Women's Health Issue

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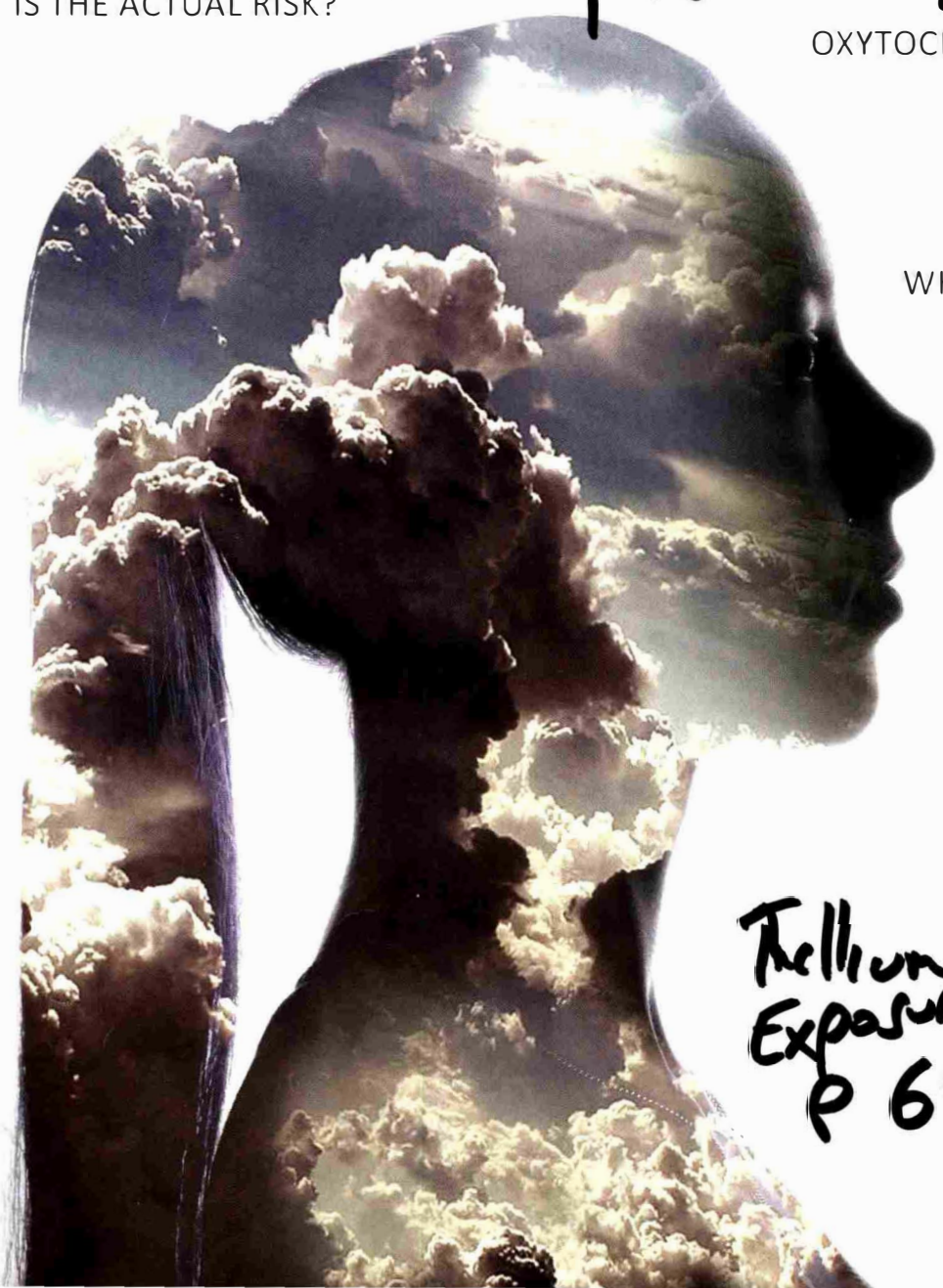

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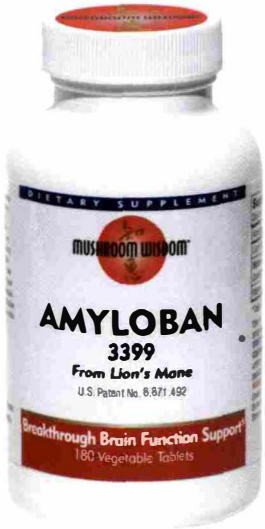

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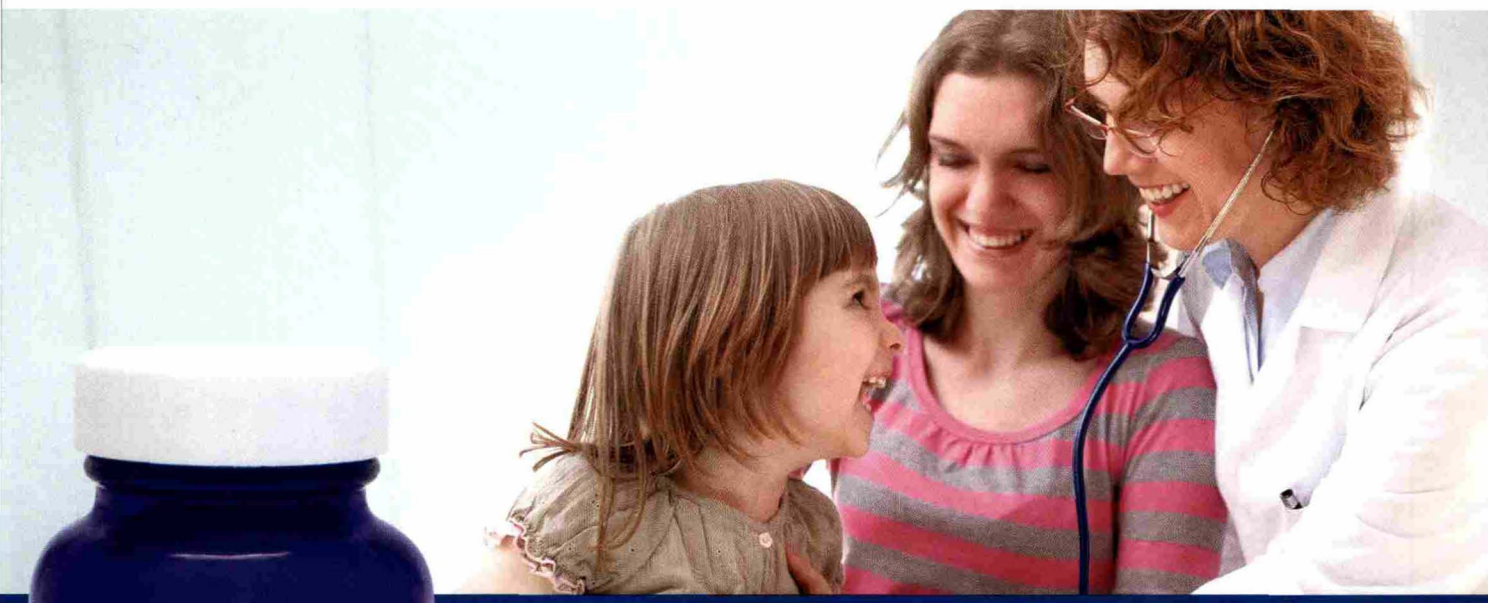

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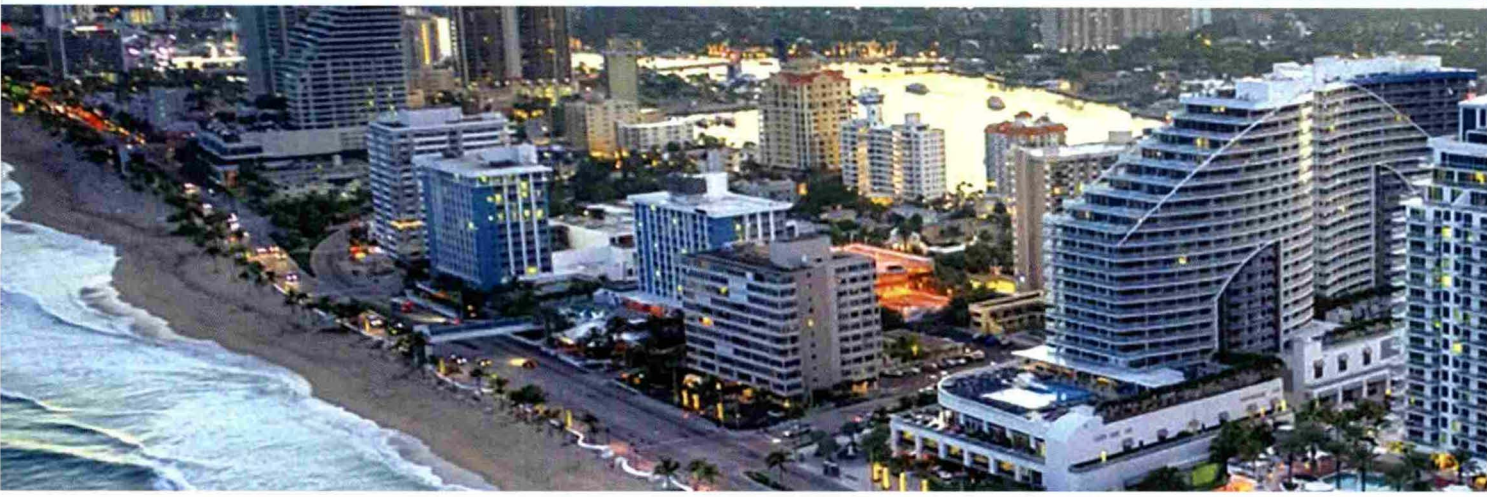

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From the Publisher

Schadenfreude

Foreign words or idioms not infrequently find themselves in use, particularly in newspaper or periodical articles and essays. When one cannot define what it is that makes something or someone attractive, particularly in romantic or intellectual encounters, instead of saying "I don't know what it is about her," one can throw up one's hands and exclaim, "She has a certain *je ne sais quoi*." While I enjoy tossing around phrases from *le français*, I am much more apt to employ a German word that does not so easily find a comparable one in English: *schadenfreude*, which is now ensconced in our lexicon. In German, "schaden" is damage or harm; "freude" is joy or happiness. Hence, schadenfreude is the joy that one experiences in another's experiencing damage or harm; pleasure in another's misfortune. Such is the state I that found myself over the holidays when the former hedge fund manager and until recently the CEO of Turing Pharmaceuticals, Martin Shkreli, was arrested for security fraud charges.

Shkreli made a big name for himself last September by loudly announcing that he was raising the cost of the antiparasitic medication Daraprim from $13.50 a pill to $750. Despite the fact that he was roundly hissed for this outrageous price hike by physicians and patients alike, Shkreli grinned unrepentantly like the Cheshire cat in media interviews, explaining that his shareholders were entitled to their profits, greedy or otherwise. On YouTube he claimed that the profits that Turing Pharmaceuticals would make in drug sales, primarily to AIDS patients suffering from toxoplasmosis, would be the seed money for developing a new antiparasitic drug. Shkreli would be spearheading these R&D efforts with his extensive education in pharmacology, parasitology, and molecular biology – which would be none, except self-study on the Internet.

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From the Publisher

➤ *continued from page 4*

Shkreli's arrest had nothing to do with his price gouging. Instead, in earlier employment with a hedge fund, his reckless stock investing proved to be disastrous, and investors were seeking reimbursement for Shkreli's losses. When Shkreli headed another drug firm from which he was fired, Retrophin, he adapted a "quasi Ponzi scheme" using Retrophin's financing to pay back the hedge fund investors. He has been released on a $5M bail, but Turing Pharmaceuticals ordered him to resign.[1]

Daraprim's price remains ridiculously inflated, based on the dubious logic that it has been underpriced given its critical need in AIDS patients. Chiefs of other pharmaceutical houses have not been oblivious to Shkreli's ploy; doxycycline and hydroxychloroquine, both inexpensive medications, have recently skyrocketed in costs.

Yes, my *je ne sais quoi* mirth upon learning of Shkreli's arrest was pure schadenfreude.

FDA Antics Continue

In 2012, due to the gross incompetency and negligence of one compounding pharmacy in Massachusetts, numerous clinics were supplied with an injectable corticosteroid adulterated with mold. The steroids were being administered intraspinally to patients primarily with chronic back pain. A large number of these patients developed fungal meningitis, requiring difficult antifungal therapies; not a few of these patients had persistent infections, and many died when the treatment failed. Needless to say, there was a huge uproar in the medical community, and the FDA demanded that it be given substantial increase in its regulation of compounding pharmacies. While Congress was feckless in accomplishing anything in 2013, it did nearly unanimously pass legislation that gave the FDA nearly free rein in its policing powers. In early 2014 the FDA announced that it intended to set up major new guidelines for compounding pharmacies, ensuring that the corticosteroid fiasco could never reoccur.

Among the many provisions that the FDA was considering was tightened oversight of two different types of compounding pharmacies: a highly regulated manufacturing "outsourcing" facility and a less regulated compounding pharmacy. The manufacturing facility would have very strict requirements for manufacturing only drugs currently not manufactured by pharmaceutical manufacturing facilities. Generally the manufacturing facility would be able to sell and ship products across state lines without limitation. The manufacturing facility would be obligated to set up a "clean" facility that would meet essentially the same standards as a drug company. It would not be permitted to compound any drugs except those approved for its manufacturing operation and would be subject to routine direct FDA inspection. The compounding pharmacy would be permitted to "compound" injectable and noninjectable drugs

continued on page 8 ➤

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

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From the Publisher

➤ *continued from page 6*

and other products if approved by the FDA; all drugs failing to be approved by the FDA would be forbidden from being compounded. The compounded pharmacy would be freely able to "compound" drugs by prescription only; no products would be made available for "office use." The compounding pharmacy would be limited to providing prescriptions primarily within the state; only 5% of the prescriptions would be permitted out of state.

Over the past two years the FDA has been meeting secretly, determining the specifics of how the manufacturing outsourcing facility and the compounding pharmacy will be regulated. An undisclosed list of acceptable and unacceptable drugs for manufacturing/compounding is being formulated. Compounding pharmacies and outsourcing facilities have applied for licensing and have begun their process of direct FDA oversight. One point of difficulty has been the conflict that exists between oversight by the local state board of pharmacy versus the FDA. State pharmacy boards must give the FDA approval for federal licensing authority; without federal authority the FDA may be onerous in its local oversight of the facility.

The bottom line: Expect that by the fall your compounding pharmacy will be experiencing a greater level of oversight that will interfere with your ability to provide injectable and noninjectable drugs for the office and the patient. Sometimes it will be simply paying a higher price for the drug or a delay in receiving it. Other times the drug will be unavailable for an extended period of time, perhaps permanently. For the compounding pharmacy's out-of-state practitioners, there may be a reduction in available drugs based on the FDA's "5% out-of-state" rule. Worse yet, some practitioners may be obliged to discontinue treatments due to unavailability of drugs from all compounding pharmacies and manufacturing facilities. Of particular concern are drugs that have never had approved status such as DMPS and DMSA or bioidentical hormones such as estriol.

It is regrettable that our political representatives in the House and Senate are largely unconcerned about these matters. They think that the only concern is public safety and that only a fully policed FDA will ensure such. Check with your compounding pharmacy to see what prescriptions are imperiled. Ask you patients to write their representatives about the threat that they face with continuing their treatment. This is a good year to confront politicians seeking reelection about FDA regulation of compounding pharmacies.

Brazilian Zika Virus Causes Alarming Microcephaly Cases

Last year Brazil has had a scary spike of women bearing children born with microcephaly, a rare condition wherein the head and brain are dramatically reduced in size. The condition has been attributed to a virus transmitted by the same mosquito responsible for causing dengue fever, yellow fever, and another

continued on page 10 ➤

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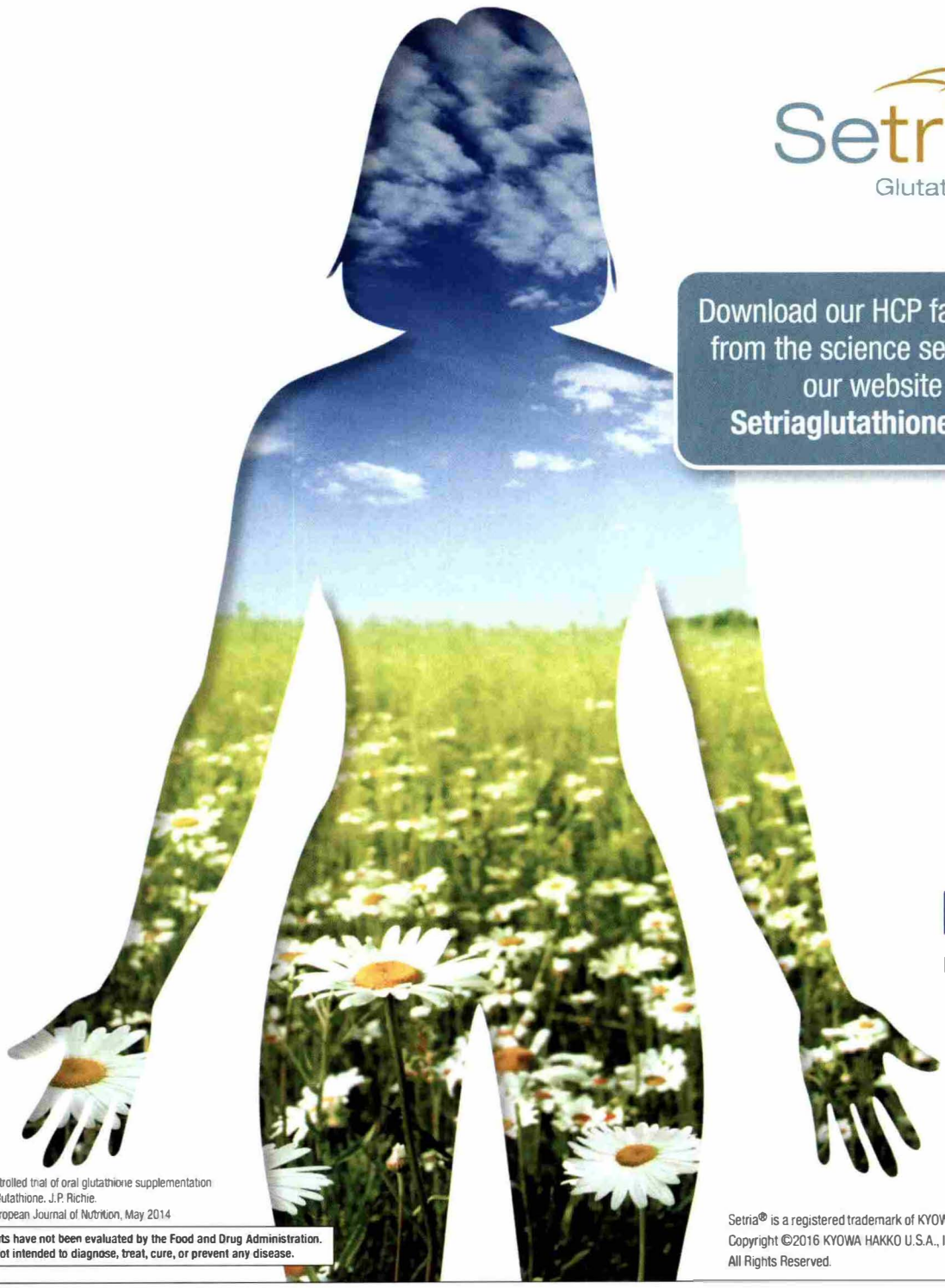

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1) Randomized controlled trial of oral glutathione supplementation on body stores of glutathione. J.P. Richie. Published in the European Journal of Nutrition, May 2014

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From the Publisher

➤ *continued from page 8*

increasingly worrisome infection, chikungunya. *Aedes aegypti* is a not-so-rare mosquito, and it widely ranges throughout South America, Latin America, the Caribbean, Africa, and Southeast Asia. Recently it has been responsible for an outbreak of dengue fever on the Big Island of Hawaii. However, while dengue fever and chikungunya are unpleasant if not incapacitating fevers and arthralgias in adults, the pregnancy complicated by Zika is a nightmare for health authorities and devastating for young families.

While Zika virus cases have been reported in French Polynesia and Africa, the virus is a new development for Brazil.[2] Epidemiologists suspect that the virus may have been brought over by Africans during the 2014 World Cup Games or by Polynesian islanders during a 2014 international canoe competition in Brazil. Still, it is unclear what pathological mechanism triggered microcephaly in pregnancies in Brazil, when the same virus did not cause it either in Africa or Polynesia. 2782 cases of microcephaly were registered in 2015, compared with only 147 cases in 2014 and 167 in 2013.

While ground zero for the Zika virus is Brazil, the virus has been found in other countries in South America, Central America, and the Caribbean. As Zika is now a major risk for pregnant women, they have been warned by the CDC to avoid travel through areas having infection. As of the late January at least one American has been identified as becoming infected. Infectious disease experts are worried that the mosquito-borne virus, that might also be transmitted sexually, may spread through North America and eventually worldwide.

The rapidly increasing number of Zika infections necessitates emergency eradication of mosquito populations as well as development of an effective vaccine.

Weird: A Dollop of *Enterobacter* During Your Brain Tumor Surgery

Like you, I don't follow the surgical medical literature, much less the neurosurgery journals. However, one of the most captivating strategies among neurosurgeons has been to intentionally inoculate the exposed surgical field of an excised glioblastoma with gut *Enterobacter* bacteria. The theory is that patients who have been diagnosed with glioblastoma multiforme (GBM) have a very grim prognosis despite advancements in surgery, radiotherapy, chemotherapy, and "biologic" treatments. (This is the conventional consensus; it ignores Dr. Stanislaw Burzynski's antineoplaston treatment for brain tumor.) In 1999 a case report in *Neurosurgery* discussed four GBM patients who developed postsurgical infections and survived for years without cancer symptoms; GBM generally has only a predicted 1-year survival. According to an article in one of my favorite medical journals, the *New Yorker*, this case report became urban legend for how to survive a brain tumor; one neurosurgeon joked, "If I ever get a GBM, put your finger in your keister and put it in the wound."[3] However, neurosurgeons at Columbia University reported in 2009 that they were unable to find evidence that GBM patients who developed postsurgery wound infection had greater survival than those who had

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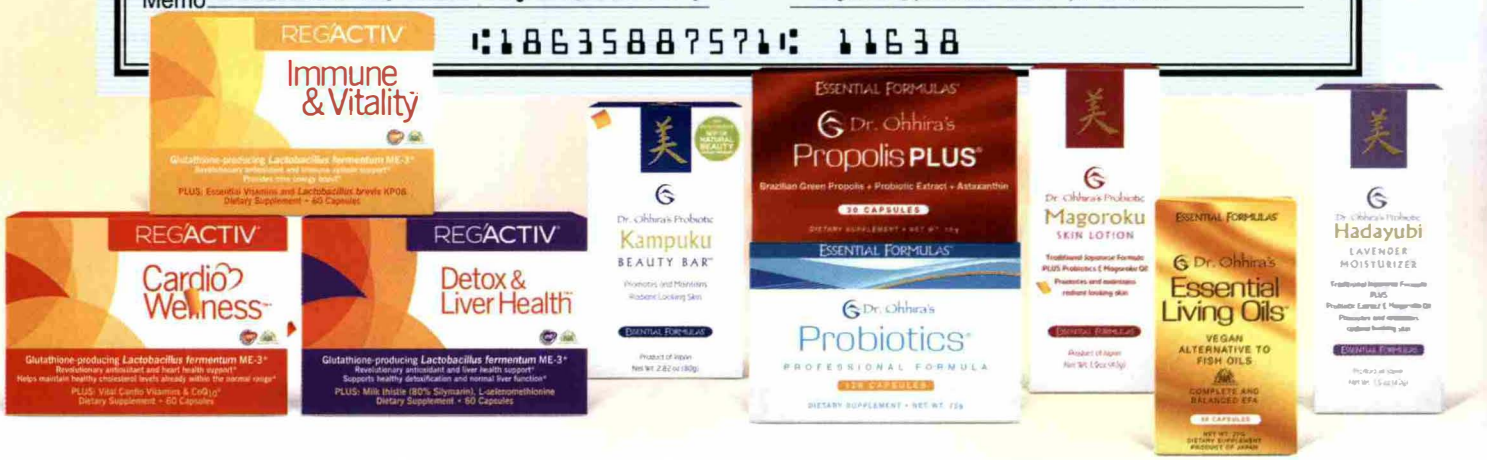

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$E = (MD)^2$ or ... $E = (DO)^2$ or ... The Fall 2015 Meeting of the International College of Integrative Medicine

by John Parks Trowbridge, MD, FACAM

We all have a passing familiarity with Einstein's famous formula that spawned the nuclear age: $E = mc^2$. As we pursue our careers in clinical medicine – with an increasing array of nutraceuticals and herbals, pharmaceuticals and operations – we gladly set aside the "theoretical" in favor of the more "practical." After all, *that's* what "makes folks better," right?

Program chair/internist Simon Yu, MD, of St. Louis, Missouri (preventionandhealing.com), would beg to differ! While we acknowledge that supplements and drugs are working at a "molecular level," we tend to view them through a *macroscopic* lens. Bioflavonoids and vitamin C help with bruising and fragile blood vessels, vitamin D helps with weakened bones, magnesium helps modulate muscle contraction and relaxation, and so on. But Nobel laureates and leading professors in basic research and clinical medicine join harmoniously in a single chorus: controlling energy in the body is the key to understanding illness and to achieving repair, recovery, and robust function.

Dr. Yu's introduction to the sterling lineup of bioenergetic medicine speakers at the 60th Congress of the International College of Integrative Medicine (ICIM; icimed.com) in Chicago this past fall proposed a new paradigm to resolve the paradox and controversy: our Western tradition has taken such a limited view of ancient understandings of energy flows (meridians) that we fail to see "the big picture." Adjusting your frame of reference acknowledges that myriad infections, deficiencies, injuries, and so on can have far-reaching effects on organs/systems seemingly unrelated and distant from the "site" of interest. When an energetic framework is applied, disparate signs and symptoms become far more clear in contributing to our better design of a path to recovery for the "whole person."

Speakers were invited to use experiences with cancer – fundamental failure of the immune system – as a lens through which to view molecular and energetic interruptions to normal physiology. Cardiologist/internist William Lee Cowden, MD, MD(H), internationally acclaimed "integrative medicine health educator," offered wide-ranging case reports to demonstrate how classical allopathic approaches are vastly enhanced by the selective addition of a myriad of "alternative" (especially bioenergetic) technologies of diagnosis and treatment (acimconnect.com).

Young Hee Ko, PhD (kocancer212@yahoo.com), and Peter L. Pederson, PhD, professor of biological chemistry and oncology at Johns Hopkins University School of Medicine, Baltimore, have worked diligently to discover natural approaches that will affect cancer cells while leaving normal cells alone. Harnessing the "Warburg effect" of oxygen deprivation on cancer phenotypes, their fascinating animal studies with the novel compound 3BP (3-bromopyruvate), an "energy blocker," show promising results with interrupting mitochondrial ATP production in PET-scan positive cancer cells, especially useful for those who have exhausted all conventional treatments.

Laboratory founder/internist Stephen E. Fry, MD (drstephenfry.com), of North Scottsdale, Arizona, is well known to many of us for his pioneering work in characterizing parasitic infections and especially intraluminal biofilms as causative agents in degenerative diseases. His continuing advances are yielding new understandings of chronic inflammatory diseases, especially their more precise diagnosis for more effective treatment.

Lee G. Woolley, DNM, of North Carolina, offered brief reviews of advanced understandings in homotoxicology and energetic diagnostics and bionetic biofeedback technologies for addressing advanced illness (thenewhuman.com). Clinical researcher Alex Mostovoy, HD, DHMS, BCCT, of the Thermography Clinic in Toronto, Canada (thermographyclinic.com), presented an overview of the convincing clinical applications of infrared thermography, long the safe and effective stepchild abandoned by conventional radiologists.

Professor James L. Oschman, PhD, has parlayed his degrees and studies in biophysics and biology into acclaimed scientific articles probing for better explanations of the results documented with "healing energy" and bodywork, particularly with frequency medicine therapies (energyresearch.us; NFAM.org). Sylvia Binder, ND, PhD (Naturopathy), CEO of the Ondamed Companies, New York and Germany, has returned to her native Germany to continue work at the Binder Institute for Personalized Medicine, helping people who are suffering with chronic illnesses in clinics around the world. The various cases presented show remarkable results with sound frequencies along with highly focused pulsed electromagnetic fields (ondamed.net).

