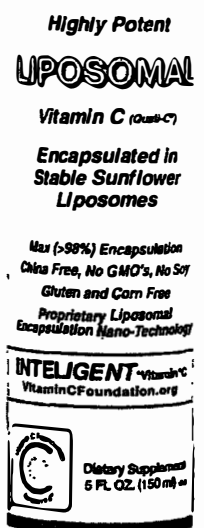
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*continued on page 112* ►





# Women's Health Update

by Tori Hudson, ND  
womanstime@aol.com

## NAC in COPD; Multivitamin-Mineral Use and Cardiovascular Disease in Women

### Multivitamin-Mineral Use Associated with Lower Risk of Death from Cardiovascular Disease in US Women

There have been only 2 randomized clinical trials on whether vitamin and mineral supplements are effective for the prevention of cardiovascular disease. One of these, the Physicians' Health Study II, did not find an association between the use of a multivitamin-mineral (MVM) supplement and cardiovascular disease (CVD) in both incidence or mortality after an average of 11 years, in male US physicians aged 50 years or older. The other study, the French SUPplementation en Vitamines et Minéraux Antioxydants (SU.VI.MAX), randomly assigned women and men (women 35–60 y.o.; men 45–60 y.o.) to receive either a daily antioxidant combination (not an MVM) or placebo, and after 7.5 years CVD incidence was not statistically different between the two arms. In 2010, a large Swedish cohort study of women found that multivitamins (MV) without minerals were associated with a reduced risk of myocardial infarction, and if they used them more than 5 years, the association was even stronger.

The current study set out to examine the association between MVN and MV use and CVD mortality in US adults who did not previously have CVD. The researchers linked the NHANES II data and the 2011 National Death Index to examine the association between MVM and MV use and mortality due to CVD. These two large surveys provide data on over 10,000 adults aged 40 years and older. Data points included history of myocardial infarction, stroke, coronary heart disease, cardiovascular disease, non-skin cancers, diabetes, alcohol, smoking, height, weight, blood pressure, cholesterol, triglyceride, glucose/glycolated hemoglobin testing, age, race, education, dietary supplements (vitamins, minerals, herbs), and over-the-counter and prescription medications. A MVM was defined as 3 or more vitamins and at least 1 mineral. A MV was a vitamin combination without minerals. There were also 3 duration categories of <1 year, 1–3 years, and > 3 years.

Approximately 45% of the individuals evaluated had used a dietary supplement in the previous 30 days. MVMs were the most frequently used (21%) and MVs (14%).

Results: Neither MVM nor MV use was associated with a lower risk of CVD mortality when they compared users with nonusers. However, when they looked at the length of time of use, there was indeed a significant inverse association for MVM use of >3 years with a more than 35% reduced risk of CVD mortality in women, but not men. MV only was not significantly associated with CVD mortality when combining men and women, although men who had used MV for 1 to 3 years did have reduced CVD related mortality.

**Comment:** It's reassuring to see some positive data for MVM users and prescribers, and useful to see that longer use, in this case >3 years, is clearly associated with reduced mortality from cardiovascular disease. All kinds of critiques can be lodged against this kind of study, since it is not the gold-standard randomized, controlled trial. However, even RCTs can be criticized because they are often of short duration and have a more homogeneous population of individuals being studied. The current study is strong in the robust diversity of individuals as well as a large sample who were older than 65, which is especially useful when looking at cardiovascular disease mortality.

There are many research studies on individual minerals, vitamins, amino acids, fish oils, and herbs that show efficacy in both prevention and intervention in different areas of cardiovascular disease. Examples include magnesium intake and an inverse association with risk of strokes, reduced risk of ischemic heart disease, and CVD mortality; protective CV effect of vitamin D; hawthorn to improve outcomes of congestive heart failure; and the many and diverse cardiovascular benefits in prevention and treatment with fish oils (strokes, CVD mortality, blood pressure, type 2 diabetes and more).

As a result of the current study, I will be more eager to recommend long-term use of MVM for women in my practice and teachings.