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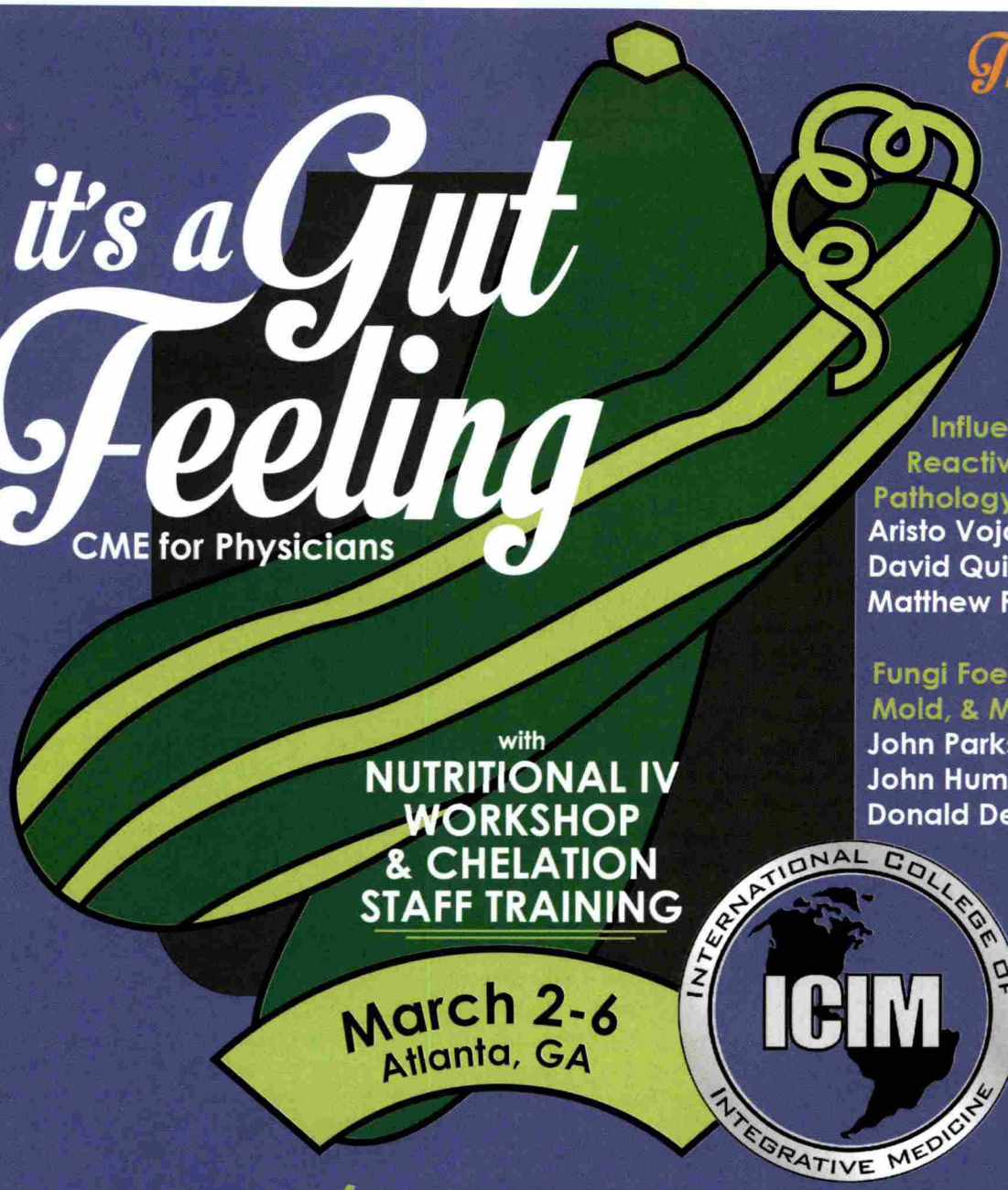

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Fall 2015 Meeting of ICIM

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Long a favorite educator for most of us, ophthalmologist Jerry Tennant, MD, MD(H), PScD, of Dallas, Texas (tennantinstitute.us), shared his elaborate simplification of the energetic model of illness and healing, integrating ancient modalities and modern applications in the treatment of cancers and other illnesses. His famous thesis: healing is voltage.

Associate Professor Magda Havas, PhD, of Trent University in Peterborough, Ontario, Canada (magdahavas.com), offered broad perspectives on the biological effects of electromagnetic pollution. Perhaps of most concern are her studies showing disturbing alterations of the sympathetic and parasympathetic systems, including heart arrhythmias and tachycardia, resulting from hypersensitivity to radiation from cordless phones found in many households.

Clinical researcher Carolyn McMakin, MA, DC, clinical director of the Fibromyalgia and Myofascial Pain Clinic of Portland, Oregon, and developer of Frequency Specific Microcurrent (FSM; frequencyspecific.com), reviewed her many successes using nontoxic, noninvasive FSM to treat fibromyalgia associated with spinal injuries and head/face/neck pain and low back pain caused by myofascial trigger points, showing reductions in pro-inflammatory mediators.

Professor of biology at Boston College, Chestnut Hill, Massachusetts, Thomas N. Seyfried, PhD (thomas.seyfried@bc.edu), presented persuasive evidence for his conclusion that cancer is best defined *and treated* as a mitochondrial metabolic disturbance rather than a genetic disease. His pioneering work with a restricted ketogenic diet shows that development of nontoxic "metabolic therapy" interventions holds great promise for *prevention* and treatment of cancers of all kinds.

Clinical chemist and laboratory director Emil K. Schandl, MD(MA), PhD, of Hollywood, Florida, is internationally known for his work in epigenetics, DNA replication, and other fields. His thesis is simple: we should look for, refine, and employ clinical and *biochemical* parameters that allow for diagnosis (and follow-up) of *pre*visual cancers. His present Cancer Profile battery of tests could lead to earlier and more effective treatments in patients in whom cancer is developing (americanmetaboliclaboratories.net).

Immunologist Donald Braun, PhD, of Cancer Treatment Centers of America (cancercenter.com), explores tumor genetics (genomics), emphasizing discovery of "how good cells go bad." His evidence suggests that apoptotic programs primarily begin in the mitochondria – of course, the essential energy factories of the cells. Profiling cellular genes, proteins, and pathway interactions elucidates critical control points in integrated cell networks, leading to more effective treatments.

ICIM member and clinical practitioner Paul Peirsal, MD (drpeirsel.com), has long subscribed to "thermodynamics" as a guiding principle in clinical practice. Reducing a complex theory down to its component parts, he presented a persuasive framework into which our diagnostic and treatment strategies can be placed. For example, the body is subject to "entropy" or wear-and-tear disruption. The sleep we enjoy at night is a "pit stop" in our race to survive degeneration and aging. 'Nuff said – you really need to hear his elegant talk to appreciate the dozens of years of study that he has invested.

Mercury-free dentist Michael Rehme, DDS, CCN, of St. Louis, Missouri, offered a holistic view of dental-medical interactions, relating restorative materials ("fillings" and such), endodontics, cavitations, and gingival infections and biofilms, comprehensively addressing the realm of tooth-body connections ("biological medicine"; toothbody.com). Diane Meyer, DDS, extensively reviewed her innovative protocol for effective treatment of osteonecrosis of the jaw (ONJ), a substantial improvement over traditional approaches (holisticdentistillinois.com).

William Pawluk, MD (drpawluk.com), lays claim to eclectic training in homeopathy, hypnosis, bodywork, acupuncture, medical use of electromagnetics, and energy medicine in his "family practice" career. His many contributions in the fields of wound healing and other applications of pulsed magnetic fields have put to rest any skepticism that the many successes of "energy medicine" are just hocus-pocus. Chelation guru Garry Gordon, DO, MD, MD(H), of the Gordon Research Institute in Payson, Arizona (gordonresearch.com), echoed these concepts in presenting his long clinical experience in pulsed electromagnetic field (PEMF) therapies for a variety of human ailments. The basis for PEMF success: production of "charge" in the tissues = "a lot more juice." Those of us with cell phones understand this idea of charge and its loss very well!

Did I mention that we also have fun? Chicago magician Dennis Watkins enthralled us at our "Quantum Physics Gala," where we humbly honored Martin Dayton, DO, Sunny Isles Beach, Florida (daytonandesmedical.com), with our Lifetime Achievement Award.

With this taste-test of what you missed, I offer just this *one* piece of advice: come join us at the next ICIM meeting, in Atlanta, Georgia, March 3–6, 2016. Yes, you just have time to register: www.icimed.com, or call Wendy Chappell-Dick, ED, at our office: 419-358-0273. ◆

John Parks Trowbridge MD, FACAM, is past president and now adviser to the board of ICIM. His totally biased views are presented in this review of the meeting, since he has long thought that these meetings are always "the best ever" in his 37-year clinical career. Look forward to his upcoming lecture on "Candida and the Gut" – fresh perspectives from the bestselling author of *The Yeast Syndrome* (and many contributions to the *Townsend Letter*.)

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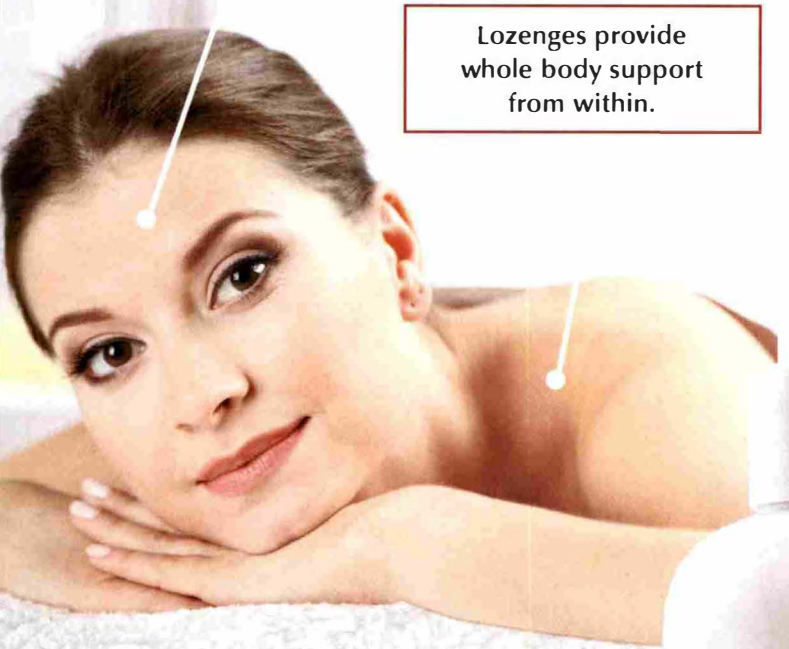

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ON THE COVER: Substance Use Disorders (52); Clinical Uses for the 'Love Hormone' (57, 62); Fat Intake and Breast Cancer (82); Weight Management in Menopause (95); Women's Health Protocols (107)

From the Publisher

➤ *continued from page 10*

no infection. Still, a 2011 report of GBM patients at Catholic University in Rome found that those patients who had infection survived twice as long as those who did not have infection. The intriguing question was whether intentional implantation of the surgical wound with *Enterobacter* would increase GBM survival.

Neurosurgeon Paul Muizelaar, MD, PhD, formerly chief of neurosurgery at University of California at Davis, was far more than "intrigued" with this question. He was of the mindset that since GBM's survival rate was so grim, the failing patient should be offered *Enterobacter* inoculation of the wound during brain surgery. In 2010 he recommended this approach to three patients, one of whom had just been diagnosed with GBM and not yet undergone therapies exhaustively. Muizelaar admits that he is a neurosurgeon who is impressed with surgery that "works," not with basic research that gradually proves underlying mechanisms. When he learned about a GBM patient whose surgical wound became infected and had a shrinking of his tumor mass, he thought that he should offer his GBM patients *Enterobacter* implantation as an option. Unfortunately, the key patient who made Muizelaar enthralled with inducing postsurgical infection did not continue to show brain tumor regression. The three patients whom Muizelaar operated upon and provided *Enterobacter* inoculation only had provisional improvement; later their brain tumors continued to grow, and each died.

Whether or not postsurgery inoculation with bacteria of the surgical wound would be helpful for GBM or other brain tumors remains conjecture that needs research with animal models. Further experimentation on humans with GBM should be deferred until there is successful animal research. Muizelaar retired from his University of California neurosurgery position and is now employed at the University of Virginia at Richmond. Two of the patient families sued the Davis medical school and settled out of court. Muizelaar maintains that *Enterobacter* implantation is still a viable option for GBM.

Tori Hudson's Women's Health Update – A Must-Read This Issue!

For those who have not been keeping abreast of the best integrative/naturopathic approaches to managing women's health issues, Dr. Hudson's "Women's Health Treatment Protocols That I Count On" in this issue is for you!

Her discussion is brief, to the point, and "ready to put to use on Monday." Endometriosis is a very challenging and painful issue for young women, and conventional gynecology does not really offer any natural alternatives. Hudson advises the use of omega-3 oils, curcumin, Pycnogenol, NAC, high-dose melatonin, antioxidants, and oral progesterone. Similarly, many younger menstruating women suffer from dysmenorrhea. Who knew that ginger and niacin are keystones to treatment? For vaginal candidiasis, we often immediately write prescriptions for antiyeast drugs. Why not consider boric acid suppositories and probiotic suppositories? Many females suffer with vaginosis. Hudson likes to use a homeopathic suppository, but when that does not work, she suggests the use of vaginally inserted metronidazole gel. Some women have been exposed to HPV. A naturopathic approach would consider indole-3-carbinol, coriolus, high-dose folic acid (or methylfolate), and green tea suppositories.

Hudson also writes about her favorite research highlights in 2015. When women are treated with antidepressive agents, it is not uncommon for them to suffer sexually. Although it may be reasonable to consider hormone replacement therapy with bioidentical hormones, Hudson suggests that the botanical maca may offer strong support for sexual dysfunction. Women suffering from PCOS are treated for hypertension, insulin resistance, and weight management. Hudson writes about the support provided by *myo*-inositol and D-*chiro*-inositol for managing PCOS. *Myo*-inositol appears to be more effective in countering metabolic dysfunctioning, while D-*chiro*-inositol works better on the excessive testosterone. Hudson also notes research using alpha-lipoic acid in treating a difficult-to-solve burning mouth syndrome.

Oxytocin: The New Hormone in the 'Hood

When we evaluate women for hormone replacement therapy, we generally consider thyroid, estrogen, progesterone, testosterone, and sometimes adrenal hormone support. The neuropeptide oxytocin is not generally part of our initial hormone diagnostic and treatment workup. Dr. Devaki Lindsey Berkson and Pushpa Larsen, ND, in separate articles in this issue, argue that perhaps we should be considering oxytocin concurrently when we prescribe hormone replacement. Berkson notes that the animal's ability to maintain monogamous relationships, mating for life, "connection," is determined by the presence of oxytocin receptors and activity in the brain. MRIs of nursing mothers reveal an increase in brain activity in areas of the brain replete with such receptors. Oxytocin is the "cuddle hormone."

Larsen examines the relationship between patients having chronic pain and their low levels of oxytocin. Fibromyalgia patients experiencing intensive pain have had reduction in symptomatology when treated with oxytocin replacement. Patients with severe headaches have had significant reduction in pain with intranasal oxytocin. Furthermore, the use of oxytocin has enabled pain patients dependent on opiates to reduce the dose of their opiate medications.

Berkson observes that oxytocin plays a key role in causing a sexually active woman experiencing satisfying orgasms strong bonding behavior with her partner. PET scan imaging studies reveal that a woman's pituitary gland is more activated following orgasm than a man's brain; oxytocin and prolactin are released in higher concentrations postorgasm. Berkson asks, if there are bonding issues, why not treat the woman with oxytocin hormone replacement? Her clinical case studies suggest that oxytocin may play a very important role in a couple's sex life!

Jonathan Collin

Notes

1. Pollack A. Chief of Turing Pharmaceuticals resigns after arrest. *New York Times*. Dec. 10. 2015.
2. Musso D. Zika virus transmission from French Polynesia to Brazil. *Emerg Infect Dis*. October 2015;21(10):1887.
3. Eakin E. Bacteria on the brain. *New Yorker*. Dec. 7, 2015:56–63.

◆

Review of Exponential Medicine Annual Meeting 2015 November, Del Coronado Hotel San Diego

by Ira L. Goodman, MD, FACS, ABIHM, FAARM

I was fortunate to attend this most unusual event last fall. The meeting is intended for physicians, basic science researchers, academics, industry, and anyone interested in what medicine will look like in the next 30 years. The technology world was well represented, especially in the area of sensors, mobile health, virtual reality, advanced diagnostics, robotics, artificial intelligence, and of course Big Data. It was like stepping into the future on steroids. The meeting originates from Singularity University, the brainchild of Peter Diamandis (founder of the XPRIZES) and Ray Kurzweil (the foremost futurist whose predictions have been over 80% accurate). Both of them spoke. The chair of the meeting was Daniel Kraft, a Stanford- and Harvard-trained physician in hematology/oncology who is also on the faculty of UCSF. He delivered several rapid-fire presentations coordinated with slides and video that were completely engaging.

On day 1, I sat next to a medical resident who had flown in from South Korea just for this meeting, and during the meeting met many people from other countries who all shared an entrepreneurial bias. There was more than enough to fill anyone's curiosity. I cannot possible cover everything in this brief review but will highlight some things that caught my attention as a functional medicine practitioner, author, and examiner:

1. A recording stethoscope. Throw away your old model. This is way cool and much better. You do not even need to listen along with it, nor do you need a physician to use it (think robo-doc and the deconstruction, democratization, and dematerialization of medicine per Eric Topol's books). It is placed on the chest and it records the heart sounds, which can be printed out and attached to the chart. You actually get a sound tracing like an EKG. No longer are you dependent on the physician's memory about how your heart sounded 6 months ago or even yesterday. It transforms auditory unrecorded data into memorialized visual data. Right now, it is not paired to a printed interpretation (as EKGs are now), but I think that is coming. The possibilities are endless for this breakthrough device. I want one, now!
2. $99 cancer tests developed in a lab in Spain that claims over 85% sensitivity and specificity via serum. If this pans out, the colonoscopy business will lose big, as will many other cancer-screening enterprises. This is a good thing, since they largely do more harm than good. Not enough space to go into this contentious topic, but I highly recommend Hadler's and Welch's books on this subject.
3. A company called First Derm that allows a patient to take a photo of any skin lesion and submit it online for rapid interpretation by a dermatologist. Compare that with a 30-day wait time, 3 hours in the office, and even after all that, facing a misdiagnosis in many cases. It is surprisingly affordable, fast, and accurate – who could want more?
4. A new cardiac CT scanning company called HeartFlow that pairs a low-radiation scan with state-of-the art graphics to produce not only a calcium score (which is what is available now) but also a 3-D image of your entire heart and its vascular tree showing in vivid color the status of every vessel. I have never seen anything like it. It will put a serious dent in the angiography and treadmill businesses, which are archaic in many ways, not to mention the nuclear scanners, which are even worse.
5. A neurostimulation device called Thync. I have investigated several of these devices and may publish a review of all of them in another post. These include the Alpha-Stim, Fisher Wallace, Tennant Biomodulator, the Muse, transcranial magnetic stimulation, and focused ultrasound of the brain. They are all used for slightly different indications and worth looking at individually, but I will limit my comments here to the Thync device. It is a small white patch placed on one side of your forehead as well as your

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neck. It is linked to a mobile device that allows you to control time, intensity, and frequency depending on what effect you desire. It can cause almost instant calm, a zenlike state, or high energy depending on the circumstances. When I first saw it advertized, I thought that it was another gadget with limited usefulness but then I tried it. After about 8 minutes, I was in an altered state that was very pleasant. It was very noticeable and lasted over 3 hours, even though the session itself was only for 10 minutes. Clearly, each individual must customize the experience in regard to settings, but I think that there is real science behind this technology. Although it is still based on the drug model (used for a symptom p.r.n.), it is far less invasive and quicker acting. This is probably where neuroscience will go in the future, and eventually these devices can be implanted so they can work behind the scenes to create any mental/emotional state you like (think Woody Allen's orgasmatron from *Sleeper*, except invisible). Is there anyone who does not want this?

In addition to all this, there were lavish meals, nighttime activities that encouraged networking, and a beach party with a bonfire. This meeting raises the bar for medical events to a standard that will be hard to beat.

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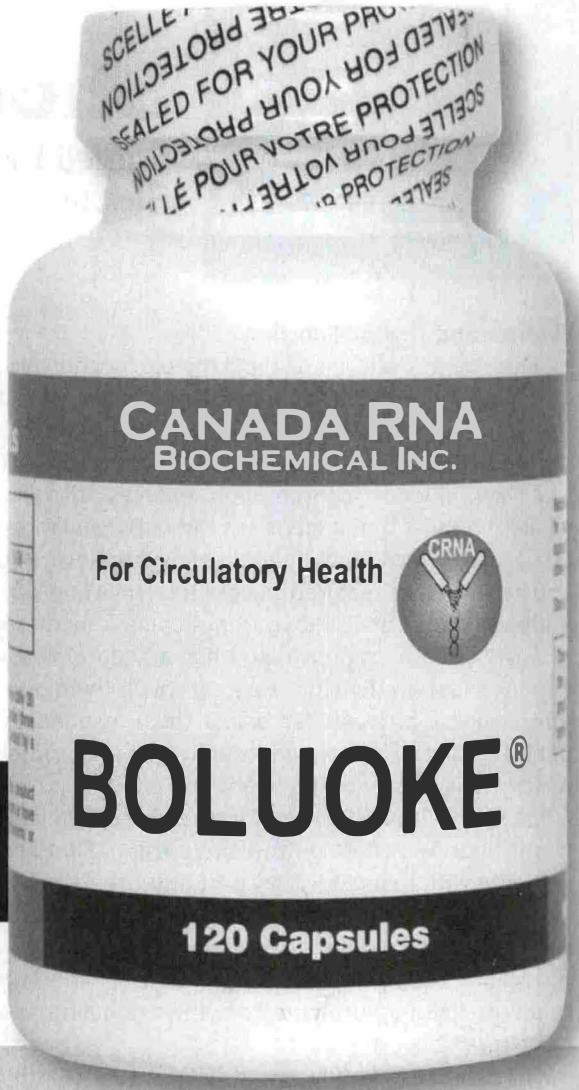

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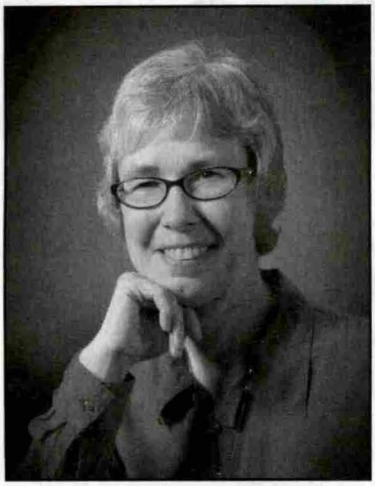

Shorts

briefed by Jule Klotter
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Fluoride and Thyroid Function

Fluoride at low levels disrupts thyroid function, according to a 2006 National Research Council (NRC) report and more recent studies. Fluoride accumulates in the thyroid and produces morphological changes. Numerous animal experiments show that high fluoride consumption reduces thyroid hormone levels (T3 and T4) and increases thyroid-stimulating hormone (TSH) levels. In addition, fluoride has other adverse endocrine effects, including impaired glucose tolerance and earlier sexual maturation. Subclinical thyroid dysfunction increases the risk of heart disease, cognitive dysfunction, depression, and bone demineralization (in the case of hyperthyroidism). These effects occur at levels far below those needed to produce dental fluorosis (discoloration and pitting in tooth enamel), which is the most recognized adverse effect.

Since the 2006 NRC report, researchers have learned more about fluoride's effect on thyroid function. Fluoride does not compete with iodine for transport into the thyroid, according to the NRC report. It does, however, inhibit the activity of Na+/K-ATPase (the enzyme needed to fuel the cellular sodium-potassium pump) and thyroid peroxidase (the enzyme that catalyzes thyroid hormone from thyroglobulin), according to more recent investigations.

In their 2013 study, Swati Singla and Shashi Aggarwal reported correlations between fluoride content of drinking water and abnormal thyroid peroxidase (TPO) and thyroid hormone levels. The Indian researchers compared 633 people with hypothyroidism and fluorosis, 227 people with hyperthyroidism and fluorosis, and 140 age- and sex-matched controls. Fluorosis and thyroid dysfunction are major problems in India. Drinking water used by the fluorotic patients had a fluoride content that ranged from 1.01 to 16.00 mg/L. Drinking water for the control group contained 0.76 to 1.00 mg/L fluoride. The US Maximum Contaminant Level Goal for fluoride in drinking water is 4.00 mg/L. (Fluoride is an industrial pollutant.)

The researchers grouped the fluorotic thyroid patients according to the level of fluoride in their drinking water. All of them had significantly higher fluoride blood levels than the nonfluorotic control group. Their urinary iodine and fluoride concentrations were higher as well. Those whose drinking water contained 1.01 to 4.00 mg/L excreted the highest concentration of fluoride in their urine (3.68 ± 0.53 mg/L). As drinking water fluoride levels increased, less fluoride and more iodine were excreted. Singla and Aggarwal found that TPO activity in the hyperthyroid and the hypothyroid groups decreased significantly as fluoride exposure increased. Thyroid hormone levels (T3, T4) also decreased with increased fluoride exposure and TSH levels rose.

The 2006 NRC chapter summary on fluoride's endocrine effects says: "'In humans effects on thyroid function were associated with fluoride exposures of 0.05-0.13 mg/kg/day when iodine intake was adequate and 0.01-0.03 mg/kg/day when iodine intake was inadequate. ..." Robert J. Carton, PhD, a retired environmental scientist, noted in his review of the 2006 report: "This simply means for a 70-kg person (often called the 'standard man'), fluoride doses as low as 3.5 mg/day for those with an adequate intake of iodine, and 0.7 mg/day for those with an inadequate intake of iodine may have an effect on the thyroid." Many Americans consume more than 0.7 mg/day via food alone.

No research study claims that fluoride is the sole cause of thyroid dysfunction, but excessive fluoride is clearly a largely unexamined – and preventable – contributor.

Carton RJ. Review of the 2006 United States National Research Council Report: Fluoride in Drinking Water. *Fluoride*. July–September 2006;39(3):163–172. Available at www.khi.org. Accessed November 25, 2015.

National Research Council. *Fluoride in Drinking Water – A Scientific Review of EPA's Standards*. Washington, DC: The National Academies Press; 2006. Available at www.nap.edu/read/11571/chapter/1. Accessed November 25, 2015.

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Maternal Stress and Epigenetics

Posttraumatic stress disorder (PTSD) produces epigenetic changes in glucocorticoid-related (e.g., NR3C1) and FKBP5 genes that are transmitted to an affected woman's offspring. Babies born to women with PTSD have lower cortisol levels and increased glucocorticoid receptor sensitivity, indicating decreased resilience to stress and increased susceptibility to developing PTSD when exposed to traumatic events. A 2014

study led by Nadir Perroud found that women who were exposed to the Tutsi genocide during pregnancy and their offspring had lower cortisol and glucocorticoid receptor levels than nonexposed women with the same ethnicity and time of pregnancy and their children. The researchers also report an association between PTSD and NR3C1 epigenetic modifications found in exposed mothers and their children. They say that these changes "may underlie the possible transmission of biological alterations of the [hypothalamic-pituitary-adrenal] axis."

Neuroscientist Rachel Yehuda, PhD, and colleagues began investigating the effect of parental PTSD on offspring in the late 1990s. They performed a series of studies involving the offspring of Holocaust survivors. Offspring with at least one parent with PTSD "displayed low urinary and plasma cortisol levels, and increased glucocorticoid responsiveness as measured by plasma cortisol levels in response to low dose dexamethasone administration [a test to assess adrenal function]," compared with those whose parents did not have PTSD. When Yehuda and colleagues compared Holocaust survivor offspring with demographically matched Jewish controls whose parents were not exposed to trauma, they found "a greater prevalence of PTSD among offspring with maternal PTSD." The highest rate of PTSD was found when both parents had PTSD. Paternal PTSD alone was associated with anxiety disorders.

Some PTSD-associated epigenetic changes were reversed in military veterans who responded to 12 weeks of psychotherapy in a small 2013 study. Higher levels of glucocorticoid receptor (GR) gene promoter methylation at pretreatment (indicating lower GR expression) were associated with a positive response to psychotherapy treatment. Although GR gene expression did not change in treatment responders, FKBP5 (a mineralocorticoid receptor gene linked to PTSD) expression did; FKBP5 promoter methylation decreased, indicating greater FKBP5 gene expression. In addition, plasma and urinary cortisol levels indicated decreased GR sensitivity. "These findings distinguish two seemingly stable epigenetic markers that may associate, respectively, with prognosis (GR gene methylation) and symptom severity (FKBP5 gene methylation)," say the authors. In addition, this study indicates that glucocorticoid-related genes respond to environmental factors – including psychotherapy – throughout life.

This small 2013 study needs to be replicated. Still, it offers hope that epigenetic stress responses passed from mother to child can be mitigated.

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Prenatal Genetic Testing Lawsuits

Malpractice lawsuits against practitioners and medical laboratories that offer prenatal genetic tests are on the rise. Parents faced with caring for a newborn with a debilitating, inheritable disease have won large settlements when practitioners failed to inform parents about available prenatal genetic tests that would have identified the condition prebirth, giving the parents the option of terminating the pregnancy. Judgments or settlements have also resulted when medical laboratories mistakenly informed parents that their unborn child was free of a screened-for inheritable disease, such as cystic fibrosis. In both cases, the lack of accurate genetic test results led to the birth of a child with a painful, incurable, and financially devastating disease. The large settlements help with the child's medical and living costs.

Although some state legislators focus on the morality of abortion implicit in these "wrongful birth lawsuits," judges and plaintiffs' attorneys view these cases as examples of medical negligence and malpractice.