Bailey R, Fakhouri T, Park Y, et al. Multivitamin-mineral use is associated with reduced risk of cardiovascular disease mortality among women in the United States. *J Nutr.* 2015. doi:10.3945/jn.114.204743



## Women's Health Update

➤

### Benefits of N-Acetylcysteine in Patients with COPD

In the current study, patients with proven and stable chronic obstructive lung disease (COPD) were randomized to treatment with either NAC 600 mg twice daily or placebo, in addition to the treatments that they were already using. Patients had a follow-up every 16 weeks for 1 year. After enrolling 120 patients with COPD who were at least 4 weeks after their last exacerbation, in the end there were 108 who completed the study, with 52 in the NAC group and 56 in the placebo group. In the analysis, patients were classified as a high exacerbation risk (a history of 2 or more exacerbations per year or a lung function forced expiratory volume < 50% or both). Those with a low exacerbation risk had a history of fewer than 2 exacerbations per year and a forced expiratory volume of 50% or more and no recent hospitalizations related to COPD.

For high-risk patients, this higher dose of NAC at 600 mg twice daily significantly reduced the exacerbation frequency at 8 and 12 months, a prolonged amount of time until the first exacerbation and an increased probability of having no exacerbations at 1 year, compared with placebo. For low risk patients, this dose of NAC did not have a significant effect.

**Comment:** COPD is frequently associated with exacerbations, which lead to a deterioration of lung function and quality of life. One of the primary management goals of COPD is to prevent exacerbations. For those with a high rate of exacerbations, corticosteroid inhalers and phosphodiesterase (PDE04) inhibitors are frequent strategies. However, these regimens may be associated with corticosteroid-inhaler induced pneumonias. Mucolytic agents have an important role in managing COPD exacerbations because increased mucus secretions causes coughing and the mucus plugs can obstruct airways and lead to increased death.

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Oral N-acetylcysteine (NAC) is known for its mucolytic effect, but also is a significant antioxidant and anti-inflammatory. NAC is also a free-radical scavenger and precursor of reduced glutathione, which contributes to the inflammatory modulatory effect. This potent antioxidant and anti-inflammatory effect is best achieved with 100 mg per day or more. In one previous study, 1200 mg/day was shown to improve exercise endurance in patients with emphysema-related COPD. In another (the HIACE study), 600 mg twice daily reduced COPD exacerbations and improved small airway function. In a large 3-year trial (the BRONCHUS study), NAC did not improve lung function or result in a decline in the frequency of COPD exacerbations; however, it is suggested that this was due to a dose of only 600 mg/day.

COPD exacerbations are multifactorial (mucus hypersecretions, inflamed ciliated epithelial cells in the airway, excessive migration of neutrophils, a high amount of oxidative stress, and lowered vital lung capacity.) I think that this leans towards a good understanding of why NAC is the perfect supplement to reduce the frequency of exacerbations and perhaps severity, due to its antioxidant and anti-inflammatory effects, mucolytic effects, and ability to inhibit the attachment of bacteria to the lung epithelium. It appears that the effect is most significant in higher-risk COPD patients.

Tse HN, Raiteri L, Wong KY, et al. Benefits of high dose N-acetylcysteine to exacerbation-prone patients with COPD. *Chest*. 2014;146(3):611-623.

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

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# Kyowa Hakko Receives Patent on L-Citrulline and L-Arginine Combination to Rapidly Increase Blood Flow

Kyowa Hakko Bio Co. Ltd. announces that it has received a patent for the combination of the amino acids L-citrulline and L-arginine. The patent protects the use of L-citrulline and L-arginine in formulations used to rapidly and effectively increase blood L-arginine levels.

L-arginine is an amino acid critical to the production of nitric oxide (NO) in the body. NO helps regulate and improve blood circulation. L-citrulline is a major precursor to L-arginine and has been shown in other studies to increase L-arginine levels, and thus improve NO production.

"We measured blood L-arginine levels and nitric oxide levels 40 minutes and 60 minutes after amino acids administration. At both time points, the combination of L-citrulline and L-arginine had a better effect than the single amino acids," said Ryusuke Nakagiri, senior director of strategic science at Kyowa Hakko USA.

A related animal study published in November 2014 in *Biochemical and Biophysical Research Communications* showed that L-citrulline plus L-arginine supplementation caused a more rapid increase in plasma L-arginine levels and marked enhancement of NO bioavailability, including plasma cGMP (Cyclic guanosine monophosphate) concentrations, than with dosage with the single amino acids.<sup>1</sup>

Kyowa Hakko Bio Co. Ltd. manufactures both L-citrulline and L-arginine at its Cape Girardeau, Missouri, facility.