McLeod PS. Clinical pathology laboratories should be aware of new malpractice risks from genetic testing [online article]. DARK Daily. July 25, 2012. Available http://www.darkdaily.com/clinical-pathology-laboratories-should-be-aware-of-new-malpractice-risks-from-genetic-testing-71512. Accessed November 25, 2015.

Thyroid Cancer Overdiagnosis

"There is an ongoing epidemic of thyroid cancer in the United States. The epidemiology of the increased incidence, however, suggests that it is not an epidemic of disease but rather an epidemic of diagnosis," according to Louise Davies, MD and H. Gilbert Welch, MD. Thyroid cancer incidence has almost tripled since 1975 (4.9 to 14.3 per 100,000) – primarily due to increased detection of papillary thyroid cancers. These small, nonaggressive cancers are common in people who display no symptoms during their lifetime and who die from causes other than thyroid cancer. Despite increased detection, death rate from thyroid cancer has not decreased, which indicates overdiagnosis.

For their 2014 study, Davies and Welch used 1975–2009 data from nine SEER (Surveillance, Epidemiology, and End Results program) areas and thyroid cancer mortality data from the National Vital Statistics System, which contains cause-of-death listed on death certificates. They found higher cancer detection rates among women compared with men: "The absolute increase in thyroid cancer in women (from 6.5 to 21.4 = 14.9 per 100,000 women) was almost 4 times greater than that of men (from 3.1 to 6.9 = 3.8 per 100000 men)." They also found that the thyroid cancer mortality rate has remained stable at about 0.5 deaths per 100,000.

Davies and Welch dispute the idea that the stable mortality rate is the result of treatment improvements. "For this explanation to be true," they write, "the improvements in treatment would have had to exactly offset the rise in incidence. If treatment improved too fast, the mortality line would fall. If treatments improved too slowly, the mortality line would rise. While this explanation is theoretically possible, it is not particularly plausible in explaining 30 years of stable mortality." The stable mortality rate suggests that many thyroid

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tumors pose no threat to life. Other evidence for overdiagnosis stems from data showing that access to medical care is directly related to thyroid cancer detection: "People with enhanced health care access tend to have not only more small cancers identified but also more thyroid cancers identified overall."

A 2015 study from Memorial Sloan Kettering Cancer Center, using data from 1950 to 2005, supports the observation that thyroid cancer survival rates have remained stable despite an increase in diagnosis. The MSKCC study also found that incidence rates of large tumors (>6 cm) and metastasis have not changed over time. The authors say that improved survival rates in recent years are due to the increased number of small, asymptomatic thyroid cancers that are being detected and treated. "Relying on survival rates to measure success in treating thyroid cancer may reinforce inappropriately aggressive management," they write. "Treatment decisions in thyroid cancer should be made based on mortality, not survival data."

Total thyroidectomy is the usual treatment for thyroid cancer, subjecting patients to risk of complications such as permanent hypoparathyroidism and vocal cord paralysis. In addition, patients require thyroid hormone therapy and monitoring for the rest of their lives when the thyroid is removed. After surgery, half of the patients also receive radiation treatment, usually in the form of radioactive iodine. Radioactive iodine is associated with increased risk of leukemia and other secondary cancers. "These aggressive therapies persist despite guidelines suggesting that partial thyroidectomy is a reasonable approach for lower risk cancers and data indicating that few patients with papillary thyroid cancer derive survival benefit from radioactive iodine," say Davies and Welch.

Davies and Welch offer several suggestions for reducing aggressive treatment of small, asymptomatic thyroid cancers. Active surveillance, an option for nonaggressive prostate cancers, is now being investigated at MSKCC and in Japan. In addition to this wait-and-see treatment approach, Davies and Welch suggest reclassifying small thyroid neoplasms with a term other than cancer, an idea that has been suggested for ductal carcinoma in situ breast neoplasms, another condition that typically leads to unnecessarily aggressive treatment. In the meantime, practitioners need to share the uncertainties surrounding small thyroid cancers and their treatment. Davies and Welch also ask clinicians to be aware of the hazards involved in "looking too hard for thyroid cancer." "Patients – and in the case of thyroid cancer, particularly women – need protection not only from the harms of unnecessary treatment but also the harms of unnecessary diagnosis," they write.

Davies L, Welch HG. Current thyroid cancer trends in the United States. *JAMA Otolaryngol Head Neck Surg.* 2014;140(4):317–322. Available at http://archotol.jamanetwork.com/article.aspx?articleid=1833060. Accessed November 25, 2015.

Ho AS, Davies L, Nixon IJ, et al. Increasing diagnosis of subclinical thyroid cancers leads to spurious improvements in survival rates [abstract]. *Cancer.* June 1, 2015;121(11):1793–1799. Available at www.ncbi.nlm.nih.gov/pubmed/25712809. Accessed November 25, 2015.

Vaccines During Pregnancy

In November 2015, FDA announced recommendations for licensing vaccines intended for use during pregnancy to prevent disease in the infant. No vaccines have FDA approval for use during pregnancy at this time, even though the CDC has recommended tetanus, diphtheria, and acellular pertussis (Tdap) vaccination during pregnancy since 2011. The rationale for the CDC recommendation is to decrease whooping cough risk in infants. (CDC also recommends flu vaccinations during pregnancy.)

Tdap vaccines Adacel (Sanofi Pasteur) and Boostrix (GlaxoSmithKline) are licensed for use in adults and older children. The manufacturer inserts for both products (available at http://www.immunize.org/packageinserts/pi_tdap.asp) state that the vaccines have not been evaluated for fetal harm or reproductive adverse effects in humans and that the vaccines "should be given to a pregnant woman only if clearly needed." Neither manufacturer knows if the vaccines are transmitted in human milk. FDA licensure means that product labeling would contain information for its safe and effective use, information that is currently lacking.

The FDA Briefing Document lists several concerns that manufacturers should address in order to license a vaccine for use during pregnancy. Adverse effects may be caused by vaccine antigens, the adjuvants and excipients used to enhance vaccine effects, and/or a mother's immune response. Pregnancy makes a woman's immune system less sensitive in order to tolerate the growth of the fetus. Vaccination incites an inflammatory reaction that "could disturb maternal mechanisms that maintain tolerance of foreign fetal antigens, potentially leading to adverse pregnancy outcomes, such as spontaneous abortion or intrauterine growth restriction or preterm birth," according to the FDA.

Detecting adverse effects can be tricky, since first trimester miscarriages, preterm births, deep vein thrombosis, and other events occur fairly often in pregnant women. Identifying safety concerns requires well-designed, controlled studies with inert placebos, such as saline. Most vaccine safety studies use the vaccine formula (containing toxic aluminum compounds, formaldehyde, and other constituents) minus the antigen as a control, or the studies compare two types of vaccines or vaccine doses/schedules.

I found on PubMed just one blinded Tdap safety study for pregnancy use that used a saline placebo. The February 2015 study led by Flor M. Munoz was, in the authors' own words, an "exploratory study that was not powered to test any specific hypotheses." Just 33 women received Tdap while pregnant (30–32 weeks), and 15 received a saline injection at the same point in their pregnancies. After delivery, treatment was switched; women who had received the placebo were given Tdap, and the vaccinated women received the saline injection.

The authors state, "There were no differences in the infants' growth and development (Tables S2 and S3), and no cases of pertussis illness occurred in mothers or infants." Considering that the incidence of whooping cough in US babies under 1 year peaked at just over 120 per 100,000 (according to CDC), it would have been surprising if pertussis had shown up. I also

question the assertion that infants showed no differences in development. Growth measures were very similar, but I noticed some differences in test results for the Bayley-III developmental screening test, which was administered to infants at 13 months. Bayley-III screens receptive and expressive communication, fine and gross motor skills, and cognition. I was troubled that the body of the article made no mention that a noticeably lower percentage of the treated infants scored "competent" in four of the five categories. For example, 63.3% of babies from vaccinated mothers compared to 78.6% of control babies were assessed competent in gross motor development (sitting, crawling, standing, and walking unassisted). Receptive communication was the exception; a smaller percentage of the control group (64.3%) received competent scores for receptive communication compared with the treated group (70.0%).

The difference between the two groups was not statistically significant; this study did not have enough participants for any definite conclusions to be made. Still, I would expect a safety study to make some comment about the need for follow-up research. Instead, the authors concluded: "Until further research provides definitive evidence of the safety and efficacy of Tdap immunization during pregnancy, our findings support current ACIP recommendations to immunize pregnant women with Tdap during pregnancy to protect infants against pertussis."

Shorts

Only a few vaccine trials posted at www.clinicaltrials.gov are designed to investigate safe vaccine use during pregnancy. Study designs make me question their usefulness in assessing the safety risks for women and their babies. A Vanderbilt University observational study on TDAP Safety in Pregnant Women (NCT 02209623) has no placebo control. A Mexican study (NCT 01445743) does have a saline control, but the sole outcome being measured is the antibody levels in infants. No studies test the cumulative effects of vaccines despite the recognized toxic effects of vaccine constituents such as aluminum compounds, formaldehyde, and the surfactant polysorbate-80. A list of excipients and adjuvants is available at CDC http://www.cdc.gov/vaccines/vac-gen/additives.htm (see Reference Materials).

FDA Vaccines and Related Biological Products Advisory Committee Meeting. Clinical development and requirements for licensure of vaccines intended for use during pregnancy to prevent disease in the infant [online document]. November 13, 2015. Available at http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/VaccinesandRelatedBiologicalProductsAdvisoryCommittee/ucm427602.htm. Accessed November 25, 2015.

Jackson BJ, Needelman H., Roberts H, Willet S, McMorris C. Bayley Scales of infant development screening test-gross motor subtest: efficacy in determining need for services. *Pediotr Phys Ther.* Spring 2012;24(1):58–62. Available at http://journals.lww.com/pedpt/Fulltext/2012/24010/Bayley_Scales_of_Infant_Development_Screening.12.aspx. Accessed January 7, 2016.

Mahoney D. CDC panel expands Tdap vaccine in pregnancy recommendation [online article]. Medscape Medical News. October 24, 2012. http://www.medscape.com/viewarticle/773230. Accessed November 25, 2015.

Munoz FM, Bond NH, Maccato M, et al. Safety and immunogenicity of tetanus diphtheria and acellular pertussis (Tdap) immunization during pregnancy in mothers and infants: a randomized clinical trial. *JAMA.* 2014 May 7;311(17):1760–1769. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4333147. Accessed January 3, 2015.

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Pathways to Healing

by Elaine Zablocki

CAM Professions Engaging with Quality Measures

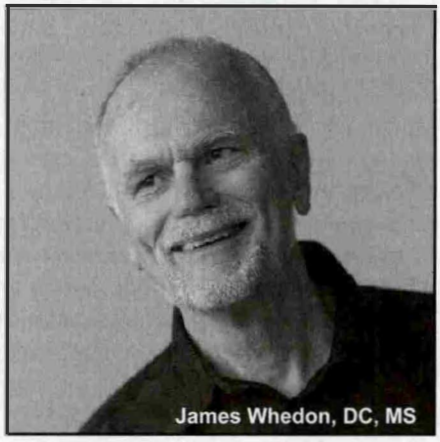
In recent years, mainstream health care has developed a variety of measures to examine and record the quality of care. These measures often look at processes (appropriate actions done at the appropriate time), and they also look at outcomes (did those actions actually improve the patient's health?). "Quality measures are constantly changing; they are a living target," says James Whedon, DC, MS. "We've had a proliferation of measures and not a whole lot of agreement on which ones we should be following in conventional medicine, let alone integrative health."

Whedon is an active member of the Academic Consortium for Complementary and Alternative Health Care's Research Working Group, which includes health-care leaders who are aware of and working on the most salient issues facing the CAM professions. He is the director of Health Services Research at Southern California University of Health Sciences (SCU), an education and training center for the CAM professions. All SCU students share their initial science classes, and then follow more specialized training as their education progresses. Whedon's research focuses on analysis of claims data, looking at subjects such as the utilization, cost, and safety of chiropractic care under Medicare, and the effect that integrative care has on the utilization of opioid medications.

Many quality measures in current use look at specific processes that are easy to measure. For example, the National Committee for Quality Assurance (NCQA) has developed a series of measures for accountable care organizations. One of them focuses on whether people with depression remained on antidepressant medications for a specific period of time. Another looks at whether people with high levels of LDL cholesterol are receiving drug therapy.

"The premises of conventional medicine are not entirely the same as the operating premises of integrative health care," Whedon notes. "One of those conventional premises is that adherence to prescribed medications is a good thing and nonadherence is a bad thing. However, in the case of antidepressants and psychotropic drugs in general, the evidence for their effectiveness and safety is questionable. In that light, adherence to antidepressant medications may not always be an unadulterated good thing. To base a quality measure on those premises flies in the face of the experience of many patients, who want to get off these medications but find no support in the medical community."

In contrast, the NCQA quality measures for wellness and health promotion include several that are fully congruent with the practice of integrative health. These include completing a health appraisal, identifying core risks, and counseling about weight reduction, increasing physical activity, and quitting smoking. "These measures are about reducing risk for chronic disease, they are about primary prevention." Whedon says. "Let's look for measures that result in effective health care. When we have a practice which promotes health such as counseling patients on diet and lifestyle, then it makes sense to institute that as a measure of quality."



James Whedon, DC, MS

On the Agenda for the CAM Professions

The CAM professions are rarely included in the current system of quality measures. For example, in the Physician Quality Reporting System (PQRS), which is used in Medicare/Medicaid, chiropractic physicians are the only CAM practitioners included. While allopathic physicians must report nine measures, in 2015 chiropractors reported two measures: "pain assessment and follow-up," and "functional outcome assessment."

"Do we want to work towards inclusion of integrative health practitioners in existing quality measures?" Whedon asks. "Do we want to supplement existing methods with others that are more congruent with integrative health? Do we want to be part of this conversation?"

At present the CAM professions seem to have a wide variety of opinions on this subject. Each profession has its own organization and structure, and its own viewpoint. In addition, there's a range of viewpoints within each profession, with some practitioners choosing to be fully integrated within

mainstream health care, while others do not take insurance and instead serve patients who are able to pay out of pocket. "For each practitioner, it's a question of what you want," Whedon says. "Do you want full integration? Do you want to work in an integrative practice setting with medical doctors and other conventional practitioners? Do you want to work in a hospital or large health system? If your answer is yes, quality measures will certainly be part of your life, because they are already part of those systems."

Right now many practitioners have only a marginal awareness of quality concerns and quality measurement. Many independent practitioners who aren't associated with larger organizations haven't been thinking about these issues. But for practitioners who do want to practice in a larger context, and for professionals currently in training, these issues are likely to grow in importance over the next decade.

What Does This Mean For Patients?

"Patients should care about quality because everyone deserves the highest quality health care. Everyone deserves the kinds of health care that they need and want," Whedon says. "Should you care about quality measures? Yes, to the extent that they measure what they're intended to measure. Are they patient-centered quality measures or are they pharmacocentric? For example, do we really want to measure use of medications, and levels of cholesterol, or do we really care more about whether or not we are preventing or reversing heart disease? Or do we want to measure patients' quality of life and satisfaction with their care? We have to ask ourselves, are we measuring what really matters most to patients?"

Is it time for CAM professionals to think about, and learn more about, quality measures in health care? "In conventional care, this train has already left the station," Whedon says. "If the integrative health communities want to participate in conventional care, we do have to start talking about it. We may or may not agree with all aspects of the current quality measures, but I think it's worth taking the time now to initiate a dialogue on these subjects."

Resources

Whedon and other experts discussed quality measures in integrative care during an online webinar in mid-June 2015, sponsored by the Project for Integrative Health and the Triple Aim (PIHTA), a project developed by the Academic Consortium for Complementary and Alternative Health Care (ACCAHC).

The webinar, "If I Ran the Zoo: Quality Measures and their Alignment with Integrative Health and Medicine," is archived on the PIHTA website at http://www.optimalintegration.org/events/events-archived-pihta-01.php.

There will be a discussion of quality measures and integrative health at the International Congress on Integrative Medicine & Health to be held in Las Vegas, May 17–20, 2016. See www.icimh.org/About-the-Congress.

For more information on PIHTA see: http://www.optimalintegration.org/project-pihta/pihta.php.

For more information on ACCAHC see: http://www.accahc.org.

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.

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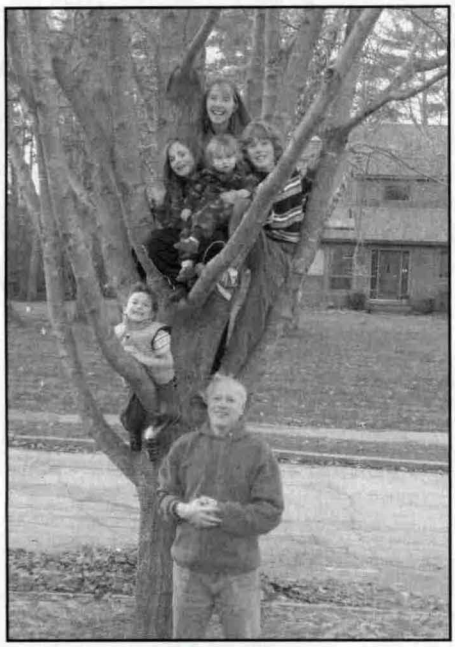

Literature Review & Commentary

by Alan R. Gaby, MD
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DHEA for Dyspareunia Associated with Menopause

Two hundred fifty-three women with dyspareunia associated with menopause were randomly assigned to receive, in double-blind fashion, placebo, 3.25 mg of dehydroepiandrosterone (DHEA), or 6.5 mg of DHEA, administered intravaginally once a day before bedtime for 12 weeks. Compared with placebo, the higher dose of DHEA decreased dyspareunia by 46% ($p < 0.02$) and decreased moderate-to-severe vaginal dryness by 42% ($p < 0.02$). The higher dose of DHEA also produced histological improvements (a 45.8% decrease in the mean percentage of parabasal cells [$p < 0.0001$] and a 4.7% increase in the percentage of superficial cells [$p < 0.0001$]) and decreased mean vaginal pH by 0.83 units ($p < 0.0001$). The effect of the lower dose of DHEA was less pronounced, and the reduction in dyspareunia compared with placebo was not statistically significant. No significant adverse effects were reported.

Comment: These results indicate that daily intravaginal administration of 6.5 mg of DHEA (but not 3.25 mg of DHEA) resulted in clinical and histological improvement in women with dyspareunia associated with menopause. DHEA is metabolized in part to estrogen and testosterone, which may account for its beneficial effect on dyspareunia. However, DHEA may also have physiological actions unrelated to its function as a precursor to estrogen and testosterone, since DHEA receptors have been identified on some human cells. In previous research, intravaginal administration of DHEA did not cause endometrial proliferation and produced little or no change in serum concentrations of estrogen and testosterone. Because it appears to be effective at low doses, intravaginal administration of DHEA may be preferable to oral or transdermal administration when treating symptoms related to vaginal atrophy.

Archer DF et al. Treatment of pain at sexual activity (dyspareunia) with intravaginal dehydroepiandrosterone (prasterone). *Menopause*. 2015;22:950–963

Vitamin D and Bone: Racial Differences

The association between serum 25-hydroxyvitamin D (25[OH]D) levels and lumbar bone mineral density (BMD) was examined in a cross-sectional study of 1773 adult participants in the Multi-Ethnic Study of Atherosclerosis (714 white, 353 black, 249 Chinese, and 457 Hispanic). Serum 25(OH)D was highest among whites and lowest among blacks, but BMD was highest among blacks. Higher serum 25(OH)D was significantly associated with higher BMD only among white and Chinese participants. Among Hispanics, higher serum 25(OH)D was nonsignificantly associated with higher BMD. Among blacks, BMD was significantly higher in those with a serum 25(OH)D level less than 20 ng/ml than in those with a serum 25(OH)D of 30 ng/ml or greater.

Comment: This is one of several studies to show that the association between 25(OH)D levels and BMD differs among different racial and ethnic groups. Whereas higher 25(OH)D was associated with greater BMD in white and Chinese participants, the opposite association was seen in blacks. Previous research has found that the concentration of vitamin D-binding protein is lower in blacks than in whites, and that this difference is largely genetically determined. Although blacks have lower 25(OH)D levels than whites do, a higher proportion of their circulating 25(OH)D is bioavailable, because less is bound to vitamin D-binding protein. The net effect is that the serum concentration of bioavailable 25(OH)D is very similar between whites and blacks (Powe CE et al. Vitamin D-binding protein and vitamin D status of black Americans and white Americans. *N Engl J Med*. 2013;369:1991–2000). Based on the available evidence, a case can be made that blacks who have normal BMD and moderately low serum 25(OH)D levels should not be given vitamin D supplements.

Van Ballegooijen AJ et al. Vitamin D metabolites and bone mineral density: The multi-ethnic study of atherosclerosis. *Bone*. 2015;78:186–193.

Vitamin D and Bone: Higher Doses Not More Effective Than Lower Doses

Two hundred thirty postmenopausal women (mean age, 61 years) who had a serum 25-hydroxyvitamin D level of 14 to 27 ng/ml were randomly assigned to receive, in double-blind fashion, placebo, low-dose vitamin D3 (800 IU per day), or high-dose vitamin D3 (800 IU per day plus twice monthly 50,000 IU; equivalent to a total of about 4000 IU per day) for 1 year. After 1 year, fractional calcium absorption (measured using 2 stable isotopes) increased by 1% (equivalent to about 10 mg per day of additional calcium absorbed) in the high-dose group, decreased by 2% in the low-dose group ($p = 0.005$ vs. high dose), and decreased by 1.3% in the placebo group ($p = 0.03$ vs. high dose). Mean changes in bone mineral density of the spine, total hip, femoral neck, and total body did not differ significantly between groups, and there was no clear trend favoring high-dose over low-dose vitamin D.

Comment: In this study of postmenopausal women with low or borderline-low serum 25-hydroxyvitamin D levels, supplementation with 4000 IU per day of vitamin D, as compared with 800 IU per day, resulted in a small increase in calcium absorption, but this increase did not translate into beneficial effects on bone mineral density. The results of this study are consistent with those of a previous study in which postmenopausal women received daily either 800 IU or 6500 IU of vitamin D3 for 1 year. While bone mineral density increased in both groups, the mean increase was nonsignificantly greater with the lower dose of vitamin D than with the higher dose. (Grimnes G et al. The effect of high-dose vitamin D on bone mineral density and bone turnover markers in postmenopausal women with low bone mass - a randomized controlled 1-year trial. *Osteoporos Int*. 2012;23:201–211). The results of these studies indicate that high-dose vitamin D is not more effective than 800 IU per day for preventing osteoporosis in postmenopausal women.

Can Inositol Prevent Gestational Diabetes?

Two hundred twenty obese pregnant women were randomly assigned to receive, in open-label fashion, 2 g of *myo*-inositol plus 200 µg of folic acid twice a day or placebo (200 µg of folic acid twice a day), starting in week 12–13 of gestation. Oral glucose tolerance tests were conducted at 24 to 28 weeks of gestation. The incidence of gestational diabetes was significantly lower by 58% in the *myo*-inositol group than in the placebo group (14.0% vs. 33.6%; $p = 0.001$). Insulin resistance improved slightly in the *myo*-inositol group and worsened slightly in the placebo group ($p < 0.05$ for the difference in the change between groups).

Comment: *Myo*-inositol (commonly referred to simply as inositol) is a compound that occurs naturally in food and is synthesized in the body. A typical daily diet contains about 1300 mg of *myo*-inositol, with beans being among the best sources. *Myo*-inositol and one of its naturally occurring stereoisomers, D-*chiro*-inositol, are each thought to play a role in regulating glucose levels. In the present study, supplementation with 4 g per day of *myo*-inositol significantly reduced the incidence of gestational diabetes and improved insulin resistance in obese pregnant women. The mechanism by which *myo*-inositol improves glycemic control is not known. Additional studies are needed to determine whether it is safe to supplement with this relatively large dose of *myo*-inositol during pregnancy.

D'Anna R et al. Myo-inositol supplementation for prevention of gestational diabetes in obese pregnant women: a randomized controlled trial. *Obstet Gynecol*. 2015;126:310–315.

Cranberry Prevents Post-Surgery Urinary Tract Infections

One hundred sixty women undergoing elective gynecological surgery involving urinary catheterization were randomly assigned to receive, in double-blind fashion, 2 cranberry capsules twice a day (equivalent to 8 ounces of cranberry juice twice a day) or placebo, beginning at the time of hospital discharge and continuing for 6 weeks. The proportion of women who developed a urinary tract infection (UTI) was significantly lower by 50% in the cranberry group than in the placebo group (19% vs. 38%; $p < 0.01$).

Comment: The incidence of UTI is 10% to 64% among women undergoing elective gynecological surgery during which a catheter is placed. Cranberry juice has been used for many years to prevent and treat UTIs. There are several different mechanisms by which cranberry juice could be beneficial. First, the proanthocyanidins in cranberry extracts have been shown to prevent the adherence of uropathogenic strains of *E. coli* to human uroepithelial cells. Second, ingestion of cranberry juice may acidify the urine, and thereby inhibit the growth of some uropathogenic bacteria. Third, cranberries contain hippuric acid, which has antibiotic activity. The results of the present study demonstrate that, among women undergoing elective gynecological surgery involving urinary catheterization, the use of cranberry extract capsules during the postoperative period reduced the incidence of urinary tract infections by 50%.

Foxman B et al. Cranberry juice capsules and urinary tract infection after surgery: results of a randomized trial. *Am J Obstet Gynecol*. 2015;213:194.e1–194.e8.

Gaby's Literature Review

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Fish Oil for Rheumatoid Arthritis

One hundred thirty-nine patients with rheumatoid arthritis for less than 12 months who had not previously received disease-modifying antirheumatic drugs (DMARDs) were randomly assigned to receive, in double-blind fashion, in a 2:1 ratio, a high dose (5.5 g per day) or a low dose (0.4 g per day) of omega-3 fatty acids (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) from fish oil. All patients also began a regimen of DMARDs (methotrexate, sulfasalazine, and hydroxychloroquine). After 12 months, the proportion of patients who had commenced leflunomide (an indicator of failure of medical therapy) was significantly lower in the high-dose group than in the low-dose group (10.5% vs. 32.1%; $p = 0.002$). The remission rate was significantly higher in the high-dose group than in the low-dose group (approximations from figure 3: 41% vs. 23%; $p = 0.03$).

Comment: EPA and DHA, the major omega-3 fatty acids present in fish oil, have anti-inflammatory activity. Numerous double-blind trials have found that supplementation with fish oil improves symptoms in patients with rheumatoid arthritis. The results of the present study demonstrate that supplementation with a high dose of fish oil (about 18 g per day) can provide additional benefits to those achieved with DMARDs. Specifically, high-dose fish oil increased the remission rate and also decreased the number of patients for whom DMARDs were ineffective.

Proudman SM et al. Fish oil in recent onset rheumatoid arthritis: a randomised, double-blind controlled trial within algorithm-based drug use. *Ann Rheum Dis.* 2015;74:89–95.

Can Cherry Juice Ameliorate Dementia?

Forty-nine elderly individuals (mean age, 79.8 years) with mild-to-moderate dementia were randomly assigned to consume 200 ml per day of cherry juice or a control juice (apple juice) for 12 weeks. The cherry juice was produced by a novel method designed to retain the anthocyanins. Compared with baseline, cherry juice significantly improved measures of verbal fluency ($p < 0.02$), short-term memory ($p < 0.02$), and long-term memory ($p = 0.001$). No significant changes were seen in the control group, but it was not stated whether the difference in the change between groups was significant.

Comment: Basic science research suggests that anthocyanins (which are present in large amounts in cherry juice) may have neuroprotective effects. The results of the present study suggest that cherry juice may improve cognitive function in elderly people with mild-to-moderate dementia. However, the study had some weaknesses. First, it was not stated whether the improvement with cherry juice relative to apple juice was statistically significant. Second, the cherry juice provided 103 kcal per day more energy and 2.8 g per day more protein than the apple juice. In elderly people, some of whom might be malnourished, a small amount of additional calories and protein could be nutritionally significant. Cognitive function depends in part on the availability of neurotransmitters, many of which are synthesized from amino acids. An increase in dietary protein, when combined with the potential protein-sparing effect of a higher caloric intake, may increase neurotransmitter synthesis. That effect, as opposed to any effect specific to cherry juice, could have contributed to the improvements observed in this study.

Kent K et al. Consumption of anthocyanin-rich cherry juice for 12 weeks improves memory and cognition in older adults with mild-to-moderate dementia. *Eur J Nutr.* Epub 2015 Oct 19.

Fish Oil Improves Muscle Mass in Elderly People

Sixty healthy elderly men and women (aged 60--85 years) were randomly assigned to receive, in double-blind fashion, in a 2:1 ratio, omega-3 fatty acid esters (Lovaza; 1.9 g per day of eicosapentaenoic acid and 1.5 g per day of docosahexaenoic acid) or placebo (corn oil) for 6 months. Compared with placebo, omega-3 fatty acids significantly increased mean thigh muscle volume by 3.6%, hand grip strength by 2.3 kg, and one-repetition maximum lower- and upper-body strength by 4.0% (all $p < 0.05$).

Comment: In this study, supplementation with omega-3 fatty acids slowed the decline in muscle mass and muscle function that typically occurs with advancing age. Increasing omega-3 fatty acid intake may therefore help maintain physical independence in elderly people. While the mechanism of action of omega-3 fatty acids is not known, it is thought to involve alterations in both anabolic and catabolic pathways.

Smith GI et al. Fish oil-derived n-3 PUFA therapy increases muscle mass and function in healthy older adults. *Am J Clin Nutr.* 2015;102:115–122.

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Optimizing Metabolism

by Ingrid Kohlstadt MD, MPH
www.INGRIDients.com

Top Ten Technologies for Improving Metabolism

The Johns Hopkins Applied Physics Lab held an open house to celebrate the first exploration of Pluto as New Horizons spacecraft zipped past 9.5 years after the crewless spacecraft's earth launch. The team members speaking to us hadn't slept for a week, but they couldn't have been happier; and in the packed auditorium, the edge-of-the-seat excitement for science was tremendous.

For a moment, the audience fell unexpectedly silent as they searched for an answer to the speaker's question: What do New Horizons and a smartphone have in common?

The answer: 8 GB data storage.

Within a decade, the technology of the galaxies was scaled to fit into a back pocket. This prompted me to reflect on how technologic advances of all kinds are being used to improve human metabolism, the underpinnings of health. Colleagues and I listed the biggest metabolism-boosting technologies and generated this eclectic list:

Smartphone: The data storage technology that embarked on a decade-long interplanetary journey, traveling 36,000 mph, can now store the inner workings of the approximately 70 trillion cells of the human body. There's another reason that it's worth knowing about apps for metabolism and health. Often preinstalled, they may be collecting and exporting your data to be anonymously incorporated into some larger database, even if you haven't knowingly agreed to it. Some people are OK with that, while others would rather not participate.

PARO: Scientists agree that stress is a metabolic monkey wrench, and we create ways to deal with that stress. But, how do you help someone with Alzheimer's or autism to reduce stress without reaching for a pill bottle? One answer, pets. Animal therapy shows great potential where animals can be cared for and don't pose physical harm to those in fragile states of health. That's where high tech has found a breakthrough with PARO, a robotic therapy that looks like a harp seal pup. PARO was approved as a medical device by the ➤

FDA in 2009, and accompanying the statistics are caretaker testimonials of stress reduction, improved appetite, and social engagements which result from the metabolic turnaround that PARO awakens. I was so impressed that I met PARO's inventor and, of course, gave PARO a hug myself.

Freeze-drying: Even though behavioral science has found that people eat chips for the salt and the fat, chip-lovers usually say that it's "the crunch!" Now these chip-lovers have an alternative : freeze-drying is a food technology that offers a more healthful crunch. Freeze-dried fruits and vegetables have the crunch of chips without the salt and fat.

Copenhagen Wheel: Active living is vital to a healthy metabolism, and getting that daily dose of exercise requires resourcefulness. Technology now overcomes one of the common barriers to exercise, "If only my workplace were 1 mile closer or not uphill, I'd commute by bike." That's when a Linked-In group member told me about the Copenhagen Wheel, which converts a bicycle into an electric hybrid. A back wheel with motor, sensors, electric batteries, and a control system flattens hills and shortens distances, making that daily bike commute possible.

Solar system technology: Technology doesn't have to travel at rapid speeds within Earth's solar system for the sun's benefits. Solar cook stoves are simple technologies with tremendous global good. Single-handedly, these stoves help people in poor communities avoid gathering ever-shrinking supplies of firewood, breathing in the soot from wood and dung-burning stoves, and going to bed hungry.

Another important technology relating to the solar system is the vitamin D research that was greatly advanced by the need for preserving bone strength in astronauts. Now vitamin D is known to be part of the metabolic underpinnings of many metabolic pathways. And in the absence of direct sunlight, its levels can be boosted by exposure to full-spectrum light with measured benefit to human health.

Nanoparticle drug delivery systems: Nanoparticles can mess up metabolism in ways that our society hasn't yet studied. For example, how long do those nanoparticles in sunscreen last? Or are the nanoparticles that make dairy products "creamier" safe even though they are considered too small to be an ingredient and are therefore unlisted on food labels?

But focusing on what we do know, medications loaded with side effects can now be delivered at remarkably smaller doses using nanoparticle technology, thereby minimizing the medications' adverse impact on metabolism. Johns Hopkins Wilmer Eye Institute is bringing this technology to their corneal transplant patients, and Johns Hopkins is conducting studies of nanoparticle-sized curry extract in the treatment of cancer and Alzheimer's disease.

Golden rice: GMO technology is used to create agricultural shortcuts with inadequately studied impacts on human health and the environment. In contrast, golden rice was developed as a genetically modified crop for its health benefits in the 1990s as an alternative to biofortification in regions with vitamin A deficiency. Tragically, because of the cloud over GMO technology, golden rice has not been able to be fully developed to improve human metabolism as originally envisioned.

Measuring the microbiome: It's a rather humbling notion that in the human body, microbes outnumber human cells. A century of scientists have waded through you know what to help us make sense of gut microbes. Now laboratory testing can tell us what medications, foods, and dietary patterns can get our metabolism back on track.

HAPI: Listening is important, especially when it comes to metabolism. Eating slowly is a way to listen to the body's satiety message. Often called *mindful eating*, slowing down with food is among the 10 health messages for NutriBee, a program that engages 10- to 12-year-olds in mindful eating. They participate in an activity wherein they eat Cheerios with chopsticks. By vibrating in response to quick movements, the HAPI fork is a robotic technology that reminds people to eat slowly in our grab-'n'-go society.

Wikipedia: Internet resources enable us to leverage sight and sound technology to find new smells and tastes to engage our metabolism. Wikipedia provides morsels for our mind that embolden us towards new and nutritious tastes. And through wikis, we can share our multisensory food experiences without being a chef or food blogger.

In Summary

Space Age technology is being applied to nutrition and medicine in order to improve human metabolism. That way, not only does the technology fit into the back pants pocket, it can help us keep fitting into that favorite pair of pants, too.

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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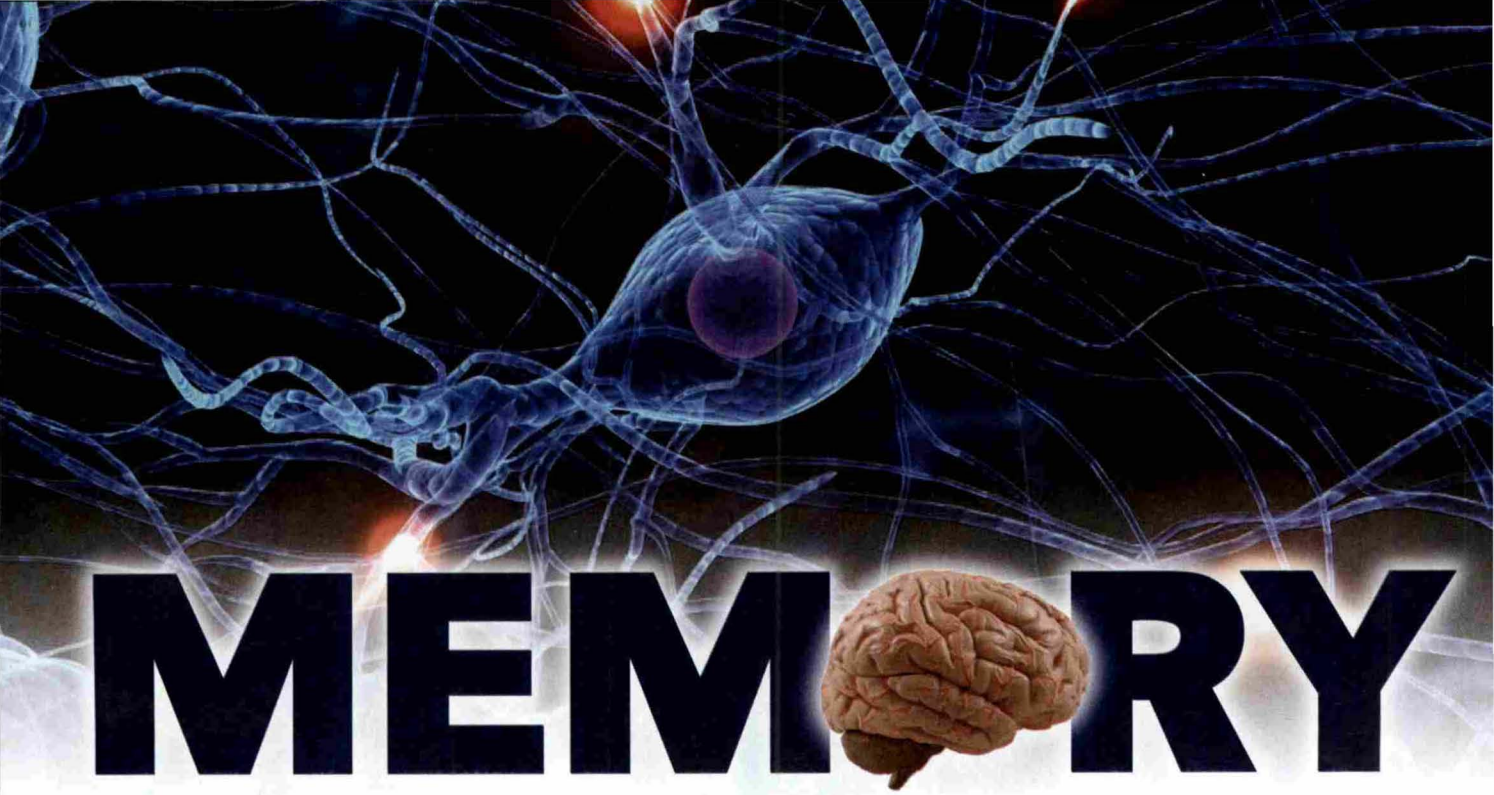

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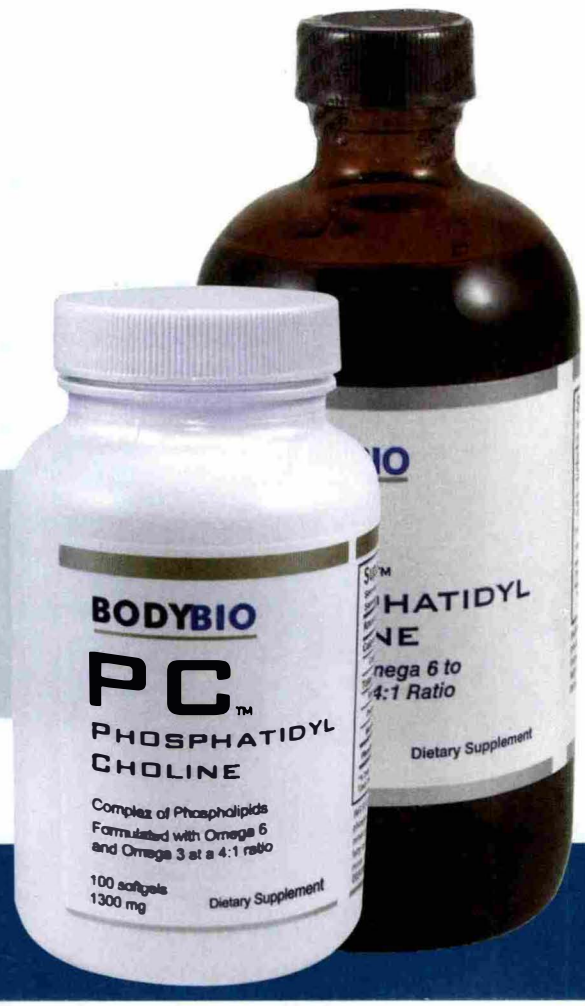

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These are a Few of My Favorite Things: Research Highlights from 2015

by Tori Hudson, ND

Throughout 2015, I have reported monthly in this column on research important to women's health. I have selected several of those research studies here as well as others, that have influenced my clinical practice in gynecological and primary care for women. In case you missed reading them this past year, I hope that these current selections benefit you and your patients.

Maca for Antidepressant-Induced Sexual Dysfunction

This study included 45 women aged 18 to 65 and a mean age of 41.5 years, who were in remission from their depression but suffering from antidepressant-induced sexual dysfunction (AISD). Patients received either 1500 mg maca root or placebo twice daily for 12 weeks. Sexual function was evaluated using the Massachusetts General Hospital-Sexual Functioning Questionnaire (MGHSFQ) and the Arizona Sexual Experience Scale (ASEX). Improvement was assessed with the Clinical Global Impression-Severity (CGI-S) and Clinical Global Impression-Improvement scales (CGI-I)

These women met the following criteria: ≤9 on the 17-item Hamilton Rating Scale for Depression (HAM-D-17) and a score of ≤9 on the Hamilton Rating Scale for Anxiety (HAM-A), which indicated that they were in remission. These patients were on current and stable doses of SSRI, venlafaxine, or a triheterocyclic antidepressant for depression for at least 4 weeks. They also had clinically significant arousal dysfunction or orgasmic dysfunction of 4 weeks or less, and the onset of these symptoms had to coincide with the subsequent use of their antidepressant. In addition, they participated in regular sexual activity at least twice monthly prior to antidepressant use and needed to be open to continued sexual activity at least once weekly during the study.

Results: The mean change in total ASEX and MGHSFQ for maca vs. placebo was not statistically significant overall, whether premenopausal or postmenopausal women. The remission rates however were higher for the maca group than the placebo group for an ASEX total score of 10 or less (maca = 9.5% and placebo = 4.8%) achieving a MGHSFQ score of 12 or less (30% vs. 20%). The higher remission rates occurred in postmenopausal women and the premenopausal women had no significant difference in remission rates between treatment groups on both of the sexual function questionnaires.

It was only the postmenopausal women who were taking the maca who had an improvement in orgasm compared with placebo and only premenopausal women taking the maca who had an improvement in arousal disorder compared with placebo. There was also a significant correlation between the testosterone levels and sexual functioning at the endpoint, on the ASEX questionnaire in women in the maca group, with a trend toward significant on the MGHSFQ in the maca group. No other significant differences were seen in the other hormones that were tested, including estrogen.

Comment: Maca root, in this dose of 1500 mg twice daily may alleviate antidepressant-induced sexual dysfunction specifically in post-menopausal women. It appears that the explanation for this is due to the maca root's altering androgen levels.

Dording C, Schettler P, Dalton E, et al. A double-blind placebo-controlled trial of maca root as treatment for antidepressant-induced sexual dysfunction in women. *Evid Based Complement Altern Med*. 2015. Article ID 949036.

Black Cohosh for Perimenopause Symptoms Induced by GnRH-a Treatment of Endometriosis

This study was designed as a prospective, randomized, controlled trial to compare the efficacy and safety of black cohosh standardized extract (Remifemin) versus tibolone. All women were treated with GnRH-a after laparoscopic ovarian cyst removal and were injected 1 week after surgery, 4 weeks later, and then a third injection before the end of the study. The black cohosh group received 20 mg tablets of a standardized extract of black cohosh, twice daily for 12 weeks. Tibolone was given 2.5 mg daily for 12 weeks. The total duration of follow-up was 12 weeks, and follow-up started 4 weeks after the first GnRH-a injection.

A total of 125 women who had undergone laparoscopic surgical treatment for their endometriosis and then were treated with GnRH-a (gonadotropin-releasing hormone agonist). In the final count, 116 women were surveyed and analyzed after 9 women discontinued treatment or were lost to follow-up. There were 56 women in the black cohosh group and 60 women in the Tibolone group.

Results: For both groups, the Kupperman menopausal index (KMI) scores after GnRH-a were significantly increased. After therapy with black cohosh or tibolone, the KMI scores and hot flash/sweating decreased in both and there was no significant difference at each juncture, between the two. Both had a very good and similar effectiveness in alleviating perimenopausal symptoms that were caused by the GnRH-a therapy. After GnRH-a therapy, the hot flash/sweating scores were 2.87 for

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black cohosh and 2.70 in the tibolone groups. After black cohosh, the scores were 0.94 and with tibolone 1.06. No statistical difference occurred between the two groups after black cohosh or tibolone with liver or renal functions or lipid profiles. Estrogen levels were lower in the black cohosh group and FSH and LH levels were higher than the tibolone group, a predictable finding. No significant difference was seen in endometrial thickness. The black cohosh though had far fewer adverse events than the tibolone group in the areas of vaginal bleeding/spotting and breast pain. The incidence of nausea, emesis, and abdominal discomfort was not significantly different between groups.

Comment: Endometriosis is a very common gynecological disorder and can range from mild to severe. In those women with either severe symptoms that significantly affect her quality of life and/or those for whom the endometriosis is the cause of their infertility, current conventional treatment options include pain management with analgesics, hormonal contraception for symptom and disease management (but not cure), surgery, and medical agents that suppress ovarian function at least temporarily (e.g., gonadotropin-releasing hormone agonists = GnRH-a). With surgery or ovarian suppressive treatments, the risk of symptom recurrence is from a low of 21.5% at 2 years to 50% at 5 years after treatment. One of the problems with GnRH-agonists is that they reduce estrogen levels that then lead to perimenopausal symptoms including hot flashes, sexual dysfunction, bone loss, and others. This definitely limits the use of these agents to short term use, usually up to 6 months and usually post endometriosis surgery. Add-back estrogen therapy is then used at low doses to mitigate these effects of the GnRH-agonist, which then has not only benefits, but potential risks. A nonhormonal alternative, such as a botanical that can alleviate the menopause symptoms, is a logical and potentially effective first approach rather than the medication tibolone (not available in the US), which has more adverse events than black cohosh, and does not have any estrogenic effect.

Chen J, Gao H, Li Q, et al. Efficacy and safety of Remifemin on peri-menopausal symptoms induced by post-operative GnRH-a therapy for endometriosis: a randomized study versus tibolone. *Med Sci Monit*. 2014;20:1950–1957.

Burning Mouth Syndrome: A New Study on Alpha-Lipoic Acid

Burning mouth syndrome is one of those occasional but difficult problems that I see in my women's health practice. This syndrome occurs more frequently in middle-aged and elderly individuals and is more prominent in women, about a 7:1 ratio. The precise cause of burning mouth syndrome is unknown, although multiple local and systemic factors exist. Local factors associated with burning mouth syndrome include hyposalivation and/or xerostomia, parafunctional habits, contact allergies, poorly fitting oral devices, *Candida albicans* oral infection, smoking, alcohol, caffeine, and hot or spicy foods. Systemic factors associated with burning mouth syndrome include menopause, nutritional deficiencies (B vitamins, iron, folic acid), type 2 diabetes, hypothyroid, and select medications (e.g., antihypertensive drugs).

Given the limited published evidence for natural medicine solutions to this condition, I was attracted to this new study on the use of alpha-lipoic acid (ALA) as a treatment, although it's not the first study on ALA for burning mouth syndrome.

This double-blind, placebo-controlled study was conducted in Madrid, Spain, in which patients were randomly allocated to either placebo or ALA. All participants were assessed for salivary flow rates, complete blood count, ferritin, vitamin B12, and folic acid. Treatment was 600 mg/day of ALA at 200 mg every 8 hours for 2 months, or placebo every 8 hours for 2 months. Patients were assessed every 15 days for changes in symptomatology and for side effects. Final results were obtained after 2 months.

Most of the patients were 55 women and 5 men over age 18, with a mean of 62 years, who had burning mouth syndrome for more than 4 months and no clinical objective signs. The duration of symptoms in patients was between 4 months and 20 years. The average intensity was 6.6, with a range of 2.5 to 10. Burning symptoms were the most common symptom in 63.3% of the patients and stinging in 20%. The rest reported itching or other symptoms, with the tongue being the most affected site. In addition to burning, 10 patients had dysgeusia, 13 had xerostomia, and 24 reported both symptoms that occurred concurrently. Stimulated and unstimulated salivary flow was found in 25 patients. About one-third of the participants associated the onset of their burning mouth syndrome symptoms with a dental treatment.

Patients were excluded if they had local oral lesions or alterations or unmanaged systemic diseases; were on cisplatin, cyclophosphamide, gentamicin, or amikacin; or were already undergoing any type of treatment for their burning mouth syndrome.

The primary outcome was measured using a visual analogue scale as mild improvement (50%–75%), great improvement (>75%), or complete amelioration of symptoms. Results were divided into three categories: slight improvement, decided improvement/resolution, and no change or worse. Eight of the 20 patients (27.5%) who received placebo showed some level of improvement, 5 worsened (17.2%), and 16 had no change (55.2%). Sixteen of the 5 patients who received ALA (64%) improved, 9 (36%) had no change, and none worsened. One month after the end of the treatment, 4 of the 8 patients who had improved in the placebo group had a relapse of burning. About one-third (5 of 16 patients) with signs of improvement taking ALA worsened 1 month after treatment was discontinued.

Previously published research on ALA has demonstrated efficacy and is probably one of the most effective treatments for burning mouth syndrome. The most common dose studied is 600 mg/day, as in the current study. Based on the current study as well as at least 6 other studies, ALA at a total day's dose of 600 mg/day should be at the top of every practitioner's list for treating burning mouth syndrome.

Palacios-Sanchez B, Moreno-Lopez L, Cerero-Lapiedra R, et al. Alpha-lipoic acid efficacy in burning mouth syndrome. A controlled clinical trial. *Med Oral Patol Oral Cir Bucal*. July 1, 2015;20(4):e435–440.

Cinnamon for Primary Dysmenorrhea

In a randomized, double-blind trial, with 114 women with moderate dysmenorrhea, 38 received placebo, 38

continued on page 38 ➤

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Research Highlights

➤ *continued from page 36*

ibuprofen, and 38 cinnamon. Ibuprofen was given in a dose of 400 mg three times daily and cinnamon was given 420 mg three times daily, as was placebo. The visual analogue scale (VAS) was used to determine the severity of pain and the Cox Menstrual Scale was used to determine the duration of pain. A VAS rating of 0 means no pain and 10 means maximum pain. Pain intensity and duration of pain were monitored during the first 72 hours of the menstrual period. Severity of pain was assessed using VAS at hourly time intervals for the first 4 hours, then 8 hours, 16 hours, 24, 28, 48, and 72 hours. Duration of pain was assessed once daily. The Cox Menstrual Scale includes 17 symptoms and gauges the severity of each symptom from 0 (no symptoms) to 4 (very severe). Duration is rated from 0 (asymptomatic) to a 4 (continued symptoms for multiple days).

Women were 18 to 30 years old, had regular menstrual cycles, moderate primary dysmenorrhea, lack of chronic disease, no vaginal discharge/itching/burning, no pelvic inflammatory disease, no pelvic masses, no recent stress, and a body mass index of 19–26. Women were excluded if they were using hormonal contraception, or had medicine or plant allergies or only mild dysmenorrhea.

Results: The mean pain severity score and mean duration of pain in ibuprofen and cinnamon were less than placebo. Four hours after intervention, there were no statistically significant differences between the cinnamon and placebo group. Eight hours after treatment, the mean severity of pain in the cinnamon group was significantly lower than the placebo group and at various time intervals the mean pain severity in the ibuprofen group was significantly less than the cinnamon and placebo groups.

Comment: While cinnamon significantly reduced the severity and duration of pain during menses, the effect was less than that of ibuprofen.

Jaafarpour M, Hatefi M, Khani A, Khajavikhan J. Comparative effect of cinnamon and ibuprofen for treatment of primary dysmenorrhea: a randomized double-blind clinical trial. *J Clin Diag Res.* 2015;April 9(4):QC04–QC07.

Green Tea Effects on Weight Reduction

Green tea has been studied for its beneficial effects on cardiovascular and metabolic diseases. Epigallocatechin gallate (EGCG) is the most abundant green tea catechin and is considered the most bioactive constituent that can reduce body weight by decreasing fat cell differentiation and proliferation. One study has demonstrated that green tea extracts and drinks could reduce body weight and body mass index in obese individuals in 2 months.[1] On the other hand, a previous study by those authors found that 302 mg of EGCG daily did not reduce weight in obese women.[2] The currently published study set out to increase the concentration of EGCG to a daily dose of 856.8 mg/day to see if this increased amount would result in weight loss in obese individuals.

This randomized, double-blind trial was conducted in 115 women with central obesity with 102 of them having a body mass index (BMI) ≥27 kg/m² and a waist circumference ≥80 cm. Women were randomized to either a high-dose green tea group or placebo group for 12 weeks. One capsule of green tea or placebo was given 3 times per day, 30 minutes after meals for a total daily dose of 856.8 mg EGCG.

Body weight decreased from 76.8 kg to 75.7 kg after 12 weeks in the EGCG group. BMI and waist circumference were reduced from 31.0 cm to 30.6 cm and 95.1 cm to 92.8 cm respectively. In the placebo group, only waist circumference and hip circumference reached significant reduction, from 95.7 cm to 91.5 cm and 107.2 cm to 103.7 cm respectively. No differences were seen in weight or BMI.

The study also demonstrated a trend of decreased total cholesterol and decreased LDL cholesterol. Significantly lower ghrelin levels and elevated adiponectin levels were also seen in the green tea group than in the placebo group.

Comment: Obesity is one of the most challenging issues in women's health care. No one strategy produces consistent results in all women. Nutritional modifications, exercise programs, behavioral therapy, and agents that can affect insulin resistance, fat burning, fat oxidation, and metabolic rates occupy central roles in efforts. Green tea and its main components, the catechins, including EGCG, are thought to influence body weight through mechanisms of thermogenesis and fat oxidation. The results of the current study with significant weight reduction and decreased ghrelin levels after EGCG treatment implies that a high dose of EGCG might increase energy metabolism and interrupt lipid accumulation and directly inhibit ghrelin secretion.

For perspective on dosing, one might look for a capsule of green tea extract of approximately 300 mg of EGCG. If 1 capsule 30 minutes after each meal (3 times per day), this would then be 900 mg of EGCG per day, slightly more than the 856.8 mg in the current study.

Chen I, Liu C, Chiu J, Hsu C. Therapeutic effect of high-dose green tea extract on weight reduction: a randomized, double-blind, placebo-controlled clinical trial. *Clin Nutr.* 2015:1–8 (in press).

Notes

1. Basu A et al. Green tea supplementation affects body weight, lipids, and lipid peroxidation in obese subjects with metabolic syndrome. *J Am Coll Nutr.* 2010;29:31–40.
2. Hsu C, Sai T, Kao Y, et al. Effect of green tea extract on obese women: a randomized, double-blind, placebo-controlled clinical trial. *Clin Nutr.* 2008;27:363–370.

Comparison of *Myo*-Inositol and D-*Chiro*-Inositol in PCOS Women

Both *myo*-inositol and D-*chiro*-inositol have been shown to affect ovarian function and metabolic factors in women with polycystic ovarian syndrome (PCOS). They have been shown to improve androgen levels, increase the action of insulin, reduce systolic blood pressure, and more.

The purpose of the current study was to compare the effects of *myo*-inositol and D-*chiro*-inositol in women with PCOS. Fifty women with a diagnosis of PCOS according to the Rotterdam criteria were enrolled. They were randomized into two groups; 25 were treated with 4 g of *myo*-inositol plus 400 mcg of folic acid daily for 6 months, and the other 25 were treated with 1 g of D-*chiro*-inositol plus 400 mcg/folic acid per day.

In the *myo*-inositol group, there were statistically significant reductions of diastolic and systolic blood pressure; lowering of luteinizing hormone (LH); lowering of the LH/FSH (follicle stimulating hormone) ratio; and lowering of total testosterone and free testosterone, androstenedione, prolactin, and the HOMA (homeostatic model assessment) to check for insulin resistance. These same patients also had

a statistically significant increase of sex hormone binding globulin (SHBG) and the glycemia/immunoreactive insulin ratio.

In the D-*chiro*-inositol group, there was a statistically significant reduction of systolic but not diastolic blood pressure and a statistically significant reduction of the Ferriman-Gallwey Score (a measure of hirsutism), LH, LH/FSH ratio, total testosterone, free testosterone, androstenedione, prolactin, and the HOMA.

Both inositols reduced systolic blood pressure, LH, LH/FSH ratio, circulating androgens, and prolactin, and increased insulin sensitivity and SHBG. *Myo*-inositol may decrease the LH/FSH ratio, total testosterone, and the HOMA in a more statistically significant way. D-*chiro*-inositol is likely to reduce mostly, but not statistically significantly, the LH and free testosterone levels and may increase, but not significantly, the glycemia/IRI ratio.

It could be concluded from this comparison that both the inositol isoforms are effective in improving the ovarian function and metabolism of women with PCOS, although *myo*-inositol showed the greater impact on the metabolic profile and D-*chiro*-inositol affected more positively the hyperandrogenism measurements. In comparing the two products pre- and posttreatment, there was a higher regularization of menstrual cycles in those treated with D-*chiro*-inositol compared with those with *myo*-inositol, although this was not statistically significant.

Comment: PCOS is one of the most common endocrine disorders in reproductive-aged women. The majority of women with PCOS (about 74%) do not ovulate, almost half (about 42%) have insulin resistance, and almost half (48%) have hyperandrogenism. It's important to remember that PCOS is a syndrome – and not all women with PCOS have any one sign or symptom. Not all actually have multiple cysts on the ovaries, not all have excess body hair, and not all have abnormal menstrual cycles. In women with PCOS, though, the insulin resistance is commonly associated with hyperinsulinemia, which then enhances the production of androgens by the ovarian theca cells, leading to a reduction in circulating levels of SHBG, which leads to increased levels of free testosterone. Nutritional, lifestyle, supplemental, and pharmaceutical strategies try to address the syndrome by targeting this core issue of improving insulin sensitivity, which thereby addresses the signs and symptoms of PCOS. Both *myo*-inositol and D-*chiro*-inositol, in the doses used in this study, improve ovarian function and metabolism in PCOS, but *myo*-inositol showed the most effect on the metabolic profile and D-*chiro*-inositol reduced the hyperandrogenism better.