## About Kyowa Hakko's L-Citrulline

L-citrulline is an amino acid that plays an important role in nitric oxide metabolism and regulation. L-citrulline is converted to L-arginine in the body, leading to sustained increases in both L-arginine and nitric oxide. An ingredient with application in the areas of heart health and sports nutrition, L-citrulline is preservative-free, allergen-free, and contains no artificial flavors or colors. It's nonhygroscopic and highly stable, and its mild taste makes it suitable for use in a variety of formulations. This pure, vegetarian ingredient is also self-affirmed GRAS. Manufactured in the US using a proprietary fermentation process, L-citrulline is an ultrapure amino acid that carries the Kyowa Quality logo, ensuring that the ingredient is backed by our commitment to the highest manufacturing standards.

## About Kyowa Hakko USA

Kyowa Hakko USA Inc. is the North American sales office for Kyowa Hakko Bio Co. Ltd., an international health ingredients manufacturer and world leader in the development, manufacturing and marketing of pharmaceuticals, nutraceuticals, and food products. Kyowa is the maker of branded ingredients including Cognizin Citicoline, Pantestin Pantethine, Setria Glutathione, and Sustamine L-Alanyl-L-Glutamine. For more information, visit <http://www.kyowa-usa.com>.

## Notes

1. Monto M, Hayashi T, Ochiai M, et al. Oral supplementation with a combination of L-citrulline and L-arginine rapidly increases plasma L-arginine concentration and enhances NO bioavailability. *Biochem Biophys Res Commun.* 7 November 2014;454(1):53-57 ISSN 0006-291X. <http://dx.doi.org/10.1016/j.bbrc.2014.10.029>.

# Metagenics Launches Ultra Calm and Ultra Energy

Ultra Calm is a dietary supplement designed to address stress-related concerns. It contains 200 mg of L-theanine to support relaxation, a sense of calm, and a healthy stress response.\* Ultra Calm is available in chocolate coconut flavor, and each box contains 12 bars.

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## Pharmaceutical Industry Gouges Americans

Total expenditures for prescription drugs in the US increased last year by 13%, to an estimated \$368 billion. That comes to about \$1150 for every man, woman, and child in the country. The year-over-year increase resulted largely from a 31% increase in spending on specialty medications, such as the recently approved drugs for hepatitis C (e.g., sofosbuvir [Sovaldi]) and the tumor necrosis factor (TNF) inhibitors (e.g., adalimumab [Humira]) used for rheumatoid arthritis, Crohn's disease, and other inflammatory conditions.

Twelve weeks of treatment with Sovaldi, when combined with other drugs such as simeprevir (Olysio), results in an apparent cure rate of 90%, a substantially higher cure rate than with previous generations of hepatitis C drugs. However, Sovaldi costs \$84,000 for a course of treatment and Olysio costs \$76,000, for a total cost of \$160,000. At those prices, the cost of treating all of the estimated 3.2 million Americans with hepatitis C would be more than half a trillion dollars. Although Sovaldi was approved by the FDA only a little more than a year ago, it has already become one of the world's largest-

selling drugs, with more than \$10 billion in annual sales. Humira costs about \$20,000 per year, and many patients are on this drug for the long term. In 2013, Humira was the top-selling drug in the world, with sales of \$11.5 billion. Combined worldwide sales of the 3 major TNF inhibitors (Humira, Remicade, and Enbrel) were more than \$30 billion, with just under half of those sales in the US. In addition, drug companies have been repeatedly raising the prices of many other popular drugs, and the increases have far outpaced inflation. For example, since 2007, the cost of Humulin R U-500 (human insulin) has increased 354%, EpiPen (epinephrine) has increased 222%, and Avonex (for multiple sclerosis) has increased 147%. Since ObamaCare mandates that everyone have medical insurance (including drug coverage), individuals and employers have little choice but to fork over more and more money in premiums, a large portion of which is being confiscated by the drug industry.

The distributors of these expensive patented drugs typically try to justify their high prices by pointing to the high cost of drug development.

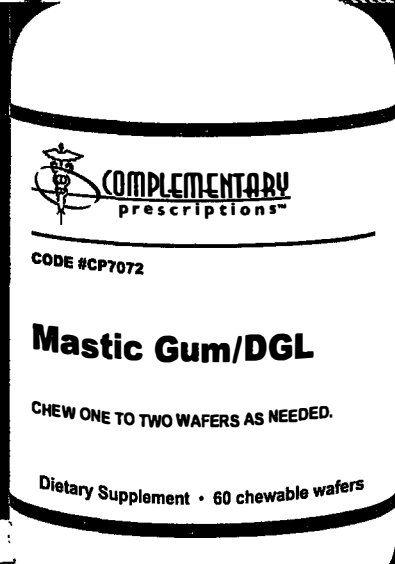
Gilead Sciences (which owns Sovaldi) also argues that the cost per patient cured is not much different than that of older, inferior drugs. Moreover, they claim, use of Sovaldi could save money by reducing the need for even more expensive liver transplants. However, it seems that the main reason Gilead Sciences has been charging \$1000 per pill for Sovaldi in the US is that it has been able to get away with it. The shallowness of Gilead Sciences' pricing justification is revealed by the fact that the company is licensing generic drug companies to manufacture and sell the drug in developing countries (but not in the US) for only \$10 per pill, a 99% discount.<sup>1</sup> And AbbVie (a spinoff of Abbott Laboratories) makes so much money on Humira that it was able to afford more than \$200 million in advertising for that one drug alone in a recent year (2012).

Some groups are beginning to fight back against the price-gouging tactics of the pharmaceutical industry. For example, Express Scripts, which manages prescription drug benefits for 85 million people and is the largest pharmacy benefits manager in the US, recently announced it will no longer

*continued on page 112 ►*

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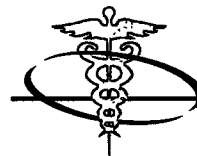
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## Editorial

► cover Sovaldi or Olysio (except in limited circumstances). Instead, it will cover a similar drug cocktail, Viekira Pak, after having negotiated a substantial discount with its distributor. Not surprisingly, the share price of Gilead stock fell 11% on the day that Express Scripts' decision was announced. Perhaps we can find some comfort in the observation that one branch of the medical-industrial complex (a pharmacy benefits manager) is duking it out with another branch of said complex (the drug industry), so that the costs being imposed on the hapless, mandated consumers and employers can be

lowered from intolerable to merely obscene.

Practitioners of natural medicine point out that safe, effective, relatively low-cost alternatives exist for many of the conditions for which expensive drugs are currently being prescribed. For example, in the treatment of chronic hepatitis C, the addition of intramuscular vitamin B12 injections once every 4 weeks to the previous generation of antiviral drugs increased the apparent cure rate (sustained viral response) from 36% to 72%.<sup>2</sup> High-dose intravenous vitamin C has an antiviral action, and might also be an effective treatment. I have only treated one hepatitis C patient with intravenous vitamin C; that patient was disease free after receiving 20 weekly infusions of 50 g each.

However, natural medicine does not always work, and many patients can benefit from what the pharmaceutical industry has to offer. It is incumbent upon us, therefore, to put the pressure on the drug companies from all directions, so that we are no longer their financial hostages.

Alan R. Gaby, MD

### Notes

1. McLain S. Gilead cuts hepatitis pill price abroad. *Wall Street Journal*. September 16, 2014:B1-B2.
2. Rocco A et al. Vitamin B12 supplementation improves rates of sustained viral response in patients chronically infected with hepatitis C virus. *Gut*. 2013;62:766-773.

## Calendar

► continued from page 106

**SEPTEMBER 30-OCTOBER 3: INTERNATIONAL PLANT-BASED NUTRITION HEALTHCARE CONFERENCE** in Anaheim, California. CONTACT: 203-594-1632; pbnhc.com

**OCTOBER 1-4: 13TH ANNUAL RESTORATIVE MEDICINE CONFERENCE** in Blaine, Washington. CONTACT: [restorativemedicine.org/conference/2015/](http://restorativemedicine.org/conference/2015/)

**OCTOBER 2-4: HORMONE REPLACEMENT THERAPY SEMINAR (Session 2)** with Dr. Neal Rouzier in Chicago, Illinois. CONTACT: [www.ducerecorp.com/Seminars.aspx](http://www.ducerecorp.com/Seminars.aspx)

**OCTOBER 9-11: 15th INTERNATIONAL CONFERENCE ON AYURVEDA & AUTOIMMUNE DISORDERS** in San Jose, California. CONTACT: [aapna.org/conferences/15th-conference-october-9-11-2015-san-jose-ca-usa](http://aapna.org/conferences/15th-conference-october-9-11-2015-san-jose-ca-usa)

**OCTOBER 14-17: MINDFUL PRACTICE ADVANCED WORKSHOP: ENHANCING QUALITY OF CARE, QUALITY OF CARING, AND RESILIENCE** in Batavia, New York. For healthcare practitioners. CONTACT: [www.urmc.rochester.edu/family-medicine/mindful-practice/presentations-workshops.aspx](http://www.urmc.rochester.edu/family-medicine/mindful-practice/presentations-workshops.aspx)