Pizzo A, Lagana A, Barbara O. Comparison between effects of myo-inositol and D-chiro-inositol on ovarian function and metabolic factors in women with PCOS. *Gynecol Endrocrinol.* 2014;30(3):205–208.

Vulvar Lichen Sclerosus: Treatment with Topical Avocado and Soybean Extracts

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

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

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

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

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

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

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

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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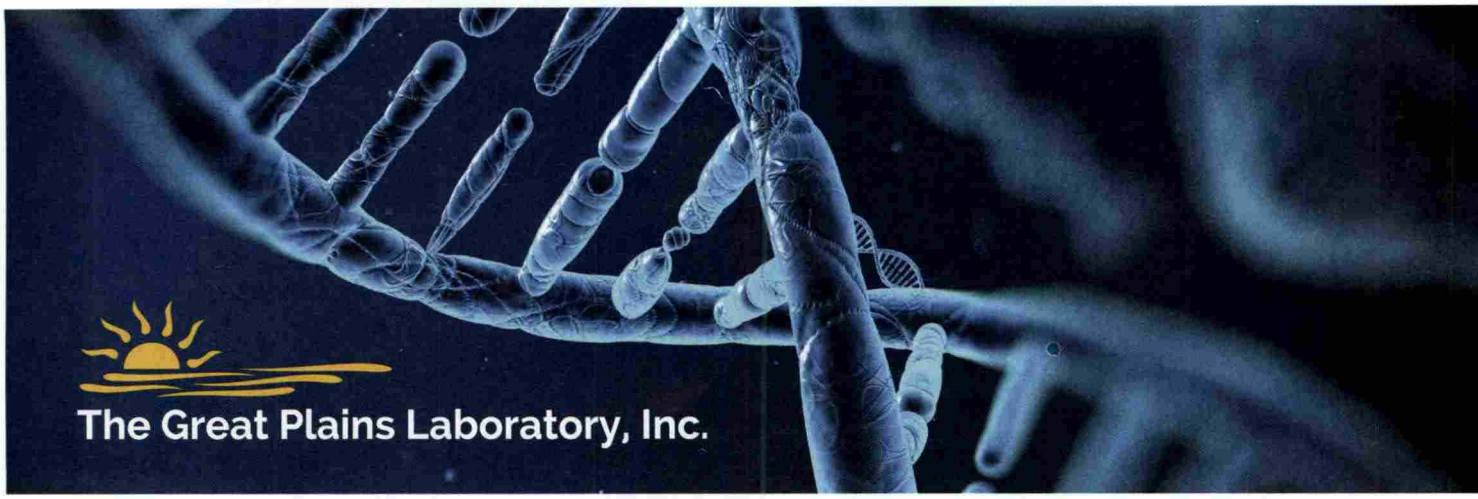

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GPL-SNP1000 will help you understand how these nine genetic pathways are performing in your patients. It will also help you determine your patients' predisposition for developing various disorders, including ADHD, adverse drug reactions, allergies, anxiety, arthritis, autism spectrum disorders, bipolar disorder, cancer, depression, heart disease, osteoporosis, oxidative stress, and schizophrenia. Test results will help guide you to better and more personalized treatment for your patients.

For additional information about GPL-SNP1000 and genetic testing, please read the article **"Genetic Testing: The Key to Truly Personalized Medicine"** by Matthew Pratt-Hyatt, PhD in this issue of Townsend.

GPL vs. Amy Yasko

	GPL-SNP1000	AMY YASKO
DNA Methylation	105	21
Oxalate Metabolism	53	8
Mental Disorders	241	0
Gluten Opioid Peptides	252	0
Autism Spectrum Genes	32	0
P450s (cyps)	48	0
Cholesterol Deficiency	101	1
Acetaminophen	72	0
Transporter Genes	130	0

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Genetic Testing: The Key to Truly Personalized Medicine

by Matthew Pratt-Hyatt, PhD

Personalized medicine has been called the future of medicine since the inception of the Human Genome Project (HGP) in the early 1990s, a project set up by the US government to sequence the complete human genome. The HGP was completed in 2003.[1] This new wealth of knowledge allowed scientists to develop tests that sequence the 3 billion base pairs and the 20,000 to 25,000 genes in the human genome.[2] Over those 25,000 genes there are over 80 million variants in the human genome.[3] These variations include single nucleotide polymorphisms (SNPs), as well as small deletions and insertions throughout the genome, and many of those variants play a significant role in patient health. The dream of personalized health care is to use genetic testing to understand a patient's predisposition for developing different conditions, and then undergo molecular diagnostic tests to determine how the environment is interacting with these genes.

At the Great Plains Laboratory Inc., we have been primarily focused on looking at the second half of this equation: finding the root cause of patient symptoms in a wide variety of chronic disorders. We have developed tests that look at hundreds of different analytes and have worked with doctors to help them interpret how these data can be used to personalize treatment for patients. Even though traditional medicine has mostly followed the philosophy that one size fits most, functional medicine says that each person is unique and deserves unique care. That is why we have developed our new genetic test, GPL-SNP$_{1000}$, which now allows us to have a more complete picture of what contributes to a patient's health status. In partnership with the genetic company Courtagen, we have developed what we think will be the next great tool for personalized medicine.

GPL-SNP$_{1000}$ uses the most recent advance in sequencing technology, Next Generation Sequencing (NGS). NGS machines can monitor what nucleotide is added at each place during the DNA chain prolongation reaction. This principle has been labeled "sequencing-by-synthesis." NGS allows for sequencing to move from about 1000 nucleotides long to about 1000 billion bases per run. This gives researchers the ability to perform a very in-depth sequence for one patient or sequence several dozen patients at a time using more pinpointed analysis.[4]

GPL-SNP$_{1000}$ is a genetic screen that covers 1048 SNPs over 144 different genes. These genes are broken up into

Figure 1: GPL-SNP$_{1000}$ Gene Groups and SNPs

Pathway	Clinical Significance	# of SNPs
DNA Methylation	Developmental delays Mental disorders Risk of homocysteinemia	105
Mental Health	Mental disorders	53
Drug Metabolism	Increased risk of adverse drug reactions	241
Autism Spectrum Genes	Developmental delays and disorders	252
Oxalate Metabolism	Primary hyperoxaluria Myoglobinuria Fibromyalgia Autism Vulvodynia	32
Gluten Sensitivity		48
Cholesterol Metabolism	Mental disorders Heart disease Increased risk of obesity	101
Acetaminophen Toxicity	Increased risk of adverse drug reactions	72
Transporters	Liver disease Coronary disease Mental disorders	130

nine different groups: DNA methylation, mental health, drug metabolism/ chemical detoxification, autism risk, oxalate metabolism, cholesterol metabolism, acetaminophen toxicity, and the transporter genes (see Figure 1, p. 41).

The GPL-SNP$_{1000}$ test report (see Figure 2) is programmed to only depict the SNPs that are mutated. We are including the gene symbol, the RS number (or reference SNP number), which indicates which SNP is mutated (so that you can look up new research on that mutation), a pathogenicity number (we look at all available research on each SNP and predict how severe a mutation at that SNP would be), genotype (what is the change in nucleotide), phenotype (whether the patient is heterozygous or homozygous [one of two mutated copies), and the disease(s) associated with that mutation (we have listed the most common conditions associated with every SNP in our assay). The report also has interpretations that are autogenerated for genes found to be mutated in the assay. One additional feature that our report has is hyperlinks to the references on PubMed used to make the interpretations. This allows both patients and health-care practitioners to review the literature about those particular mutations, without having to search the Internet for these articles.

We were very strategic about selecting the nine specific groups of genes and SNPs that our test evaluates. We talked to dozens of functional medicine professionals and asked them what groups of genes would help them the most in their practices. The top answer was the DNA methylation pathway, which was not surprising, because the most utilized genetic tests on the market are currently the MTHFR tests. The MTHFR pathway is a process by which carbons are added onto folic acid from amino acids and redistributed onto other compounds throughout the body. This process is responsible for the formation of methionine, S-adenosylmethionine (SAMe), and thymidylate monophosphate (dTMP). These compounds play critical roles in nucleotide synthesis, neurotransmitter function, detoxification, and numerous other processes.[5] We believed that we could provide better coverage of these genes than previously done by other genetic tests. We knew that no other test had more than 35 SNPs in its assay for the MTHFR gene, so we redesigned our existing DNA Methylation Profile by increasing the number of SNPs from 32 to 105. One reason why this test is so popular is the very common occurrence of one of the more serious SNPs of the MTHFR gene, rs1801133 (C667T). This mutation has a mutant allele frequency of 39% for the heterozygous genotype and a 17% frequency for the homozygous mutant. It can decrease the enzyme's functionality by 90%, causing patients to have an increased risk of developmental delay, mental retardation, vascular disease, and stroke.[6]

Our second most requested group of genes was those that correlate with mental health. Mutations to these genes can predispose patients to a variety of ailments, including depression, schizophrenia, anxiety, and bipolar disorder. We designed this group to include the 9 genes and 53 SNPs that are most commonly the cause of mental disorders. One of the more important genes in this group is the catechol-O-methyltransferase (COMT) gene. This enzyme is responsible for the degradation of catecholamines, which include dopamine, epinephrine, and norepinephrine. Mutations to COMT can lead to bipolar disorder, anxiety, obsessive compulsive disorder, and attention deficit/hyperactivity disorder. One of the more common mutations of COMT is the Val108Met mutation (rs4680), which can cause a heightened risk of developing anxiety.[7]

The next gene group we focus on is the group for drug metabolism/ chemical detoxification. These enzymes include the cytochrome P450s, sulfur transferases, glutathione transferases, and the methyltransferases. The P450s are important for multiple molecular functions including drug metabolism, hormone production, toxicant detoxification, and more. The P450s are expressed throughout the body, but primarily in the liver. There are 57 different genes for the cytochrome P450 enzymes; however, eight are responsible for most of the drug metabolism done by the body. The P450 enzymes are responsible for 75% of all drug metabolism.[8] Mutations to P450s can cause changes in the rate of metabolism of some medications, causing decreased effectiveness and other dangerous complications. Some medications known to be affected by drug mutations include but are certainly not limited to warfarin, diazepam, antiarrhythmic drugs, antidepressants, and antipsychotics.[12,13] P450s that are known to have alleles in the population that dramatically affect drug metabolism include CYP2C9, CYP2C19, and CYP2D6.[9] Besides the P450s, which are considered phase I detoxification, GPL-SNP$_{1000}$ covers phase II detoxification enzymes that include glutathione S-transferse, sulfotransferase 1a1, betaine-homocysteine methyltransferase 2, and UDP glucuronosyltransferease 1A1.

The next group of genes that we analyze tells parents if they or their children may have a mutation that is commonly found in autistic patients. It has been reported that the prevalence of autism has increased dramatically in the last two decades.[10] We looked at many different studies to determine what mutations are more commonly found in autistic patients, but not found in the neurotypical, nonautistic public. Three

Figure 2: GPL-SNP$_{1000}$ Report

Gene	RS Number	Pathogenicity	Genotype	Phenotype	Disease Associated
IDI1	rs7075141		G,A	+ —	Increased risk of Alzheimer's disease
FDPS	rs11264359		A,G	+ —	Increased risk of Crohn's disease

large studies that were done using over 3000 participants were very useful in developing this panel.[11–13] We selected 252 SNPs that cover 33 genes that were found in these three studies. These genes cover many different pathways, including glucose metabolism, ion and calcium channels, DNA transcription regulation, and nervous system genes.

Next, we included a group of genes that are involved with oxalate metabolism. Oxalate and its acidic form, oxalic acid, are formed from diet, human metabolism, and yeast/fungal overgrowth. Oxalates are known to combine with calcium to form crystals that can cause kidney stones. These crystals may also form in the bones, joints, blood vessels, lungs, and even brain.[14] The oxalate group from our test analyzes 32 SNPs that cover 5 different genes. One of these genes is alanine-glyoxylate aminotransferase (AGXT). Mutations to AGXT can lead to kidney stones and primary hyperoxaluria.[15]

In addition to these groups of genes, our new test also looks at genes for cholesterol metabolism, as well as transporters. Both of these pathways are important for the body to regulate itself properly. Cholesterol is important because it is critical for producing cellular membranes, hormones, and bile acids. There are numerous recent articles discussing the importance of these cholesterol-produced molecules that regulate sugar metabolism and our metabolic rate. Transporters are also necessary because they move large molecules and other chemicals into and out of the cell, which are not able to move across cellular membranes without assistance. Without transporters, cells are not able to attain the proper building blocks necessary for optimum functionality or dispose of toxic cellular waste.

Truly personalized medicine may not be a reality today; however, I believe the recent developments in genetic testing are the biggest leaps that we've made in a long time. GPL-SNP$_{1000}$ helps health-care professionals know what problems their patients may have now or in the future due to genetic mutations, as well as what specific treatments may be beneficial. The Great Plains Laboratory Inc. offers cutting-edge diagnostic tools that help identify underlying causes of many chronic conditions and provides recommendations for treatment based on test results. In addition to our new genetic test, we offer other comprehensive biomedical testing, including our organic acids test (OAT), IgG food allergy test, GPL-TOX (our toxic organic chemical profile), and many more. Utilizing a combination of our genetic and molecular diagnostics, we can now see a more complete picture of a patient's overall health, both at present and potential problems for the future, which can all be addressed now. I truly believe that the sun is now rising on a new horizon of health.

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Matthew Pratt-Hyatt, PhD, received his PhD in cellular and molecular biology from the University of Michigan. He has trained under Dr. Paul Hollenberg, a prominent researcher on drug metabolism, and Dr. Curtis Klaassen, one of the world's leading toxicologists. He has over a dozen publications in well-known research journals such as the *PNAS* and *Cell Metabolism*. He is currently associate laboratory director at the Great Plains Laboratory Inc. in Lenexa, Kansas, focused on diagnosis and treatment of mitochondrial disorders, neurological diseases, chronic immune diseases, and more. He specializes in developing tools that examine factors at the interface between genetics and toxicology. His work is bringing new insight into how genes and toxicants interact and how that may lead to mental health disorders, chronic health issues, and metabolism disorders.

Omega-3 Fatty Acids and the Menopausal Transition: Clinical Efficacy in Depression and Beyond

by Leah Gillingham, PhD

Introduction

Natural menopause is defined as 12 consecutive months of amenorrhea after the final menstrual period.[1] Perimenopause, also called the menopausal transition, refers to the time period of changing ovarian function and estrogen levels occurring 2 to 8 years prior to the final menstrual period. The onset of menopause has a wide range (42–58 years) with an average age of 51 years. The prevalence of depression or mood swings; hot flashes; and joint aches, pain, and stiffness increases during the menopausal transition.[2] The symptoms of menopause are closely linked to the fluctuating and declining levels of estrogen and associated changes in serotonergic transmission.[3] In addition, many women experience sleep disturbances, decreased libido, vaginal dryness, dry eye symptoms, and increased cardiovascular risk; namely, hypertriglyceridemia and arrhythmias. The use of complementary and alternative medicine (CAM) to improve quality of life during the menopausal transition has increased in light of the demonstrated or perceived risks of hormone replacement therapy.[4]

Considerable clinical interest has focused on the health benefits of omega-3 polyunsaturated fatty acids (PUFAs), one of the most widely used dietary supplements on the CAM market. Omega-3 fatty acids are classified as essential PUFAs because they cannot be synthesized by humans and thus must be consumed in the diet. The most important bioactive omega-3 PUFAs include the long-chain forms eicosapentaenoic acid (EPA; 20:5ω-3) and docosahexaenoic acid (DHA; 22:6ω-3), predominantly found in fish and fish oils. EPA and DHA play a vital role in cellular membranes, maintaining fluidity, protein, and cellular functions, as well as influencing eicosanoid metabolism, gene expression, and cell signaling.[5] In addition, endogenous EPA and DHA levels are associated with estrogen status and serotonin metabolism.[6–8] Therefore, this review investigates the efficacy of EPA and DHA supplementation for common symptoms of the menopausal transition.

Depression

Depression is a chronic and recurrent illness twice as prevalent in women as in men.[9] Moreover, women are particularly susceptible to psychological distress and depressive symptoms during the menopausal transition and early menopause.[10] More than 20% of women will experience a major depressive disorder during their lifetime, with 15% to 18% of perimenopausal women and 8% to 12% of premenopausal women affected by persistent mood symptoms.[9,11,12] Antidepressant medication effectiveness is directly correlated with the severity of depression symptoms, with minimal or no effect in patients with mild or moderate symptoms, and an observed 19% to 34% of patients failing to respond to medications.[13,14] Moreover, in the Women's Health Initiative prospective cohort study of 136,293 community-dwelling postmenopausal women investigating antidepressant use and the risk of incident cardiovascular morbidity and mortality, selective serotonin reuptake inhibitor (SSRI) use was associated with increased stroke risk (HR = 1.45; 95% CI: 1.08–1.97) and all-cause mortality (HR = 1.32; 95% CI: 1.10–1.59), and tricyclic antidepressant use was associated with increased risk of all-cause mortality (HR = 1.67; 95% CI: 1.33–2.09).[15] Considering this, CAM treatment is necessary, particularly in menopausal depression.

Observational studies reported an increased prevalence of depression associated with decreased concentrations of EPA, DHA, or both in cell membranes or plasma.[16,17] Mechanistically, incorporation of EPA and DHA in neuronal membranes decreases the reuptake rate of serotonin, similar to the effects of SSRIs.[7,8] Low plasma DHA levels have been shown to be associated with low levels of 5-hydroxytryptamine (or serotonin) and the pathophysiology of depression and impulsive behavior.[18] In addition, oral estrogen therapy results in an upregulation of endogenous conversion of alpha-linolenic acid (ALA; 18:3ω-3) to DHA, resulting in increased EPA and DHA plasma concentrations, and may contribute to a role in antidepressant effects.[19]

In a small preliminary open trial, Freeman et al. investigated the effects of omega-3 supplementation for major depressive disorder associated with the menopausal transition.[19] After 8 weeks, supplementing with 2 g/day omega-3 capsules (providing 930 mg ethyl-EPA + 750 mg ethyl-DHA daily) resulted in a

56% decrease in the Montgomery-Åsberg Depression Rating Scale (MADRS; $p < 0.0001$), with 14 of 20 women having their MADRS score decrease by 50% or more. In a study of 60 outpatient men and women, supplementing 1000 mg of EPA or 20 mg fluoxetine for 8 weeks demonstrated equal therapeutic effects in major depression disorders, with response rates of 50%, 56%, and 81% in the fluoxetine, EPA, and combination (fluoxetine + EPA) groups, respectively.[20] A recent meta-analysis of 8 double-blind, randomized, controlled trials reported that the combination of EPA and DHA as monotherapy (range of EPA+DHA supplementation from 1.2 to 6.6 g/d; average daily dose of ~3 g EPA+DHA) for 8 weeks effectively treated depression in women as compared with placebo (0.65; 95% CI =0.18–1.12, $p = 0.007$).[21] Of interest, 7 of the 8 studies used a higher dose of EPA than DHA (approximately 2:1 ratio of EPA:DHA in 5 of the trials).

DHA is structurally the most abundant omega-3 long-chain PUFA in the brain, comprising approximately 40% of all PUFAs in the brain.[22] Therefore, one might assume that supplementing the major structural component of neuronal membranes, being DHA, would exert the most beneficial effect on brain function and depression. However, supplementation with higher concentrations of EPA over DHA has been shown to be responsible for the efficacy of omega-3 long-chain PUFA supplementation in depression.[23] A meta-analysis by Martins et al. reported a significant reduction in depression symptoms in studies of supplementing more than 50% EPA or using pure ethyl-EPA, whereas supplements containing more than 50% DHA or pure DHA were ineffective.[23] The authors proposed that the cell signaling mechanisms of EPA might explain the enhanced efficacy over DHA in depression. EPA increases the production of anti-inflammatory eicosanoids, decreases the secretion of pro-inflammatory cytokines (i.e., tumor necrosis factor [TNF]-α, interleukin[IL]-6, IL-1β) via inhibition of nuclear factor (NF)-κB, decreases mitochondrial membrane permeability, prevents cytochrome C release, and decreases neuronal apoptosis.[23]

With respect to clinical efficacy, subgroup analyses by Martins et al. demonstrated improved efficacy for major depression versus mild-to-moderate depression, therapeutic versus preventative intervention, adjunctive versus monotherapy, and supplement type, with higher EPA showing significant improvements.[23] Supplements containing EPA (≥60%) in excess of DHA, with a suggested daily dose of ≥1g EPA, provide optimal efficacy for primary depression,a primary symptom of the menopausal transition.[23–25]

Hot Flashes

Hot flashes, as well as night sweats, are one of the most frequent and distressing vasomotor symptoms of the menopausal transition. Hot flashes, or hot flushes, are primarily characterized by a subjective heat sensation, including sweating, cutaneous vasodilatation, increased heart rate, and an associated drop in core temperature.[1] Approximately 80% of all women are affected by hot flashes, with 40% of women pursuing medical care due to the severity of symptoms.[2,3] Hot flashes are a physical symptom reflecting the brain's sensitivity to the changes in the hormonal environment during the menopausal transition, namely the rapid decline in estrogen levels.[26] In addition, there is a direct correlation between women who suffer from hot flashes during the menopausal transition and a greater risk of developing a major depressive disorder.[27] Perimenopausal women, but not postmenopausal, experiencing vasomotor symptoms are 4.39 times more likely to be depressed than those without vasomotor symptoms (95% CI, 1.40–13.83).[26] In light of potential risks of hormonal interventions and bothersome side effects of SSRIs, many women pursue CAM treatments for vasomotor symptoms. EPA and DHA alter serotonin transmission, similar to that of SSRIs, and therefore may effectively reduce vasomotor symptoms, namely the frequency and intensity of hot flashes.[2,7,8,28]

Campagnoli et al. first observed the beneficial effects of polyunsaturated fatty acids on hot flushes in women.[29] PUFA supplementation (providing 400 mg fish oil (30% EPA plus 20% DHA), 100 mg borage oil (20% GLA) and a mix of 15 mg vitamin E, and 25 mg of policosanols plus lipoic acid) twice daily in addition to either 60 mg/d isoflavones or placebo for 24 weeks reduced the number of moderate-to-severe hot flashes by 28.3 to 38.5% ($p < 0.05$) in 29 women (age 51 ± 5 years). The effects of PUFA supplementation on vasomotor symptoms were independent of isoflavone or placebo supplementation. The authors concluded, "PUFAs, particularly omega-3 fatty acids, could reduce hot flushes through their influence on neuronal membranes and/or the modulation of the neurotransmitter function and the serotoninergic system."[29]

Similarly, Lucas et al. investigated the effects of ethyl-EPA supplementation (1005 mg ethyl-EPA + 150 mg ethyl-DHA per day) on the frequency and intensity of hot flashes and quality of life scores in 120 emotionally distressed middle-aged women (40–55 years of age) with hot flashes using a double-blind, placebo-controlled, randomized clinical trial.[1] The average number of hot flashes was 2.8 per day at baseline. After 8 weeks, hot flash frequency decreased by a mean of 1.58 per day (95% CI, −2.18 to −0.98) corresponding to a significant 55% decrease in the ethyl-EPA group, compared with a mean decrease of 0.50 per day (95% CI, −1.20 to 0.20) or 25% decrease in the placebo group. There was a significant reduction in hot flash score (frequency × intensity) in the ethyl-EPA group compared with placebo; however, no change in hot flash intensity between groups. Menopause-Specific Quality of Life scores improved with both groups, however, was not significantly different between groups at end point.

In a preliminary open trial, Freeman et al. observed a reduction in the number of daily hot flashes and 24-hour hot flash scores (frequency and severity) with supplementation of 2 g/d omega-3 fatty acids (930 mg/d EPA + 750 mg/d DHA) for 8 weeks in 15 menopausal women.[19] However, a follow-up study by the same research group using a 12-week randomized placebo controlled trial observed no effect of 1.8 g/day (1275 mg EPA + 300 mg DHA) of fish oil supplementation ($n = 177$) for the reduction in frequency or bother of vasomotor symptoms in peri- and postmenopausal women compared with an olive oil placebo ($n = 178$).[30] Therefore, due to the limited number of studies to date, more high-quality

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randomized controlled trials are needed to substantiate the efficacy of omega-3 long-chain PUFA for vasomotor symptom relief.

Hypertriglyceridemia and Cardiovascular Risk

Cardiovascular disease (CVD) is the leading cause of death in women worldwide, particularly postmenopausal women.[31] Estrogen loss plays a major role in the increased risk of CVD.[32] However, hormone replacement therapy has not been shown to be effective in reducing CVD risk in postmenopausal women and is associated with an increase risk of stroke and venous thromboembolic events; and questions remain as to the long-term effects in perimenopausal women.[33–35] Cardiovascular symptoms of menopause include increased heart rate, heart pounding or racing, irregular heartbeat, arrhythmias, atrial fibrillation, and blood lipid levels. Moreover, triglycerides (TG) are higher in postmenopausal women compared with premenopausal women, and increase blood TG levels occurs particularly in women receiving oral estrogen therapy, but not transdermal estrogen.[36,37]

Omega-3 fatty acids can reduce TG levels by up to 45% in patients with severe hypertriglyceridemia (TGs ≥ 500 mg/dL).[36] Monitoring the lipid profile during the menopausal transition is critical and omega-3 EPA+DHA supplementation offer a well-tolerated option for hypertriglyceridemia. A randomized, double-blind, placebo-controlled crossover trial investigated the effects of 2.8 g/d of DHA for 4 weeks in postmenopausal women receiving and not receiving hormone replacement therapy.[38] In all women, regardless of hormone replacement therapy status, DHA supplementation resulted in a 20% decrease in TG, 8% increase in HDL-C, 28% decrease in the TG:HDL-C ratio, and a 7% decrease in heart rate as compared with placebo.

Mozaffarian and Wu reviewed the individual cardiovascular effects of EPA and DHA from human studies.[39] With respect to physiological risk factors, both EPA and DHA decreased TG levels, whereas EPA decreased HDL3 cholesterol and DHA increased LDL particle size and HDL2 cholesterol. In addition, DHA decreased blood pressure and heart rate, whereas EPA had minimal blood pressure effects and no clear effect on heart rate. For clinical endpoints, DHA reduced risk of atrial fibrillation and fatal CHD or sudden death, whereas EPA reduced risk of nonfatal coronary syndromes and congestive heart failure. The authors concluded, "the present evidence suggests that EPA and DHA have both shared and complementary benefits. Based on current evidence, increasing consumption of either would be advantageous compared to little or no consumption".[39]

The American Heart Association guidelines for the prevention of coronary heart disease in women recommends supplementation of omega-3 PUFAs to provide 850 to 1000 mg of EPA plus DHA daily, and higher doses of 2 to 4 g of EPA plus DHA daily for the treatment of women with high triglyceride levels.[40] Antiarrhythmic effects may be achieved with 500 to 1000 mg EPA + DHA per day.[41]

Joint Health

Over half of peri- and postmenopausal women experience some degree of joint pain and inflammation, fueled by a decline in estrogen levels and corresponding low serotonin levels.[2,42] *Menopause arthritis* is another term for joint pain during menopause; can affect the knees, hips, back, neck, shoulders and extremities; and may be associated with osteoporosis. Omega-3 EPA and DHA are effective in decreasing joint swelling and pain, tender joints, duration of morning stiffness, patients assessments of pain, and use of nonsteroidal anti-inflammatory drugs (NSAIDs).[43] Mechanistically, EPA and DHA provide immune-modulating and anti-inflammatory action (inhibit the production of prostaglandin [PG] E2 and leukotriene [LT]B4), promote the resolution of inflammation through production of resolvins and protectins, and reduce the production of inflammatory cytokines (i.e., IL-1β, IL-6, and TNF-α).[43]

In a study of 125 patients with nonsurgical neck or back pain, supplementation of 1200 mg to 2400 mg EPA+DHA for an average of 75 days resulted in a 59% reduction in NSAID and pain medicine use and a 60% improvement in joint pain, with 80% patient satisfaction and no significant side effects.[44] Research has substantiated the beneficial effects of EPA plus DHA on symptoms of arthritis. Results from meta-analysis suggest supplementing with >2.7 g/day of omega-3 EPA + DHA for >3 months, specifically in the reduction of NSAID consumption in rheumatoid arthritis patients, as well as improvements in tender joint count, swollen joints, morning stiffness, and physical function.[45,46] While the majority of clinical studies surround efficacy of EPA plus DHA for joint health in male and female patients, results may be extrapolated to the menopausal women.

Dry Eye Syndrome

Changes in hormonal balance during the menopausal transition are associated with a reduction in tear production and the onset of dry eye syndrome (DES). Patients with DES may experience a reduction of the quantity and quality of tears, an unstable tear film, ocular surface damage, and ocular symptoms such as irritation, dryness, fatigue, and variable visual disturbances.[47] DES affects approximately 7.8% of women 50 years or older in the US, compared with 4.7% of men.[47] Extended periods of dry eye is associated with inflammation of the ocular surface. Due to the role that omega-3 EPA and DHA play in modifying the inflammatory process, much interest surrounds the use of omega-3 supplementation in the treatment of DES.

Currently, there are no clinical trials that investigate the effects of omega-3 PUFA supplementation on DES in peri- or postmenopausal women only. However, in a small randomized controlled trial, Kawakita et al. assigned either fish oil supplementation (1245 mg EPA plus 540 mg DHA daily) (n = 15) or placebo (n = 12) to patients with DES.[48] After 12 weeks, there was a significant improvement in eye pain subjective symptoms and measures of tear stability with fish oil supplementation compared with placebo. Results suggest that fish oil supplementation accelerates

recovery and effectively treats DES. While Wojtowicz et al. did not observe a change in tear stability, supplementation of omega-3 fatty acids (450 mg EPA, 300 mg DHA, and 100 mg flaxseed oil daily) for 90 days increased the average tear production and tear volume in 36 patients with DES compared with placebo.[49] In addition, 70% of patients supplementing with omega-3 fatty acids became asymptomatic at the end of the study, compared with 7% in the placebo group. A short-term study supplementing 180 mg EPA plus 120 mg DHA twice daily for 30 days observed a 71% improvement in tear evaporation, a 26% improvement in dry eye symptoms, and a 22% improvement in measures of tear secretion, results significantly better than the placebo group.[50] Therefore, EPA plus DHA supplementation shows much promise for effectiveness in DES in the menopausal transition.

Conclusion

The research reviewed supports the use of omega-3 PUFAs, specifically EPA and DHA, as effective CAM for symptom relief in the menopausal transition. More specifically, women who are experiencing depression should supplement with higher levels of EPA to DHA and target a minimum daily dose of 1 g EPA for optimal efficacy. While daily supplementation of >3 g/d of EPA plus DHA are ideal for hypertriglyceridemia and joint health, more research is needed to substantiate the efficacy and optimal dose for hot flashes and dry eye syndrome in perimenopausal women. Inclusion of a high-quality fish oil supplement, providing targeted doses of EPA and DHA, in a patient's treatment protocol may provide synergistic benefits and improve quality of life during the menopausal transition.

Notes

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Study of Insulin Responses to Carbohydrate and Noncarbohydrate Challenges In Insulin-Based Care of Metabolic Disorders

by Majid Ali, MD; Sabitha Dasoju, MB, BS; Naila Karim, MD; J. Amin; and Daawar Chaudhry

We present our initial experience with measurements of insulin responses to carbohydrate and noncarbohydrate challenges for patient education and improved compliance to insulin-focused integrative plans for insulin modification and reversal of diabetes type 2. Predominantly carbohydrate meals produce blood glucose spikes, which trigger insulin spikes. Such changes are not observed with predominantly noncarbohydrate meals. Measurements of such insulin responses, designated insulin responses ratio (IRR), provide for insights into the meal–insulin dynamics and a deeper understanding of crank-and-crankshaft model of insulin receptor dysfunction and its clinical significance.[1-6]

The study included 30 consecutive adult patients with chronic metabolic, inflammatory-immune, and degenerative disorders who underwent IRR testing. The study data, though limited, offer an opportunity to assess the benefits of insulin-focused patient education and care, shifting from the prevailing glucose-focused clinical discourse.

Table 1: Insulin and Glucose Profiles with Insulin Responses to 75 Gram Glucose (Upper) and 300-Calorie Noncarbohydrate (Lower) Challenges of a 52-Year-Old 5' 2" Woman Weighing 228 Lbs. Presenting with Recurrent Sinusitis, Hypothyroidism, Chronic Fatigue, and Urticaria

	Fasting	1 Hr	2 Hrs	3 Hrs
Insulin	6	50	50	10
Glucose	85	92	87	52
Insulin and Glucose Responses to a 300-Calorie Noncarbohydrate Load				
	Fasting	**1 Hr**	**Insulin Responses Ratio (IRR)**	
Insulin	14	20	2.5	
Glucose	97	83		

Table 2: Insulin and Glucose Profiles with Insulin Responses to 75 Gram Glucose (Upper) and 300-Calorie Noncarbohydrate (Lower) Challenges of a 71 Year-Old 5'2" Woman Weighing 175 Lbs. Presenting with Rapid Weight Gain, Hypothyroidism, and Prehypertension

	Fasting	1 Hr	2 Hrs	3 Hrs
Insulin	5.8	60.1	36.3	53
Glucose	87	91	76	51
Insulin and Glucose Responses to a 300-Calorie Noncarbohydrate Load				
	Fasting	**1 Hr**	**Insulin Responses Ratio (IRR)**	
Insulin	4.73	17.7	3.3	
Glucose	98	98		

The study data also allow exploration of any relationship that might exist between increasing IRR values and worsening degrees of hyperinsulinism and diabetes type 2. Specifically, what light, if any, might such a relationship shed on insulin receptor and pancreatic beta cell dynamics that would deepen patients' understanding of insulin homeostasis in health and disease?

The term *insulin responses ratio* (IRR) was coined by one of the authors (MA) for the ratio between blood insulin concentrations measured 1 hour after 75 grams of glucose and a 300-calorie noncarbohydrate load.[7] We used protein powder, lecithin, ground flaxseed, and organic vegetable juice for the 300-calorie noncarbohydrate load. For some years, we have employed the IRR values for: (1) an initial assessment of insulin homeostasis status of the patient; (2) a simple, easy-to-understand, and objective metric for patient education; (3) improving the patient compliance to integrative plans for hyperinsulinism modification and diabetes reversal plans; and (4) establishing the crucial importance of insulin homeostasis for health preservation, reversal of chronic diseases, and healthful aging.

Hyperinsulinism modification and reversal of diabetes type 2 require a "food philosophy" based on a deeper understanding of cellular bioenergetics and insulin homeostasis. The necessary dietary, detox, and lifestyle changes for success usually take several months. There is a need for a clear, easy-to-understand metric for the patient's

individualized metabolic responses to fats, proteins, and carbohydrates in the dietary plan. The IRR value seems suitable for this purpose and in our early experience materially improved patient compliance.

Results

Tables 1 through 3 present the results of the IRR test for three patients: first with mild hyperinsulinism, the second with severe hyperinsulinism, and the third with diabetes type 2.

Discussion

From an evolutionary perspective of cellular energy economy, the lowest insulin concentrations associated with unimpaired glucose tolerance can be considered as optimal insulin homeostasis. Therefore, the optimal management of the insulin-resistance-hyperinsulinism-diabetes spectrum should be focused on insulin dynamics. In reality, in the prevailing medical model, insulin resistance and hyperinsulinism are completely ignored. (How can it be different unless proper insulin testing is done?) As for diabetes type 2, it is treated with drugs that lower blood glucose levels by increasing insulin activity. So, the treatment compounds the underlying problems of hyperinsulinism.

Shifting from Sugar-Talk to Insulin Conversations

As discussed at length in previous publications from our center, hyperinsulinism modification and reversal of diabetes type 2 requires "insulin conversations."[1-9] Within this broader context, there are the matters of dietary, environmental, detox, and spiritual components of integrative plans focused on restoring insulin receptor function, beta cell dynamics, and related aspects of insulin homeostasis. We introduced IRR measurements in our clinical practice in order to expand the range of such conversations, underscoring the need for a shift away from "sugar problems."

Patient Rating of the IRR Test

We expected that explanation of the mechanics of the IRR test and the effort required to complete the study would deepen the patient's interest in learning about insulin dynamics in health, hyperinsulinism, and diabetes type 2. This indeed was the case. A comparative study of a patient's glucose and insulin profiles with selected examples from our IRR files allowed us to discuss in simple terms the matters of the pathogenesis and reversal of the hyperinsulinism-diabetes continuum with improved patient compliance.

In actual practice in the study, the IRR data were discussed with patients in two successive visits and they were given appropriate write-ups and lent DVDs on the subject suitable for home study. In the third visit, patients were asked to rate the value of the test in: (1) understanding the relationships between types of foods consumed and the blood sugar and insulin responses; and (2) its influence on their food choices. Only 4 of 30 patients asked

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Table 3: Insulin and Glucose Profiles with Insulin Responses to 75 Gram Glucose (Upper) And 300-Calorie Noncarbohydrate (Lower) Challenges of a 72-Year-Old 5' 6" Woman Weighing 165 Lbs. Presenting with Diabetes, Hypertension, Arthritis

	Fasting	1 Hr	2 Hrs	3 Hrs
Insulin	35	65	55	55
Glucose	155	236	305	281
Insulin and Glucose Responses to a 300-Calorie Noncarbohydrate Load				
4/27/14	Fasting	1 Hr	2 Hrs	IRR
Insulin	7.4	N/D	9.7	6.7
Glucose	155		174	

Table 4: Distribution of IRR Values of 18 Patients In 3 Groups with Peak Blood Insulin Concentrations (In uIU/mL) of: (1) up to 60; (2) 61 to 200; (3) over 200

Patient #	Peak Glucose (mg/dL)	Peak Insulin Post Glucose (uIU/mL)	Peak Insulin Post Nonglucose (uIU/mL)	IRR	Major Diagnoses
1	78	18.1	<2	9	Allergy, IBS, Eczema
2	100	24.6	7.8	3.1	GERD, Anxiety, Fatigue, Allergy
3	146	51.1	21.86	4.2	Atrial Fibrillation, CFS, BPH
4	117	38.3	11.0	3.4	Colitis, Fatigue, Arthralgia. Allergy
5	82	49	<2	1.7	GERD, Anxiety, Fatigue, Sinusitis
6	82	48	<2	1.7	Allergy, Myalgia. Headache
7	131	37.7	15.3	3.5	Anxiety, Mold Allergy, Headache
8	163	54	9.2	3.0	Allergy, Memory loss, UTI
9	178	54.6	17.7	3.2	Hypothyroid, Prehypertension
10	92	50	10	5	Sinusitis, Urticaria, Hypothyroidism
Insulin Category 2 with Peak Insulin Concentration Between 60 and 200 uIU/mL, Mean IRR 8.2					
1	87	69	6	11.5	Colitis, Cystitis, Hypothyroidism
2	81	69	7	10	Rosacea, Eczema, Fatigue, Hypothyroidism, Backache
3	136	86.7	5.6	15.5	Neuropathy, Fatigue, Hypertension
4	161	125	23.5	5.3	Neuropathy, Hypertension, CAD* Allergy
5	165	132	44	5.3	CAD,* Hepatitis C, Neuropathy
6	178	84.7	25	2.1	Weight gain, Neuropathy, Eczema
Insulin Category 3 with Peak Concentration Over 200 uIU/mL, Mean IRR 3.0					
1	109	218	87.2	2.5	Diabetes, Anxiety, Hypertension,
2	112	230	63	3.5	Weight Gain, Fatty Liver, Neuropathy

* Coronary Artery Disease

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for further clarification of the test in subsequent visits.

Dietary Plans for Insulin Modification

In our experience, the prevailing notion of counting calories, caloric intake of various food items is not the critical issue in hyperinsulinism modification and diabetes reversal. Rather, attention should be focused on: (1) how different foods in different combinations create sugar spikes with consequent insulin spikes; and (2) how such spikes create undesirable hunger responses, as well as sugar and carbohydrate craving. Specifically, what is needed is the knowledge of how the healthy fats and proteins can be combined with limited amounts of carbohydrates and fruits to prevent or attenuate sugar and insulin spiking. For example, a slice of toast generates a sugar spike but not when it is eaten with an egg. A snack of blueberries, notwithstanding the benefits of berries, generates sugar and insulin spikes, which can be prevented or attenuated when cheese is added to the snack.

Correlation of IRR Value with Degree of Hyperinsulinism

The data in Tables 1 through 3 suggest a correlation between increasing degrees of hyperinsulinism and rising IRR values. This correlation is supported by additional data presented in Tables 4 and 5. In Table 4, mean IRR values in insulin groups 1 and 2 (low-insulin and moderate-insulin groups) are 3.8 and 8.2 respectively. The mean IRR value of the diabetes group of 7 is consistent with the relationship between the carbohydrate and noncarbohydrate responses. The low (3) IRR value in the third insulin group (only 2 patients with extreme hyperinsulinism) is not consistent and may point to as yet unrecognized aspect of such hyperinsulinism. Clearly no inferences can be drawn from just two case studies.

To our knowledge, no studies of relationship between insulin responses to carbohydrate and noncarbohydrate responses have been reported. However, this correlation is not unexpected in light of the crank-and-crankshaft model of insulin resistance and hyperinsulinism – the greater the resistance of insulin receptor embedded in the cell membrane, the larger the expected differential between insulin responses to glucose and noncarbohydrate challenges.[1]

Glycemic Index

The knowledge of glycemic indices of foods and glycemic loads of meals are very valuable for the general education of the patient. However, these values do not reveal anything about the insulin homeostasis status of the patient, which must be the focus in reversing hyperinsulinism and diabetes.

The value of glycemic indices in metabolic studies has been decried by some influential writers. To cite one recent example, consider the following telling text from the conclusion section of a recent *JAMA* report on the subject of glycemic index: "In this 5-week controlled feeding study, diets with low glycemic index of dietary carbohydrates, compared with high glycemic index of dietary carbohydrates, did not result in improvements in insulin sensitivity, lipid levels, or systolic blood pressure. In the context of an overall DASH-type diet, using glycemic index to select specific foods may not improve cardiovascular risk factors or insulin resistance."[10]

Many readers of *Townsend Letter* who practice integrated healing arts use glycemic indices and glycemic loads in their clinical work. Such readers might be chagrined by the above citation of the 2014 Harvard study that clearly challenges their use of the index. They are likely to ask, how can any serious student of human nutrition and insulin homeostasis ever think that a mere 5-week study of obese individuals with hypertension (as described in the paper) will yield useful data about the benefits of the use of glycemic indices of foods? For the amusement of such *Townsend* readers, we include below an excerpt from an op-ed article published in the *New York Times* on February 21, 2015[11]:

Bad Diet Advice – for Decades

The article was titled "The Government's Bad Diet Advice." It would have been more appropriate if were titled "Harvard School of Public Health Bad Diet Advice – for Decades." No, we do not take a cheap shot at Harvard here. Consider this text from the same article of the *New York Times*: "Much of the epidemiological data underpinning the government's dietary advice comes from studies run by Harvard's School of Public Health. In 2011, directors of the National Institute of Statistical Sciences analyzed many of Harvard's most important findings and found

Table 5: Distribution of IRR Values of 18 Patients with Diabetes Type 2. Blood Glucose and Insulin Values Are Expressed in mg/dL and uIU/mL respectively. Mean IRR 7.0

Patient	Peak Glucose	Peak Insulin Post -Glucose	Peak Insulin Post Non-Glucose	IRR	Major Diagnoses
1	399	29.5	15.5	2.3	Diabetes Type 2, CAD,* Hypertension, Fatigue, Leg edema
2	334	57	24	2.3	Diabetes , Cancer Prostate, GERD
3	326	44.9	4.6	7.3	Diabetes Type 2, CAD,* Arthritis,
4	313	79	5.6	15.5	Diabetes Type 2, CAD,* Blood creatinine 2.6mg/dL
5	305	65	9.7	6.7	Diabetes Type 2, Hypertension, arthritis
6	242	41	3.3	12.4	Diabetes, Prehypertension, Obesity
7	217	100	29.5	3.4	Diabetes Type 2, Headache, Prehypertension
8	213	125	23.5	5.3	Diabetes, Type 2 Colonic Diverticulitis, IBS
9	205	119	14.8	8.0	Diabetes Type 2, CAD*, Hypertension, Hepatic Steatosis, and Neuropathy

that they could not be reproduced in clinical trials. ... It's no surprise that longstanding nutritional guidelines are now being challenged."

Statistical Sciences analyzed many of Harvard's most important findings and found that they could not be reproduced in clinical trials!

The *Times* here is being politically polite; it could have been forthright and stated that Harvard has done a great disservice and should come clean by publically apologizing for having misled the American people for decades.

In closing, hyperinsulinism modification and reversal of diabetes type 2 require a degree of insulin literacy for designing dietary, environmental, detox, and spiritual guidelines for individual patients. There is a need for a clear, easy-to-understand metric for the patient's individualized metabolic responses to fats, proteins, and carbohydrates in the dietary plan. The IRR value, an objective, quantifiable, and modifiable parameter, seems suitable for this purpose. In our early experience, it materially improved patient compliance.

Notes

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Updates on the Treatment of Drug Addiction

by Carolyn Ross, MD, MPH

Mark presented in my office in withdrawal from opiate use disorder (heroin). He reported using up to 2 grams a day of heroin intravenously. His opiate use disorder began when he was 18, when he was injured in a football game and had to have shoulder surgery. He felt really good right away when taking Percocet. After his doctor stopped prescribing the prescription pain pill, he started buying it on the street. Three years later, he had escalated to using heroin, which was cheaper than Percocet. He had missed his chance to go to college on scholarship. He had served 6 months in jail for possession and he had been to one rehab facility, staying clean only 1 month after discharge. His parents were frustrated and angry that he could not stop using heroin. They had kicked him out of the house multiple times, but their fears of losing him meant that he kept getting back into their good graces, even if only for a month – until once again he would steal from them or relapse. Mark's withdrawals included sweats, chills, goosebumps, runny nose and tearing eyes, nausea, tremors, dilated pupils, anxiety, and irritability. He wanted help but he also felt hopeless.

Mark's story is not an uncommon one in my office, where I treat addictions, eating disorders, and mood and anxiety disorders. Opiate addiction in particular has become an epidemic in certain parts of the US. Addiction to prescription pain pills such as Percocet, Oxycontin, hydrocodone, Norco, and others has skyrocketed, with 4.3 million Americans abusing prescription pain pills in the last month. Most (50.5%) get their pain pills from a friend or relative and some (22.1%) get them from a doctor. Heroin is a powerful opiate drug that is cut or diluted with sugar, starch, powdered milk, quinine, or other drugs before snorting, injecting, or smoking. There are 4.8 million Americans who have used heroin in their lifetime. Over 200,000 people over age 12 have used heroin for the first time in the past year and over 400,000 people were regular users of heroin at the end of 2015.

It is not uncommon that individuals with substance use disorders will also have some type of mental illness. They are called "dual diagnosis" clients. Almost 8 million adults are in this category. Often symptoms of the mental health disorder are masked by substance use. It is important to address both disorders and to screen for other cooccurring disorders such as attention-deficit/hyperactivity disorder, trauma, posttraumatic stress disorder, and eating disorders when you treat a patient with a substance use disorder. People with substance use disorders also suffer from nutrient deficiencies, insomnia, and problems with digestion. Therefore, an integrative approach to treating substance use disorders and

their cooccurring diagnoses is very important. The 8 Cornerstones of an Integrative Medicine Approach to treating addictions and other mental health disorders will give you a good overview of what a whole-person approach might look like:

1. Make a complete diagnosis by taking a complete history and using screening tests to identify cooccurring diagnoses.
2. Consider whether prescription medication is needed for stabilization of the patient.
3. Use integrative therapies to help with body-mind integration, emotional release, and deeper healing.
4. Teach patients new skills to cope with their stress and to regulate their emotions to reduce the risk of relapse.
5. Identify nutritional deficiencies and evaluate gut health.
6. Recommend psychotherapy to help patients gain insight into their behaviors and get at the root causes of their disorder.
7. Have patients use supplements to replace missing nutrients, support mood, and improve gut health.
8. Encourage physical activity to reconnect with body cues and to learn healthy, stress-reducing coping skills.

Unfortunately, in the space of this article, I will not be able to cover each of these Cornerstones. For more information, you can refer to my book, *The Binge Eating and Compulsive Overeating Workbook* (New Harbinger; 2008). I would like to mention that if you are thinking that many of these Cornerstones are not in your wheelhouse, you should consider having a team of people you could refer to who can help you treat the whole person. Your team may include an acupuncturist, nutritionist or dietician, chiropractor, therapist, psychologist, and others. Begin slowly and over time assess what you can do and what needs to be referred to other experts.

In the section below, I will cover some of the cornerstones that might help you to initiate a treatment plan for some of the complex patients whom you may see with addictions.

Make a complete diagnosis by taking a complete history and using screening tests to identify cooccurring diagnoses.

To screen your patients for substance use disorders (SUD) and other co-occurring disorders, there are a few very short screening tests that you can use. They can easily be included in your patient history form[1,2]:

Screening for SUD

1. Do you sometimes drink beer, wine or other alcoholic beverages?
   ❑ Yes ❑ No
2. How many times in the past year have you have 5 (for men)/4 (for women) or more drinks in a day?

   _____
3. How many times in the past year have you used an illegal drug or a prescription medication for nonmedical reasons?

   _____

Simple Screen for Depression

In the past 2 weeks, how often have you been bothered by any of the following problems:

1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless

Scoring: 0 for not at all, 1 for several days, 2 for more than half the days, and 3 for nearly every day. The screen is positive if the client scores 3 or more points.

Screening for Eating Disorders[3]

1. How many diets have you been on in the past year?
2. Do you think you should be dieting?
3. Are you dissatisfied with your body size?
4. Does your weight affect the way you think about yourself?

A positive response to any of these questions warrants further evaluation. This may require you to refer the patient to a therapist or other provider who specializes in eating disorders.

Consider whether prescription medication is needed for stabilization of the patient.

It is important to be aware of the medications that are available for treating SUD and to know something about how they are used. The primary medications used in treating opiate use disorder are Suboxone and methadone. Both are used for detoxification from heroin or prescription pain pills and also used for opiate replacement/ maintenance therapy. Suboxone is the newer of the two, the most well tolerated by patients, and rapidly becoming the first choice for opiate replacement therapy. This medication has literally saved lives of people who relapse repeatedly and are unable to deal with the cravings and obsessive thoughts about using drugs that lead to relapse. Methadone is a full opiate agonist, and overdose-related deaths due to respiratory depression are a significant concern. Suboxone is a combination of the partial opiate agonist buprenorphine and the opiate blocker naloxone. Because of its weak activity as an opiate agonist, it does not give the same euphoria or analgesia that methadone does. It causes less dysphoria than methadone and is better tolerated for this reason by patients. People with opiate use disorder who use opiates while taking Suboxone won't get a high, and this could lead to overuse of opiates that can lead to overdose. Opiates should not be prescribed to people taking Suboxone unless they are off Suboxone for at least 2 or 3 days. Overall overdose potential is much lower with Suboxone. Suboxone has been a lifesaver to many opiate addicts because, if it is dosed correctly, people feel "normal" and are free of cravings and thoughts of using drugs, allowing them to stay in recovery longer without having to constantly fight cravings to use.

For alcoholics, naltrexone (an opiate blocker) in oral (Revia) or intramuscular (Vivitrol) form has some evidence of efficacy by reducing the desire to drink alcohol and decreasing heavy drinking.[4] It may be a good adjunct to treating someone with alcoholism, for

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example, in conjunction with Twelve-Step meetings, therapy sessions, and other modalities. Naltrexone has also been used more recently for treatment of opiate use disorder. Opiate users have to be opiate-free for 10 days before using naltrexone or they will go into withdrawals. There is less evidence of the efficacy of naltrexone alone for opiate use disorder. However, the injectable Vivitrol form does offer 30-day coverage that is attractive to some.

Other uses of prescription medications could include the use of antidepressants and/or mood stabilizers, especially in individuals with bipolar disorder and those with depression who are unable to function. Discussion of these medications is beyond the scope of this article.

Identify nutritional deficiencies.

Alcohol is one of the major causes of nutritional deficiency in the US. It can account for up to 50% of dietary caloric intake and lead to deficiencies in B vitamins and vitamins C, K, A, and D. Other deficiencies include calcium, phosphorus, and magnesium. These deficiencies can lead to anemia, high or low blood glucose levels, decreased ability to produce neurotransmitters in the brain, and subsequent substance-induced mood disorders and other neurological disorders, including Wernicke/Korsakoff syndrome. Alcoholics also suffer from poor digestion and absorption of nutrients due to inflammation in the gut. If alcohol intake represents at least 25% of total calories, there can be significant decreases in carbohydrate, protein, and fat intake.[5]

Chronic marijuana use and "huffing," or glue sniffing, can lead to zinc deficiency that affects smell and taste and the metabolism of the omega-3 fatty acids. Chronic dieters can also be zinc deficient. Zinc deficiency is also associated with depression and poor appetite. Cocaine abuse can lead to deficiencies in B vitamins and vitamin C. Stimulants can also cause loss of appetite, and many stimulant addicts are underweight and undernourished.[6]

Individuals with SUD who also have eating disorders can have nutritional deficits, including B vitamins, vitamins D, C, and E, calcium, copper, and essential fatty acids.

Alcohol and other substance use disorders and eating disorders are all associated with abnormal glucose metabolism. Dips in blood sugar can lead to depression, anxiety, moodiness, and cravings to use drugs, drink, or overeat.[7] It is important to replace missing nutrients, stabilize blood sugar, support mood, and help heal the gut and brain in a targeted nutritional approach to treating these individuals.

Testing for nutritional deficits can be done through SpectraCell. Several studies have demonstrated a correlation between nutrition education and therapy during recovery and improved outcomes for individuals with substance use disorders.[8]

Use supplements to replace missing nutrients, support mood, and improve gut health.

Supplements can be used to replace missing nutrients detailed in the section above, to offer mood support and to treat depression and anxiety. Supplements can also be used to help improve gut health and brain health.

Once stable, some but not all of these patients may be treated with natural therapies for depression and anxiety. The regimen for mood support includes the use of the following supplements for maintenance therapy:

- Vitamin D – In alcoholics, serum vitamin D levels below 30 ng/ml are associated with greater long-term mortality.[9] Vitamin D deficiency can be associated with musculoskeletal pain syndromes (such as fibromyalgia), depression and other mood disorders, loss of bone density (which people with eating disorders and alcohol use disorders are already at higher risk for), and decreased immune function.
- Omega 3 fatty acids – Studies have linked essential fatty acid deficiency to anxiety, relapse, and suicidality. Up to 63% of all completed suicides suffered from substance use disorders.[10] Omega-3 fatty acids have been shown in studies to reduce the risk for suicide. [11] Low intake of omega-3s (DHA) also is associated with higher risk for alcoholic fatty liver in animal models.[12] A higher omega-3 level in substance abusers was associated with decreased anxiety and anger and lower rates of relapse.[13]
- B-complex vitamin – B-vitamins are necessary cofactors in the production of neurotransmitters in the brain. Symptoms of B-vitamin deficiencies can include poor appetite, fatigue, poor sleep, weakness, irritability and depression.

For depression, you can choose one of the supplements below:

- SAMe, a methyl donor that contributes to the synthesis, activation and/or metabolism of such compounds as hormones, neurotransmitters, nucleic acids, proteins, phospholipids, and certain drugs. SAMe is superior to placebo and possibly as effective as prescription antidepressants. Dosages range from 400 to 1600 mg per day given in 2 doses.
- For bipolar disorder, TrueHope's EMPowerplus has been shown in a number of studies to be effective for bipolar disorder, attention deficit disorder, and possibly major depressive disorder.
- 5-HTP – can help with sleep and mood in doses of 100–300 mg daily. 5-HTP is a serotonin precursor so caution should be used when prescribing 5-HTP in individuals who are on an SSRI or taking other serotonin precursors such as L-tryptophan.
- St. John's wort – works mainly on serotonin system. Dosage should be 300 mg three times daily. It is highly effective for mild-moderate depression and the most widely used antidepressant in Europe.

Caution: All of these supplements can trigger mania in individuals with bipolar disorder.

Patient with **anxiety** may benefit from:

- L-theanine 200–400 mg per day as needed
- Valerian – 300–400 mg 2 to 3 times daily

Insomnia can be treated with:

- Melatonin – 1–3 mg at bedtime
- Valerian – 900–1600 mg at bedtime
- Kava-kava tea made from bulk root

Supplements for Individuals with Substance Use Disorders

Here are some other specific nutrients shown in research to have benefits to those with SUD:

1. Taurine: 1 gram 3 times a day reduces the toxic byproducts found in alcohol and may decrease the severity of alcohol withdrawal symptoms. Taurine may also reduce the risk of addiction in cocaine abusers.
2. Acetyl-L-carnitine (2 grams daily) may improve memory in abstinent alcoholics.[14]
3. Co-Q10 may reduce neurotoxicity caused by methamphetamine and cocaine.
4. N-acetyl cysteine (NAC) may reduce cravings for cocaine.[15]

Supplements for Gut and Brain Health

Dysfunctions in the "gut–brain axis" may be involved in a number of metabolic and mental disorders. The gastrointestinal tract has over 100 million neurons and has the second largest collection of neural tissue in the body (after the brain). Stress can affect the homeostasis between the gut-brain and the stress hormone cortisol can increase gut permeability. As well, imbalances in the gut microbiome can produce inflammatory molecules called cytokines that can have a significant effect on brain function, leading to depression, anxiety, and cognitive dysfunction.[16] GI complaints are present in half of individuals with substance use disorders and eating disorders. It is often difficult to distinguish true GI diseases from complaints related to eating disorders, the majority of which resolve with refeeding.[17] Some GI complaints in those with SUD will be resolved with abstinence but this may take time. Supplements can help improve gut function sooner:

1. The use of pancreatic digestive enzymes may be useful in conditions associated with poor digestion, including eating disorders. Digestive enzymes help break down carbohydrates, fat and protein. A small study done in an inpatient eating disorder unit of patients on a combination of a plant-based pancreatic enzyme product and probiotics resulted in a decrease in reports of GI complaints (from 15% to 5%) and a decrease in the use of conventional medications (from 15% to 2%) to treat GI complaints.[18]
2. Constipation is a common side effect in opiate use disorder. The easiest treatment is the daily use of magnesium oxide 400–800 mg at bedtime. This should be taken as a preventive therapy rather than only taken when constipation occurs.
3. Studies in probiotics used in individuals with eating disorders and SUD showed a significant decrease in GI complaints.[19] Probiotics have also been shown to restore bowel flora and improve liver enzymes in alcoholics.[20] Consumption of foods high in probiotics can also improve brain function.[21] Bacteria in probiotics also produce anti-inflammatory cytokines that can have a positive impact on mood. The use of probiotics and a friendly yeast (*Saccharomyces boulardii*) enhance the production of salivary IgA (sIgA) which can be decreased by emotion, frustration and stress. sIgA helps fight inflammation that can cause depression.
4. To reduce inflammatory cytokines, use vitamins C, E, and N-acetyl cysteine, green and black tea, and curcumin.