**OCTOBER 21-24: 10TH ANNUAL CARDIOMETABOLIC HEALTH CONGRESS** in Boston, Massachusetts. CONTACT: [www.cardiometabolichealth.org/register.asp](http://www.cardiometabolichealth.org/register.asp)

**OCTOBER 23-24: CONCORDIA: The Legacy Continuum 2015-BioEnergetic Functional Medicine** in Santa Barbara, California. CONTACT: [physicaenergetics.com/dv/pages/Annual-Conferences.html](http://physicaenergetics.com/dv/pages/Annual-Conferences.html)

**OCTOBER 24-29: 16TH ANNUAL SCIENCE AND CLINICAL APPLICATION OF INTEGRATIVE HOLISTIC MEDICINE** in San Diego, California. CONTACT: [www.scripps.org/events/people-planet-purpose-global-practitioners-united-in-health-healing-october-25-2015](http://www.scripps.org/events/people-planet-purpose-global-practitioners-united-in-health-healing-october-25-2015)

**OCTOBER 27 - NOVEMBER 2: 42nd BIOLOGICAL MEDICINE TOUR TO GERMANY & BADEN-BADEN MEDICINE WEEK - "Clinical Applications in Biological Medicine."** Includes "Medicine Week" Congress, exclusive OIRF English language lectures, and

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**OCTOBER 28-NOVEMBER 1: ICIM CONFERENCE – IENERGY & MEDICINE: PARADOX & CONTROVERSY** in Chicago, Illinois. CONTACT: [www.IntegrativeMedicineConference.com](http://www.IntegrativeMedicineConference.com)

**NOVEMBER 7-8: ARIZONA NATUROPATHIC MEDICAL ASSOCIATION 2015 FALL CONTINUING MEDICAL EDUCATION CONFERENCE** in Scottsdale, Arizona. CONTACT: [www.aznma.org](http://www.aznma.org)

**NOVEMBER 11-14: 56TH AMERICAN COLLEGE OF NUTRITION ANNUAL CONFERENCE** in Orlando, Florida. CONTACT: [www.naturalhealthresearch.org/annual-conference/](http://www.naturalhealthresearch.org/annual-conference/)

**NOVEMBER 12-14: SOCIETY FOR ACUPUNCTURE RESEARCH 2015 CONFERENCE** in Boston, Massachusetts. CONTACT: [www.acupunctureresearch.org/events](http://www.acupunctureresearch.org/events)

**NOVEMBER 12-15: AMERICAN FUNCTIONAL MEDICINE ASSOCIATION ANNUAL CONFERENCE** in Atlanta, Georgia. CONTACT: 1-855-500-2362; [www.afmassociation.com/calendar/](http://www.afmassociation.com/calendar/)

**NOVEMBER 13-15: IGNITE CONFERENCE 2015 – The Business of Better Medicine** in San Diego, California. CONTACT: [eeignite.com/coming-soon-the-business-of-better-medicine](http://eeignite.com/coming-soon-the-business-of-better-medicine)

**NOVEMBER 14-16: 12TH INTERNATIONAL CONFERENCE OF THE SOCIETY FOR INTEGRATIVE ONCOLOGY** in Boston, Massachusetts. CONTACT: [www.integrativeonc.org/annual-international-conference](http://www.integrativeonc.org/annual-international-conference)

**NOVEMBER 19-22: 5TH ANNUAL PRO-AGING EUROPE CONFERENCE** with Dr. Thierry Hertoghe in Brussels, Belgium. CONTACT: <https://www.weezevent.com/pro-aging-europe-2015>

**DECEMBER 10-13: 23RD ANNUAL WORLD CONGRESS ON ANTI-AGING MEDICINE** in Las Vegas, Nevada. CONTACT: 561-893-8626; [www.A4M.com](http://www.A4M.com)

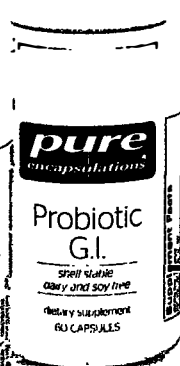
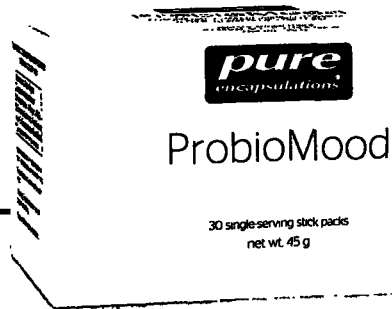


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