Brain Healing

Brain-derived neurotrophic factor (BdNF) is a protein that is important for survival of nervous system neurons

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and can serve as a marker of brain health. The more BDNF present, the healthier the brain is. Exposure to the stress hormone cortisol has been shown to decrease BdNF. BdNF regulates the psychological dependence in drug addiction. It is involved in the brain reward circuitry that is negatively affected by drugs of abuse. Stress, smoking, poor sleep, inflammation in the body, and low or high blood sugar all decrease BdNF. Modern foods and the modern lifestyle accelerate brain decay by decreasing BdNF.[22]

A newer supplement for brain healing is the natural product Synaptamine, developed by Ken Blum, who has been a noted researcher and coined the phrase *reward deficiency syndrome* to describe the impulsive and compulsive disorders and personality disorders associated with a decrease in dopamine (DRD2) receptors in the brain.

Synaptamine contains amino acids, cofactors, and vitamins that help improve reward deficiency syndrome. It is unclear at present whether long-term abstinence is better with the use of Synaptamine; however, it has some anecdotal reports of efficacy in detoxing patients from opiates and other drugs. Studies on earlier versions of this product showed efficacy in obese patients who had been on severe calorie-restricted diets (Optifast) in terms of reducing weight regain and binge behavior. This product is available online and shows a lot of promise in helping the brain heal from addictions.

Conclusion

Substance use disorders, particularly opiate use disorder, are a significant problem in our society. An integrative approach to treating SUD and their cooccuring disorders can enhance modalities such as Twelve-Step meetings, psychotherapy, and other approaches. Below are listed a summary of recommendations that form the basis of this approach.

Recommendations

1. Avoid rancid fats and trans fats; use good fats such as olive oil and omega-3-containing foods.
2. Eat more foods that are anti-inflammatory such as fruits, vegetables, nuts, and seeds.
3. Add spices that are anti-inflammatory; e.g., ginger and turmeric.
4. Green and black tea should be part of an anti-inflammatory diet.
5. Consume probiotics: bifidobacteria, lactic acid bacteria, *Saccharomyces boulardii*.
6. Take a good multivitamin and -mineral product to replace missing nutrients and offer antioxidants such as Vitamins C and E as noted above.
7. Support mood with omega-3 fatty acids, a B-complex vitamin, and vitamin D.
8. Consider Synaptamine to help the brain heal.
9. Use specific supplements as listed in this article for insomnia, depression, anxiety, constipation, etc.
10. To increase BdNF:
    a. Exercise regularly.
    b. Keep your blood sugar steady by eating frequent small meals and decreasing your intake of sugary foods and processed foods.
    c. Get enough sleep.
    d. Take omega-3 fatty acids.

Dr. Ross is a nationally known author, speaker, and expert in the field of eating disorders and integrative medicine. She went to the University of Michigan Medical School, completed a residency in preventive medicine at Loma Linda University, and set up practice in San Diego, California, where she eventually opened three women's centers, and practiced primary care and office gynecology. These centers integrated the best of Western medicine with complementary and alternative therapies such as yoga, acupuncture, chiropractic, and nutrition counseling. She developed and ran a weight management program for weight loss therapy that offered a holistic approach to treating obesity. During that time, she also served as the medical director of the Rader Institute's inpatient eating disorder program. Dr. Ross later completed a two-year fellowship the University of Arizona's Center for Integrative Medicine, studying with Dr. Andrew Weil. Her path then led her to work as the head of the Eating Disorders Program and the Integrative Medicine Department at world-renowned inpatient hospital Sierra Tucson, where she pioneered the integrative medicine approach to eating disorder treatment. She currently works in private practice in Denver, Colorado, as a weight loss therapist, addiction medicine specialist, and Suboxone doctor who specializes in opioid addiction treatment. She also is a consultant for treatment centers across the country on eating disorders and integrative medicine. Her most recent book is *The Binge Eating & Compulsive Overeating Workbook: An Integrative Approach to Overcoming Disordered Eating.*

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Beyond Sex, Birth, and Breastfeeding: Promising Clinical Uses for Oxytocin

by Pushpa Larsen, ND

It's been called the "hug hormone," the "cuddle chemical," and a "hormone of happiness", but it's most commonly known in the popular media as the "hormone of love."[1–3] Oxytocin *is* an important hormone that is released by hugging and cuddling, but a plethora of recent research is revealing that it may have far broader effects than those we typically associate with this hormone. These effects hold promise for treating some of society's major health issues: diabetes, obesity, osteoporosis, chronic pain, and heart disease. Oxytocin may also play an important role in the alleviation of migraines, anxiety, posttraumatic stress disorder, autism, erectile function, anorgasmia, vaginal atrophy, reproductive function, maintenance of muscle mass, inflammation, mood and mental disorders, recovery from addiction, and nerve regeneration.

Oxytocin is a peptide hormone made of nine amino acids. It is primarily synthesized in the paraventricular and supraoptic nuclei (PVN and SON) of the hypothalamus. Hypothalamic neurons terminating in the posterior pituitary release oxytocin into circulation. Hypothalamic oxytocin neurons project likewise to the hindbrain. Oxytocin is also produced in peripheral tissues, including the uterus, ovaries, testes, retina, and heart. In humans, oxytocin release in the brain has a diurnal rhythm, peaking around noon.[4] Painful stimuli are another trigger for oxytocin release.[5] The oxytocin receptor is expressed in a wide range of tissues: cardiac muscle, vascular endothelium, kidney, pancreas, thymus, pain-sensing neurons, adipocytes, prostate, adrenal, and osteoblasts.[6,7] Oxytocin is highly conserved, an oxytocinlike peptide being found in all vertebrate species.[6]

Oxytocin and Pain

According to the American Academy of Pain Medicine, 100 million people in the US suffer from chronic pain. This number is greater than the combined numbers who suffer from diabetes (diagnosed and estimated undiagnosed), heart disease, stroke, and all forms of cancer.[8] Patients with chronic pain have significantly lower endogenous oxytocin levels and greater pain sensitivity than healthy controls. Low levels of oxytocin are likely to be associated with greater subjective pain, stress, and depression in women with fibromyalgia. Exogenous oxytocin has improved tolerance to painful stimuli in clinical trials. Other studies have found that oxytocin increased pain thresholds in patients with irritable bowel syndrome and reduced pain in patients with chronic or acute back pain.[9]

A Chinese study of oxytocin's efficacy in treating headaches tested three different doses of intranasal oxytocin against placebo in 112 patients. Patients receiving 400 ng of oxytocin had the best response, with 20 of the 28 experiencing complete remission and the remaining 8 experiencing partial remission of headache pain. Of those patients receiving 200 ng of oxytocin, 14 had complete remission of pain, 12 had partial remission, and 2 experienced no improvement in their headache pain. This dose-response effect continued to be observed in those receiving 100 ng of oxytocin or placebo (Figure 1).[10]

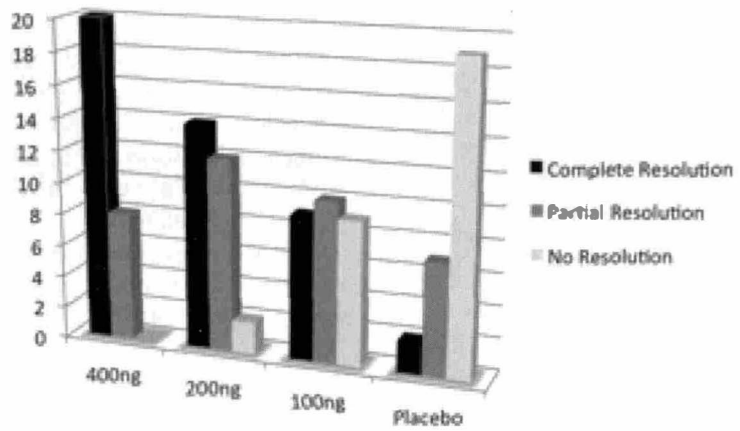

Figure 1. Dose-response in study of intranasal oxytocin used to treat migraines and tension headaches.

One pilot study conducted by an outpatient center for patients with chronic pain demonstrated a 30% to 40% reduction in opioid use and baseline pain in 7 out of 9 participants with the administration of sublingual oxytocin (10 units 2–4 times daily) in combination with sublingual hCG (250–500 units daily). Most patients requested to continue with the regimen after the completion of the study.[11] Related research on the use of oxytocin to reduce withdrawal symptoms from alcohol and drugs suggests that oxytocin might be of great benefit in fighting the current epidemic of those addicted to pain medications.[12–14]

Case Report A

A physician client of Meridian Valley Lab called for a clinical consult on Patient A with a history of cluster headaches and migraines 4 or more days a week for the past 30 years. A variety of pharmacological and nonpharmacological treatments had been tried over the years with little relief. A notable result on the patient's 24-hour urine hormone panel was of oxytocin low out of the reference range. A trial of intranasal oxytocin was suggested, at a starting dose of 20 IU daily. In August 2015, the physician reported that Patient A had experienced only one headache since commencing oxytocin treatment 3 weeks previously. Three months later, the physician reported that, while the patient continued to experience occasional headaches, they were greatly decreased in both frequency and intensity.

Oxytocin, Obesity, and Diabetes

It is well documented that individuals who are overweight or obese have elevated circulating leptin, and leptin resistance is generally understood to play an important part in the pathophysiology of obesity.[15] Leptin receptors are found on the oxytocin-synthesizing neurons of the PVN. Leptin-activated oxytocin neurons innervating the hindbrain then downregulate food intake. It has been theorized that because oxytocin is downstream from leptin, oxytocin administration could be used to "bypass" leptin resistance as well as improve body fat mass in those with genetic leptin or leptin-receptor deficiencies. Several animal studies and two human studies would seem to support this hypothesis.[16] Interestingly, at least in the animal studies, the resulting weight loss appears to be independent of food intake. Oxytocin receptors are expressed in adipose tissue at levels similar to those found in the breast, uterus, and other tissues traditionally thought to be the targets for oxytocin stimulation. Oxytocin receptor expression on adipocytes also appears to be higher in obese mice than in lean mice. Thus long-term oxytocin administration in lean mice had little effect on feeding behavior and weight beyond the first day. Glucose metabolism and insulin sensitivity in obese mice was also improved with oxytocin administration.

In a study of 20 normal-weight men, 24 units of intranasal oxytocin or placebo was administered after more than 13 hours of fasting and 45 minutes prior to having access to a breakfast buffet. Approximately 2 hours after eating breakfast, participants in the study were presented with a variety of snack foods which they were encouraged to eat at will. Ten days later, the experiment was repeated using placebo or oxytocin. Each participant served as his own control. Quantity of food intake and macronutrient balance during breakfast after fasting did not differ between oxytocin and placebo. Consumption of snacks, particularly chocolate cookies, was decreased on oxytocin vs. placebo. This suggests that exogenous oxytocin can be safely used without fear of abnormally suppressing hunger-driven eating.[17]

In the second human trial, 20 men and women with a BMI of 30 or higher were randomized to two groups. Nine participants received 24 units of intranasal oxytocin 20 minutes before 3 meals and before sleep. Eleven participants used a placebo saline nasal spray on the same schedule. Participants were asked not to make any changes to diet and exercise habits. At the end of 4 weeks, there was an average weight loss of 10.14 pounds in the oxytocin group, while no therapeutic effect was found in the placebo group. At 8 weeks, the average weight loss in the oxytocin group was 19.62 pounds. There were significant reductions in BMI and waist and hip circumference. The therapeutic effect of oxytocin appeared to be greater in participants with a higher initial BMI.[18]

James Blevins reports that, as of September 2013, there were "225 completed, ongoing or future investigations in humans [listing] oxytocin in studies of caloric intake, gastric emptying, or obesity." He also reports that oxytocin "may preferentially inhibit the intake of carbohydrates."[19]

As noted above, oxytocin receptors are expressed in many different body tissues. In adipose tissue, oxytocin stimulates fatty acid oxidation and lipolysis, resulting in smaller adipocytes. This increases adiponectin levels and decreases leptin levels, which leads to improved insulin sensitivity and increased glucose uptake in muscle cells. Oxytocin stimulates insulin secretion in the pancreas and appears to play a role in ß-cell regeneration.[20]

Oxytocin and Osteoporosis

Oxytocin receptors are expressed in both osteoblasts and osteoclasts. Osteoblasts share a common precursor cell with adipocytes. This is seen in postmenopausal osteopenia as the decrease in osteoblasts is balanced by an increase of fat cells in bone marrow.[21] Severe osteoporosis also develops in both male and female mice that either do not produce oxytocin or do not express oxytocin receptors.[22] Oxytocin administration has been demonstrated in animal studies to reverse osteopenia in animals that had been ovariectomized to simulate menopause.[23]

A study of postmenopausal women compared 20 women who had severe osteoporosis with 16 healthy controls. Bone mineral density was correlated with oxytocin but no other measured parameters, including age. Women with severe osteoporosis had the lowest levels of oxytocin.[24] Lower oxytocin

levels, poor trabecular structure, and poor bone strength compared with controls have also been found in amenorrheic young women with anorexia nervosa and amenorrheic young female athletes. In amenorrheic young female athletes, this finding was most pronounced in non-weight-bearing bones.[25,26]

Oxytocin and Mental Health

Second to its role in childbirth and lactation, oxytocin is perhaps best understood for its importance to social behavior. There is increasing evidence that oxytocin dysfunction plays a part in many mental health disorders, including schizophrenia, autism, anxiety disorders, mood disorders, and personality disorders, although what part exactly is far from clear. At this point, oxytocin looks fairly promising as a treatment for autism spectrum disorders. The evidence for its use with schizophrenia, anxiety disorders, and PTSD is thin but also promising.[27,28] On the other hand, the evidence for using oxytocin with patients with mood or personality disorders is contradictory, sometimes showing more negative than positive effects.

A number of studies support the potential of exogenous oxytocin to improve social functioning in autism. Most studies are small and have shown some improvement on measures of social function, social recognition, empathy, social recognition, repetitive behaviors, and anxiety.[29] In at least one study, 10 out of 15 children had overall improvement at week 12. Seven of those children maintained their improvement for 3 months after stopping oxytocin.[30] In another study, 11 men and 2 women with Asperger syndrome, ranging in age from 17 to 39, showed improvement in social cooperation and time spent gazing at the eyes after a single 24 IU dose of intranasal oxytocin.[31] Oxytocin appears to be safe, with no adverse effects being reported at any dose given. Still, a February 2015 article in *Science*, "Can Oxytocin Treat Autism?" cautions that "there are insufficient data for physicians to prescribe oxytocin to patients or for parents to seek oxytocin for their autistic child."[32]

Case Report B

A physician client of Meridian Valley Lab called for a clinical consult on Patient B with symptoms of extreme mental stress, anxiety, and social isolation. The patient's 24-urine oxytocin levels were low out of range. The physician decided on a trial of oxytocin. In a follow-up consultation, the physician reported that the patient had had an apparent positive response to oxytocin therapy, feeling more happiness and joy than she had for several months. It was unclear whether the response was entirely due to oxytocin, as it also coincided with her going on an extended vacation. The improvement in feelings of anxiousness and stress began shortly after starting on oxytocin and before leaving on vacation. On the way back from vacation, the patient lost her oxytocin. She subsequently noticed an increase in anxiety and feeling "disconnected."

Case Report C

A physician client of Meridian Valley Lab called for a clinical consult on Patient C with symptoms of social isolation and lack of trust and a history of sexual abuse. The patient's 24-urine oxytocin levels were in the low-normal range. A trial of oxytocin was decided on by the physician. In a follow-up consultation, the physician reported that the patient had had a "night and day" response to oxytocin. The patient was feeling so much better that her neighbor made an appointment to see the physician because she wanted "whatever [Patient C] got."

Oxytocin and the Heart

Oxytocin receptors are expressed in all chambers of the heart as well as in the cardiac vasculature. Oxytocin administered to heart tissue in vitro has been shown to stimulate the release of atrial natriuretic peptide and nitric oxide. Oxytocin is present in abundance in the fetal heart tissue and can trigger the development of cardiomyocytes from murine (mouse and rat) embryonic stem cells. An extended form of oxytocin, Oxytocin-Gly-Lys-Arg, has been described as "the most potent inducer of cardiac differentiation."[33] The actions of oxytocin on the cardiovascular system include reduction of blood pressure, decreasing heart rate and force of contraction, and vasodilation.[33,34]

Multiple animal studies have shown cardiovascular benefits from oxytocin treatment. One such study was done with diabetic mice, which were treated with either saline or oxytocin for 12 weeks starting at 4 weeks of age. Saline-treated mice developed cardiac hypertrophy, fibrosis, death of cardiac myocytes, and systolic and diastolic abnormalities. Oxytocin prevented all these effects as well as reducing inflammation and oxidative stress on the heart.[35] Other animal studies have demonstrated that oxytocin can reduce ischemia-reperfusion injury. In one study, perfusion with oxytocin prior to ischemia resulted in an infarct size 66% smaller than in the control group.[36,37]

In a study done with 28 early postpartum (human) mothers, oxytocin

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levels were measured before and during two stressful situations. In the first, each mother was asked to give a 3-minute speech on a recent situation in which she was angry or stressed. In the second task, the mothers were asked to hold a plastic bag of ice and water on their foreheads for 2.5 minutes, a task which elicits vasoconstriction and pain. Those mothers with higher oxytocin levels had a smaller increase in cardiovascular stress in response to both tasks, as measured by vasodilation, stroke volume, and heart rate.[38]

It is well established that oxytocin levels rise with sexual activity, especially with orgasm. Perhaps the cardioprotective effects of oxytocin are the underlying reason for the finding of a 2010 epidemiological study which reported that men who have sex twice or more a week are at lower risk of cardiovascular disease than men who had sex once a month or less.[39]

Oxytocin and Sexual Function

One of the cardiovascular effects of oxytocin, as mentioned previously, is that it stimulates the release of nitric oxide. The resulting vasodilation can have a salutary effect on erectile function, and improved erectile function is a known effect of oxytocin. It is interesting to note that a 2007 study demonstrated that Sildenafil (a.k.a. Viagra) stimulates the release of oxytocin from hypothalamic neurons.[40] No reports have been found of oxytocin causing erections lasting more than 4 hours.

Two published case reports suggest that oxytocin is certainly worth consideration for male sexual dysfunction. In the first, a 32-year old married father of three with social inhibition and probable Asperger syndrome was treated with 20 IU of intranasal oxytocin twice daily. Although the treatment did not greatly improve his social phobia, he did experience noticeable changes in his sexual relationship with his wife, which she confirmed. "The patient reported that while using [oxytocin], he was more spontaneously affectionate with his wife, which led to increased sexual intimacy. Importantly, these effects were present when using the spray, disappeared on discontinuation, and reappeared each of the several times he restarted the medication [after refilling his prescription]." His sexual function, as measured on the Arizona Sexual Experience Scale, improved by 46%. Libido moved from "very weak" to "somewhat strong"; sexual arousal from "somewhat difficult" to "somewhat easy"; erectile function from "somewhat difficult" to "very easily"; and satisfaction with orgasm from "somewhat satisfying" to "very satisfying." The patient continued to use the oxytocin spray daily with no problems and continued benefits.[41]

In the second case, an 82-year-old man had been unable to consistently achieve orgasm since age 78, although he was still sexually active with his wife. Several treatments had been tried with only temporary positive success. After determining that there were no pharmaceutical or psychological reasons inhibiting orgasm, the patient was given oxytocin nasal spray (20–24 IU) and instructed to use it during intercourse at the point when orgasm was desired. This resulted in the man being able to achieve orgasm multiple times per week. At the time the report was published, the patient had had continuing success over a period of 8 months.[42]

In women and men, oxytocin has been shown to increase the intensity of orgasm and contentment after intercourse, with the effects being more pronounced in men. Women felt more relaxed after intercourse and were more able to share sexual desires and to empathize with their partners.[43]

A small trial of 20 postmenopausal women investigated the use of a topical oxytocin gel to treat vaginal atrophy. The women were at least 2 years postmenopause and had significant symptoms of dryness, pain, itching, and bleeding during intercourse. Seven days of oxytocin gel normalized vaginal tissue, as confirmed by colposcopy and biopsy, in 7 of 10 participants in the oxytocin group. No such improvement was seen in the placebo group. Seven participants in the oxytocin group and 4 in the placebo group also reported a relief of symptoms. It is noteworthy that there was no difference in circulating levels of oxytocin or estradiol after treatment.[44] This suggests that topical oxytocin could be of great benefit to those women with vaginal atrophy for whom topical estrogen is not advised or desired.

In Conclusion

The research literature on oxytocin is vast, and only touched upon in this article. Two other areas in which oxytocin may hold great promise are hinted at in the following article titles:

"Oxytocin Is an Age-Specific Circulating Hormone That Is Necessary for Muscle Maintenance and Regeneration."[45]

"Effect of Oxytocin Administration on Nerve Recovery in the Rat Sciatic Nerve Damage Model."[46]

Oxytocin has a very short half-life, only 2 to 3 minutes in plasma, although its effects last considerably longer. This short half-life may undermine the meaningfulness of serum testing, especially given a normal peak at midday. As with many hormones, a 24-hour urine collection may afford the best assessment of a patient's oxytocin levels.

Although there is much research into oxytocin biochemistry, oxytocin receptor genetic polymorphism, and a multitude of animal studies exploring clinical effects of oxytocin, clinical utility in human patients is in most cases considered unproven. However, given the potentially large benefits and the lack of adverse effects noted in clinical trials to date, it may be worth considering making use of the love hormone.

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Oxytocin: The New Hormonal Kid on the Clinical Block

by Dr. Devaki Lindsey Berkson

Modern Dilemma

In America today, marital relationships and personal moods seem pretty hard to hold together. Fifty percent of marriages end in divorce.[1] Studies say that 20% to 72% of husbands commit adultery and 10% to 54% of wives do likewise.[2] Try as we may to achieve happy relationships, many fail.[3]

Moods are murky. Anxiety disorders affect 40 million adults and cost one-third of all monies spent on mental health. The National Center for Health Statistics shows that 1 in 10 Americans (and 1 out of 4 women in their 40s and 50s) take antidepressants.[4]

What if there was a safe nasal spray (of all things) that could enhance relationship harmony and loyalty, heighten desire and orgasms, stabilize moods, and make us feel more right with our world? [5–8] What if it wasn't addictive? And didn't have rebound issues?

Enter Oxytocin

In science, this hormone is referred to as the official neuropeptide of "attachment." This article brings you up to snuff (the bulk of research on oxytocin is on the *intranasal* delivery mode) on the clinical applications of oxytocin replacement. You will learn that it is a team player with our sex steroid hormones, our ability to be lean and *not* mean, and as part of the Buddha (vagal) pathway between the brain and gut.[9]

Oxytocin is a peptide hormone. Peptide hormones are made of amino acids. A peptide is a link of two or more amino acids. As far as peptide hormones go, oxytocin is a small thing, with only nine amino acids. In comparison, thyroid-stimulating hormone (TSH) contains 201. Sometimes oxytocin is referred to as a *nonapeptide*, since *nona* means "nine."

Oxytocin is historically appreciated for its role in pregnancy. It signals uterine contractions, lets down milk for lactation, and deepens bonding between mother and child.[10,11] But there's more. Emergent research and clinical evidence reveal ever-expanding possibilities for oxytocin replacement in the clinical trenches. For example, oxytocin therapy is being used to treat autism spectrum disorder, schizophrenia, obesity, addiction, erectile dysfunction, and orgasm disorders, and as a libido, orgasm, and emotional "bonding" enhancer.[12–14]

Viagra has become a household word. It's an effective, best-selling sexual medication. Viagra has also been looked at for treating depression and other mental disorders.[15,16] Why? It boosts oxytocin production.[17]

Oxytocin Receptors

Hormones are signaling molecules, or "e-mailers" in the body's physiologic Internet system. Hormones are made in various organs throughout the body. For example, oxytocin is made in the brain. These hormones are then secreted into the watery highways of the blood, where they swim to specific tissues in search of perfectly fitting receptors. Receptors are proteins shaped like malleable satellite dishes. Hormones swim into their exact receptor. Once inside, the hormone docks into specific binding domains. Marching orders are delivered to genes. Based on these directives, cells take action.

Much of the cross-talk communication that takes place to nudge life to unfold is due to hormonal (ligand to receptor) and genomic (delivering to genes) signaling. There are other forms of signaling, such as receptor-free and nongenomic signaling, but they are beyond the scope of this article.

Oxytocin (OT) delivers messages to specific oxytocin receptors (OTR). We have oxytocin receptors globally in our human biologic real estate, not just in reproductive tissues. I have been using oxytocin replacement in practice for 5 years and have some startling case histories as well as some duds. Five summaries are presented later in this article.

Brain

Oxytocin is produced in the hypothalamus.[18] It is made by the neurons of the paraventricular and supraoptic nuclei of the hypothalamus (the same areas of the brain turned on by orgasm; the bigger the orgasm, the more these cells are "turned on").[19,20] These hypothalamic neurons have axons that deliver OT both locally and peripherally.

The brain has high levels of OTRs to receive a wide array of signals. Oxytocin acts as a neurotransmitter signaling the amygdala (seat of faith vs. fear), the nucleus accumbens (sense of well-being), and the hippocampus (home of short-term memory and confidence).[21]

Oxytocin traverses cerebral regions by diffusing across neural tissue, like you would cut across lanes to get to an off-ramp on a freeway.[22] There are OTR receptors throughout the entire spinal cord.[23]

Connection

Animal model research emphasizes a strong relationship between the expression of OT in the brain and the ability to have socially monogamous *attachment* behavior. These investigations began with the vole. It's amazing research.

Two closely related species of voles have exact opposite relationship styles: one is monogamous, mating for life, while the other is promiscuous, choosing to be a forever player. What's the biological difference? The monogamous prairie vole has many more oxytocin and vasopressin (a playmate with oxytocin) receptors and activity in the brain. In comparison, the polygamous vole has far fewer such bonding receptors, and thus, more sleuthing mating behaviors.

Researchers have gone to the trouble of reversing these mating behaviors. They accomplished this by reengineering Mother Nature. By altering OT genes, they could morph typically promiscuous male voles into becoming devoted monogamous voles, and mate-for-life type voles into tomcat types. How? They altered the numbers of oxytocin genes. By reducing or increasing oxytocin signals (and its cohort, vasopressin) in the brain, they could reproducibly alter biologic desire for either monogamy or bigamy (though some say this should be dubbed "pig-amy").[24,25]

Moving forward from these findings, Young and Wang manipulated three attachment hormone musketeers (oxytocin, vasopressin, and dopamine) and influenced preference of one beloved over another. They "gene-jury-rigged" whom the animals would choose to mate with. They named this the neurobiological model of pair bonding.[26] A number of researchers have pleaded the case that this is how humans basically meet, mingle, and mate, too.[27,28]

We know that moms and babes bond through oxytocin. Magnetic imaging of the brains of mothers who see photos of their own infants (compared with pics of matched control infants unknown to them) show that the areas of the brain that "activate" are flush with oxytocin, vasopressin, and dopamine receptors.[29]

It's clear. Oxytocin deserves to be called "the cuddle hormone," "the love hormone," or "the cuddle chemical."

Stress

Oxytocin helps buffer stress. It has hormonal influence over the hypothalamus/pituitary/adrenal axis (HPA axis). At various levels OT helps the host cope with stress and promotes anti-anxious reactions.[30] In other words, OT signaling reduces the font size of suffering caused by stress.

Sex Hormones and Oxytocin

Sex steroid hormones – estrogen, testosterone, and progesterone – intimately interact with OTR and are part of sex hormonal influence over human emotions. Estrogens act synergistically with OT by enhancing its anxiolytic effects and increasing OTR levels. A single dose of estradiol increases plasma OT levels in women (one of the many reasons that estrogen replacement makes many women enjoy happier moods and avoid antidepressants) and a metabolite of testosterone (nicknamed 3beta-diol) has similar input in the brain and other critical areas, such as within the HPA axis.

Estrogen Receptor β

Estrogen has two major receptors that receive estrogen signals: ER alpha and ER beta. ER beta is an oncogene suppressor (protects against cancer) and anti-inflammatory molecule balancing out the pro-growth signals of ER alpha. Areas in the brain with OTRs stunningly overlap with exactly where ER beta-receptors live.[32]

Activation of ER beta normalizes HPA axis activity and acts to buffer stress and anxiety. Approximately 85% of OT neurons in the pituitary coexpress ER beta! There is grand crosstalk between OT and ER beta throughout the body. The multiple interplays are just now being explored. I prophesy that the "good" and "bad" roles of oxytocin and estrogen receptor beta will takes twists and turns because in some cellular places (such as the breast, prostate and brain), *ER beta dominance* (having many of these receptors) is what we want for tissue protection, but in other conditions (such as endometriotic implants and dysfunctional endothelium) this is not the case.

There also appears to be a "threesome" between a metabolite of testosterone (3B-diol – itself a promoter of ER beta) and ER beta and OT. All three synergize, especially in the brain and the vagus nerve.

Vagal or Buddhist Nerve Highway

In utero, when the fetus is developing, a mass of cells that are to become our brain and gut divide in half, and one cellular clump travels northerly to the brain and the other southerly to the gut. What connects the two throughout life is the vagus nerve. It's the second largest nerve system after the spinal cord. It's the longest cranial nerve, extending from the brain to the gut and other crucial organs. It starts in the brainstem behind the ears, travels down each side of the neck, across the chest, and throughout the abdomen. It connects the brain to the stomach and digestive tract and many other organs such as the lungs and the heart.

The vagus nerve is a bundle of multiple thousands of nerve fibers, of which 80% are sensory, meaning that these nerves report and reinforce back to the brain what's going on in the gut and the rest of the body. It's *cellular Big Brother*. The vagus nerve is a crucial part of the parasympathetic nervous system (though some is sympathetic, too). It is mostly the *opposite* of flight and fight.

Healthy vagal tone creates calm. Everyone has their own vagal footprint. The better the vagal tone, the less ruffled we are by stress and the more cast-iron stomachs we seem to enjoy. A healthy digestive tract is mostly parasympathetically "vagal."

The healthier your vagal tone, the lower your level of cellular inflammation, or the faster you bring

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inflamed tissues back to normal after infection, or the more peaceful your moods or the faster recovery back to calm after an emotional storm has hit.[33]

Oxytocin appears to be a major hormone player traveling vagal highways, maintaining calm, hormonal satiety and peace, suppressing inflammation, and more.[34] Being a hormone of connectivity, oxytocin upregulation in the vagal nerve – this massive internal feedback loop – may be part of feeling well and right with the world. Meditation boosts vagal tone and oxytocin.[35]

Again, crosstalk abounds. The vagus nerve is not only flush with oxytocin receptors, this large feedback nerve also influences the number of estrogen receptors in the nervous system and brain.[36] Remarkable!

Romantic Love

Adults shown photos of a romantic partner with whom they are "intensely in love" light up brain areas flush with oxytocin, vasopressin, and dopamine receptors.[37]

A number of studies have looked at mating under experimental conditions, before and after orgasm, and when giving couples nasal administration of oxytocin, which delivers it directly to the brain. These have been done in both observational manners (not randomized controlled) and in double-blind, placebo-controlled scientific experimental design. These studies are where the hormonal rubber meets the enhancement effectiveness road.

Oxytocin replacement has been shown to create more pleasurable orgasms and a stronger sense of empathy in both men and women. Men given OT intranasally report the biggest bang, perhaps since during orgasm they naturally make less oxytocin than women, so any bump *up* might be more noticed.

Since men produce less oxytocin, a bonding hormone, they are less vulnerable to intimacy attachment compared with women.[38,39] The highest experimental recorded levels of oxytocin, by the way, were shown to be achieved in women who were multiorgasmic.[40] The more oxytocin, the more orgasms – if a woman is capable of having these types of releases. (My theory is that all women are capable, but not all are hormonally replete, or in shape emotionally or physically, or they or their partners have simply not been taught how. I have a new book coming out that outlines exact details.)

Orgasm

During orgasm, oxytocin levels are significantly increased in the brains of both men and women. But, oh, so much more in ladies. Oxytocin remains elevated for about 5 minutes and then levels rapidly decline. Much less is produced by masturbation or sex without orgasm.[41,42] If you are solo, you can love the one you're with, but you won't get as much oxytocin signaling.

During orgasm, the woman wins out in that her brain, proved by PET neuroimaging, activates the pituitary more than the guy's.[43] When she orgasms, her pituitary is tremendously *turned on* to secrete more oxytocin and prolactin. So, when she orgasms, she longs to bond and has deep satisfaction (from the prolactin, a satiety hormone in this scenario) with that sensation. The man's pituitary is less turned on and produces less oxytocin, and less bonding sensation.

No matter how much a "friend with benefits" male lover might insist a liaison is only a friendly wham-bang, if it's done repetitively enough, and she orgasms enough, she'll bond with him. Her brain and hormones make her do it. He will only bond if his emotions come along for the ride. But he does not bond based on orgasms alone.

Social Attachment

If oxytocin helps bond, why not use it clinically when there are social bonding issues? Some forward-thinking neurologists and functional medicine docs are using oxytocin replacement therapy to treat specific conditions of "disrupted attachment," such as schizophrenia, eye contact disorders, social discomfort, and phobias. It's even being used to boost decision-making processes when the lack of this ability is disabling.

Case Studies: Hormones Are Stranger Than Fiction

(I've had patients in whom oxytocin replacement therapy did not improve their problems, but the following are a few examples of effective responses, some rather startling.)

Patient 1. Woman with an attachment disorder that first started when she was pregnant with her first child, in her first marriage. At the end of the first trimester she had an episode that landed her in the ER. She felt that she had a ministroke and half of her body went numb. Nothing significant was found on imaging or exams. Since that time, she claimed that she had a flat affect and was unable to bond. When her child was born, she could not bond. She no longer wanted intimacy or even to interact socially with her husband, who eventually left her. She was then in a second marriage and had the one daughter from the previous marriage. She couldn't seem to bond with either her daughter or the new husband, who she said was a very good man. She now feared losing this marriage, too. She thought the fault was hers and she wanted to know if hormone therapy could help her.

She was put on a 200 IU oxytocin lozenge (at that time I was unaware of the better clinical responses with nasal applications). Within 1 month she returned and reported that both relationships with her daughter and husband were improved. She wanted sex and enjoyed it. She had good feelings during sex, which she hadn't experienced for years. She was now doing things with her daughter, like dance classes and hugging her. This was amazing to her. She cried in the office as she described feeling human for the first time in many years. She finally had hope.

Patients 2 and 3. 39-year-old woman was married to a 25-year-old man who was a photographer in the model industry. She had gained weight and he had lost interest. He was used to looking at slim models all day long. They were religious, positive people, devoted to

each other. In the office they spoke kindly and frankly in front of each other discussing their conundrum. He loved her but he no longer desired or enjoyed sex as much with her. She was on lifelong antidepressants (which she thought had put on her weight) and couldn't get off due to fierce historical rebound issues. They wanted her to lose weight and him to gain interest, and perhaps even for her to get off antidepressants.

They both went on oxytocin (24 IU in one nostril t.i.d.) and also before and during any sexual encounter. They informed me that within several days their intimacy was better than it had been in years. They thought that their marriage was back on track. It's half a year later and they are doing better than ever. She has still not tapered off the antidepressant.

Patient 4. I worked with this 36-year-old intelligent woman for a year and got nowhere. She had a lifelong history of severe constipation that severely reduced the quality of her life. She had numerous colonoscopies, and the gastroenterologists had consistently reported to her that she had a "dead" area in her sigmoid colon. It could not be "revived" and surgery was her only answer. She had tried hormone replacement, fermented foods, fiber and seeds, neurotransmitter balancing, exercise, colonic therapy, and thyroid replacement, and still she was limited in what she could eat and prone to severe and constant flatulence and pain. She only eliminated once every 2 weeks. It took a lot to achieve that. She had tried numerous digestive enzymes and stomach acid replacement, and was down to only being able to eat a handful of foods without constant pain and bloat. I offered oxytocin as a last resort.

The first week she did 24 IU (twice a day) in one nostril, which changed nothing. I happened to ask her, after that first week, if the oxytocin by chance had made her feel any more intimate or sexy with her husband. It was then, for the first time in a year, that she confided that she did not view herself as a very "connected" person. That even though she loved her husband and her children and did right by them, she was not connected to them as she thought a true loving person would be. On the third week, her dosage was increased to 1 spray in each nostril (3 times a day) and before sex and during sex, which she reported they did once a week. A follow-up phone call within a week found her feeling more at peace with life, and miraculously going easily to the bathroom twice daily for the first time in her life. She now had no gas or belly pain, and could consume a more diverse diet without issues.

The intestinal area is lined with oxytocin receptors. Studies have shown oxytocin to have anticolitis action in rats. In vitro studies have shown it to protect enterocytes and to have protective gut anti-inflammatory, motility, and gut wall enhancing permeability actions.[44,45]

Patient 5. Woman in her late 20s with trouble with portion control. She had a history of ulcerative colitis and would have flare-ups if she ate too much, which kept her in a flare-up loop, as she continuously ate too much. One week on 24 IU intranasal spray in one nostril b.i.d. accomplished nothing, but when we increased it to one spray in each nostril t.i.d. right before eating, she was able to eat less, lose weight, and avoid continuous flare-ups. Oxytocin has also been shown to act as an anti-inflammatory in the gut.

Future Applications

Because oxytocin receptors are so global, stimulation of them by intranasal oxytocin replacement is being looked at for diverse disorders. Oxytocin cream lubricates the vaginal vault in similar ways to that of estrogens, healing, soothing, and lubricating the mucosa, but without activating the estrogen receptor. Thus, OT is safe for high-risk women to reverse vaginal atrophy.[46]

Oxytocin signaling is being investigated as an anti-aging tool to protect muscle mass as we age (muscles are exceptionally flush with OTR and signaling helps maintain fiber mass), to reduce overeating by reducing caloric intake, maybe even to decrease leaky gut and systemic inflammation, and possibly as breast tissue protector.[47–50] Oxytocin might even be linked to stimulating the newly found *happiness epicenter* in the brain.[51,52]

Oxytocin

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Up with oxytocin. Or shall I say, up your nose with it.

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Stay tuned for my new books:

- *Sex: Why Your Brain and Hormones Want You to Do It*. The neuroendocrinology of intimacy.
- *Digestive Freedom: Eat Your Way to Intestinal Wellness.* Introducing "Nutritional Gastroenterology."

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Clinically Effective, Evidence-Based, Non-HRT/BHRT Treatment Options for Perimenopause

by Todd A. Born, ND

As health-care practitioners, we see the following scenario play out in our practice a few times a week: 48-year-old female presents with chief concerns of hot flashes, night sweats, irritability, xerosis, dry eyes, vaginal atrophy, dyspareunia, sleep dysfunction, mood swings, an irregular menstrual cycle, and memory concerns.

You run some blood chemistries, and everything is unremarkable besides decreasing estrogen and progesterone, with an increase in FSH. This woman clearly is in the throes of perimenopause. She's hesitant to start hormone or biological hormone replacement therapy because of what she has heard and read online about side effects and risks of prolonged hormone replacement.

You begin to comb the Rolodex of treatment options that actually work and have a very low side effect profile and minimal if any long-term risks, but you can't think of any that work quite as well as hormones.

This article will discuss the definition of menopause, clinical signs and symptoms, long-term consequences of estrogen deficiency, conventional treatments, and finally, evidence-based, nonhormonal approaches.

The average onset of perimenopause in the US is at the age of 47.5 years. The average duration of perimenopause is 4 years, with the median age of 12 months of amenorrhea occurring at 51.4 years of age.[1] An article in February 2015 in *JAMA* looking at 3302 women showed that vasomotor symptoms lasted for more than 7 years in more than half the women, and persisted for 4.5 years after the final menstrual period.[2]

The most common symptoms that women experience are hot flashes, night sweats, sleep disturbances, vaginal dryness, and mood changes. Less common, but still prevalent, are recent onset depression, arthralgias, memory loss, breast pain and menstrual migraines.[3]

The long-term consequences of estrogen deficiency include osteopenia/osteoporosis, dementia (but only in those who have artificially induced premature menopause), dyslipidemia, and cardiovascular diseases.[4–9]

Although the evidence varies for the risks of prolonged (>5 years) use of hormone replacement therapy (HRT), at this time the preponderance of data indicate that HRT, particularly unopposed estrogens, should not be used long term.[10] The risks and consequences include endometrial hyperplasia, coronary heart disease (CHD), stroke, venous thromboembolism (VTE), and breast cancer.[11,12]

There is a major misconception amongst many health-care providers and the general public that bioidentical hormone replacement therapy (BHRT) is safer than HRT. Albeit this makes sense logically, particularly to integrative health-care practitioners, in that one would want to use a hormone with the same molecular structure as a hormone that is endogenously produced, versus one that is completely synthetic, but both carry similar risk profiles, except for medroxyprogesterone acetate (MPA).[13–16] It is believed that MPA increases the risk of breast cancer, while this has not yet been seen in bioidentical use of progesterone.[17–19]

More and more clinicians, as well as more and more patients, are looking into safe and effective alternatives as a first-line intervention to alleviate menopausal symptoms. Let's take a look at what natural agents have some of the strongest human efficacy, while also carrying a strong safety profile, even in the long term.

- Patented extract from *Humulus lupulus*, high in prenylflavonoids, particularly 8-prenylnaringenin (8-PN).
  - A 2006 double-blind, randomized, placebo-controlled trial in 67 menopausal women given the extract for 12 weeks significantly reduced hot flashes over placebo.[20]
  - A 2010 double-blind, placebo-controlled crossover study in 36 menopausal women followed for 16 weeks showed improvement in most menopausal complaints.[21]
- Combination of three Korean herbs: *Cynanchum wilfordii*, *Phlomis umbrosa*, and *Angelica gigas* Nakai.
  - Human trials have shown increase in bone mass, while relieving menopausal symptoms.
    - In a 2005 prospective RCT, 48 perimenopausal women were given the extract twice a day, or placebo, for 12 months. By the end of the study, it was shown that the group that took the extract had improved bone density, increased human growth hormone, and improved triglycerides. At the 3-month mark, 57% reported improvements in hot flashes, dyspareunia, sleep disorders, and fatigue. Only 17% of the control group reported improvements.[22]

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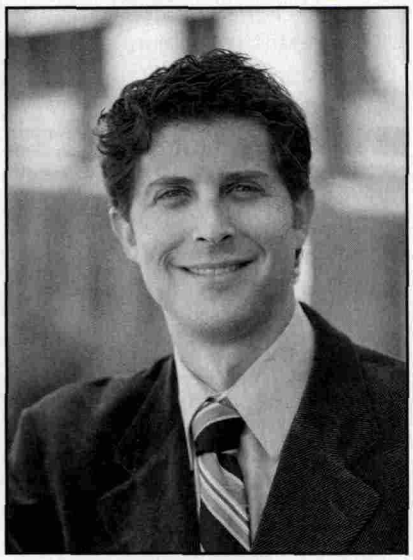
- A 2012, phase II double-blind, placebo-controlled safety study in 64 pre-, peri-, and postmenopausal women followed for 12 weeks showed that "the constituting symptoms of vasomotor, paresthesia, insomnia, nervousness, melancholia, vertigo, fatigue and rheumatic pain were significantly improved in the EstroG-100 group in comparison with the placebo group ($p < 0.05$). Statistically significant improvement in vaginal dryness in the EstroG-100 group was also observed compared with that of the placebo group ($p < 0.05$). In conclusion, EstroG-100 significantly improved the menopausal symptoms of pre-, peri-, and post-menopausal women without weight gain or any serious side effects."[23]

- Patented grapeseed extract high in proanthocyanidins.
  - A 2014, randomized, double-blind, placebo-controlled pilot study enrolled 96 women aged 40 to 60, who had at least one menopausal symptom. They were given 100 mg/day, 200 mg/day, or placebo for 8 weeks. It was shown that in the 200 mg/day group, hot flashes reduced, anxiety improved, systolic and diastolic blood pressures decreased, and in both 100 mg and 200 mg group, lean muscle mass increased.[24]
  - Although not a human trial, in 1999, rabbits fed a high-cholesterol diet and that developed atherosclerotic lesions had these lesions significantly reduced when adding in the grapeseed extract to their diets.[25]

Conclusion

The variability of what women will experience through the menopausal transition is vast, but given that most experience at least one of the aforementioned symptoms, with an average duration of 4 years, it makes sense that we have a duty as clinicians to alleviate their symptoms as much as possible, as safely and effectively as possible. One can see that this can be done without going straight to hormone replacement therapies, although this intervention may be needed for certain individuals.

We have a responsibility to use tools in our toolbox that work and have human data to support efficacy. Here, I have shown that these natural therapeutics do exist.



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Thallium Exposure: Environmental Issues

Michael Rosenbaum, MD, and Ernest Hubbard

Based on an interview with Nancy Faass, MSW, MPH

Overview

Results are presented from toxic heavy metals analyses of extractions from fresh vegetables and other foods grown and sold in Marin and Sonoma Counties, California, in 2014 and 2015.[1] Laboratory findings from these samples (Pilot Study 3) indicated that 6 of 25 foods tested for thallium exhibited levels of thallium in excess of 0.26 ppm. In the human body, thallium levels above 0.5 ppm are considered excessive. Thallium has a half-life of 60 days, so the consumption of foods with thallium content of 0.26 ppm has the potential for harmful bioaccumulation in the body.

A majority of these elevated findings occurred in samples of kale (*Brassica oleracea*) sourced from local farms (both organic and non-organic), procured in farmer's markets and from food retailers. In parallel studies of heavy metals in humans (Pilot Studies 1 and 2), subjects exhibiting high urine thallium were found to be high consumers of some of the foods testing high in thallium, particularly cruciferous vegetables. Cessation of consumption of these foods resulted in reductions in urine thallium and reduction in symptoms associated with thallium toxicity. Further discussion regarding this pilot sample includes the possibility of toxic heavy metals in the food supply and hypotheses on sources of these heavy metals.

The genesis of this environmental pilot study (Pilot 3) dates to 2010 when the authors and colleagues were asked to conduct an independent clinical study of oral chelation (Pilot 1). This research was designed to document responses to a naturally-derived detoxification product developed by LifeHealth Science, LLC, a Cleveland, Ohio-based enterprise. The initial study indicated that the detoxification agent was effective in removing a spectrum of heavy metals from study participants, and no side effects of the chelator were observed.

Following the initial study, a second human study (Pilot 2) was undertaken in 2014 involving a refined version of the detoxification agent. During this follow-up study, a percentage of the participants exhibited higher-than-normal levels of toxic heavy metals, particularly thallium, aluminum, and cesium. The subjects with higher-than-normal thallium levels also exhibited varying degrees of symptoms consistent with thallium toxicity including cardiac arrhythmias, fatigue, and hair loss. No obvious sources for the detected thallium could be identified in Marin or Sonoma Counties (i.e. high concentration of coal-burning power plants and/or cement manufacturing facilities).

When research was found in the medical literature linking high levels of thallium to kale and other cruciferous vegetables, a survey of study participants was conducted and a high correlation was found between elevated urine thallium and high consumption of kale, cabbage, broccoli and other cruciferous vegetables.

Benchmarks for Thallium Toxicity in Humans

MR: We have good research on toxicity levels for thallium because cardiologists use thallium in cardiovascular studies, scans, and stress tests of the heart. Why thallium? Because thallium mimics potassium and there is a great deal of potassium in the heart. However, these tests use 1/4,000 of the amount that is considered to be toxic.

EH: Dosage and toxicity levels came from these medical studies, because the prescribed amount of thallium for the heart scan must take into account the half-life of thallium. That has provided benchmarks for toxicity.

Given the half-life of thallium, you can see how it starts to accumulate in the body. For example, simply having a kale smoothie every morning could create an exposure if the kale contains thallium. For an average kale user, half a bunch of kale a week is not a great deal. So we used the medical data as our baseline and found that within six to eight months you start seeing sub-clinical symptoms. That is what we actually were seeing in patients in our first and second pilot studies.

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Thallium

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From a biochemical perspective, imagine what happens when a thallium atom lands where a potassium atom should have been, given that its atomic mass is about five times greater than that of a potassium atom with many more electrons. This is a hugely disruptive process in a very delicate mechanism, whether it is a nerve cell or a heart cell. Thallium is an enormously heavy metal that can bind to sulphur and lock up the potassium receptor sites, so it is no wonder that it can be so lethal.

Yet this is just one heavy metal. You could probably tell the same story about all the heavy metals in one way or another and then you must deal with all the combinations. Many of these patients have elevated levels of five or six toxic heavy metals; thallium is just one of them.

Search for the Source of the Thallium

EH: I began connecting the dots on these issues in 2014 when I came across a research paper from the Czech Republic entitled "Uptake of Thallium from Artificially Contaminated Soils by Kale." Once we realized that the thallium exposure might be present in the food chain, we decided to do a third pilot, procuring and preparing food samples for analysis, working with two different laboratories. By the end of 2014, we had submitted most of the food samples. As the lab reports came in, we found significant observable levels of thallium in some of the food, particularly in samples of cruciferous vegetables, primarily in kale. That led to all sorts of interesting questions. Were the samples that tested positive for thallium nonorganic or organic? What was the soil and the soil profile? Were the produce samples from different farms, and were they using different growing methods? We were in a scramble to find the source or sources of the thallium.

Pilot Study 3 of Sample Foods

In this pilot, food samples were prepared and submitted to two laboratories (Curtis & Thompkins and Doctor's Data) to analyze for the presence of thallium. These samples included 15 vegetables, 3 fruits, 3 protein sources, and 4 samples of commercial baby food.

Thallium. Of these, 24% showed evidence of thallium at levels with the potential for toxic effects, given the half-life of thallium in the body. Of the 10 dry-weight kale samples, 5 showed toxic levels of thallium.

Aluminum. Selected samples of kale and of commercial baby food were subjected to greater scrutiny, evaluated by Doctor's Data for 20 toxic metals. All 5 samples were found to have elevated levels of aluminum 15 to 25 times higher than the reference range.

Nickel. Two kale samples (of different varieties) evaluated for 20 metals had nickel levels 2 to 3 times the reference range.

Bioaccumulation in Crucifers

MR: We analyzed six different varieties and types of kale and the uptake was different in each of them. So we were not only looking at a particular plant, but all of the varieties of that plant.

EH: What we know now is that certain species of kale can absorb 15 times the thallium from low thallium soil and sequester so much thallium that it is probably not healthy to consume kale—especially raw kale—in large quantities. Kale is a hyper-accumulator, and there is genetic variation for this. Of the different types of kale that we have tested, we have seen significant variation in the uptake of metals in kale, even in different kale species grown in the same soil. Once you see the preponderance of information on the capacity of the crucifers as bioaccumulators, it is almost undeniable. Biochemically, it is easy to understand how they would be hyper-accumulators of thallium.

The bottom line is that anyone who is developing symptoms and eating a lot of crucifers should change their diet and get tested for heavy metal exposure.

Plant Biosorption and Bioaccumulation

The capacity of certain plants as bioaccumulators has been recognized for more than a decade. Researchers have studied both the risk of toxicity and the potential role of these plants in the remediation of toxic soils. A German study published in 2004 explored the removal of heavy metals from the environment by plant biosorption. Brassica species in particular have been evaluated for their bioaccumulation capacity: A Polish study published in the *International Journal of Molecular Sciences* in 2011, explored the role of mustard seed in toxic clean-up. Other Polish research published in 2012 documented absorption of heavy metals, nitrates, and nitrites by various species of cabbage. Additional research in this area has focused on food safety in the context of novel soil media. A 2006 U. of Illinois study of heavy metals in garden vegetables, including broccoli, evaluated the safety of river sediment as a food medium, finding levels of molybdenum three-fold higher than those associated with toxicity in grazing animals. A 2008 Chinese study evaluated the safety of cabbage grown in sludge, reporting toxic levels of arsenic, cadmium, chromium, and zinc. There is a need for comparable studies on cruciferous vegetables and other bioaccumulating plants grown in soils with heavy metal accumulation.

Environmental Contaminants

Thallium in Fertilizer

EH: We have reason to believe that some growers (on both non-organic and organic farms) may be using coal-ash-based fertilizer or manure that contains thallium. You can track the history of the coal-ash industry, the rise of coal-fired electrical generating plants in this country, and their track record on waste disposal. The picture that emerges is that

the environment has been polluted by toxic heavy metals, including thallium, for at least a decade.

Coal Ash in the Environment

By 2007, the EPA had tracked at least 70 cases in which coal ash had caused fish kills, or tainted drinking water and land.[2] In 2008, coal ash overflowed a holding pond at a power plant in Tennessee, engulfing over 300 acres in sludge, and contaminating drinking water with arsenic and radioactive radium. (The cleanup was projected to cost about $1 billion.) A spill occurred in Alabama just a few weeks later. In Virginia, a golf course built on 1.5 million tons of fly ash was considered a model of landfill recycling until tests of nearby ground water wells showed arsenic and lead levels exceeding safety standards.[3] In 2011 the Tennessee Valley Authority reevaluated groundwater sources for toxins and found contaminants leaching out of coal ash dumps at eight of the nine plants being monitored.

Synthetic Gypsum

One form of coal ash is known as synthetic gypsum, a whitish, calcium-rich material also termed flue gas desulfurization (FGD) gypsum.[4] The Environmental Protection Agency has formally stated, "EPA believes that the use of FGD gypsum in agriculture is safe in appropriate soil and hydrogeologic conditions." The EPA indicates that heavy metals in the material are far less than the amount considered a threat to human health. Field studies have shown that mercury, the primary heavy metal of concern, does not accumulate in crops or run off fields in surface water at "significant" levels.

EH: Coal ash has been used in agriculture since the 1990s as a fertilizer that is labeled as coal-ash or fly-ash, approved by the USDA. There are numerous agronomic studies that show just how much you can use before it is toxic to plants. But there is a major story in Georgia about a dairy farmer who lost about 600 head of cattle because the city of Atlanta had given him all their coal-ash to use as fertilizer. He lost his entire herd and went bankrupt. His neighbor, who was using the same coal ash, had the common sense to have his own herd's milk tested, and it turned out that it was extremely high in thallium. They did necropsies on the cattle and found high thallium. There was a huge settlement with this farmer over the thallium poisoning.

There is a history of thallium use in agriculture and its toxic effects, but no one is really regulating it. *60 Minutes* did a piece on Duke Energy in North Carolina because there was a toxic spill of coal-ash sludge in a pond and it destroyed an entire ecosystem in North Carolina. Yet we know that the American Coal Ash Association petitioned the EPA, requesting that coal ash be officially approved by the USDA for use as an organic fertilizer.

Final EPA Ruling on Coal Combustion Residuals

On April 17, 2015, EPA published its final rule establishing comprehensive regulations for the disposal of CCRs [Coal Combustion Residual] from coal-fired power plants under subtitle D of the Resource Conservation and Recovery Act (RCRA), classifying CCRs as nonhazardous solid waste. EPA issued the final rule under a self-implementing approach because EPA lacks the authority under subtitle D of the RCRA to require states to issue permits in this context. Therefore, EPA requires the minimum federal criteria to be administered by each owner and/or operator that manages CCRs in surface impoundments and landfills. The final rule continues to exclude the beneficial use of CCRs from regulation.[5]

EH: The landfills and the ponds are overflowing with coal ash, so industry turned to agriculture for disposal, and now these metals are showing up in our food supply. Periodically Michael and I step back and say, 'This is just thallium, and this is just kale. Let's look at baby food, let's look at flesh foods, at fish.' The discovery that we made in these pilot studies was the proverbial tip of the iceberg.

Thallium in Chicken Waste Fertilizer

EH: Consider a large poultry operation like Foster Farms, which has a subsidiary named Organic Farms. Foster Farms recycles the manure from their poultry operations. What they've learned is that the organic industry does not require manure used for certified organic production to be certified organic manure. It was exempted when the standards were set. So Foster Farms is now producing one-ton bags of Organic Farms chicken manure, which is advertised on organic certified websites. The sites for CCOF (California Certified Organic Farmers), for example, reference this particular brand of chicken manure.

Farmers franchised with Foster Farms obtain their feed from the Midwest in the form of corn and soybeans. On the West Coast, that feed is trucked into Southern California, into Livingston and their main poultry plants by the hundreds-of-train-car loads every month. Much of that corn and soybeans is grown with coal-ash fertilizer. So the theory has it that the manure being used by organic farmers could contain thallium derived from manure from the feed grown using coal-ash as a fertilizer. At certain levels coal ash does not kill plants, it actually promotes their growth by providing minerals.

EH: It is also possible that farmed fish are raised on feed grown on fertilizer with high thallium content.

MR: It has been shown that Atlantic salmon have very high amounts of thallium, but Pacific wild salmon does not. Atlantic salmon is farmed-raised.

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EH: "Atlantic" is actually a species of fish, like a petunia.

NF: Shameful. They call it "Atlantic" salmon to make it sound as if it were wild-caught in the Atlantic Ocean, when actually it is farmed fish.

Thallium in Organic Produce

MR: To my mind, it is also shameful that organic certification agencies such as the USDA and CCOF have allowed this to happen and did not ever once ask whether that was potentially putting consumers at risk. I have surveyed hundreds of consumers and I guarantee you, when they buy "organic" they think they're buying safe food. We have a breach in the certification process, which allows toxic levels of heavy metals into the food chain through manures that are not certified. They could also contain human hormones, hormone disrupters, and various pesticides—we do not know.

NF: Does the CCOF have a testing process in place that they use to check a product that farmers are going to use in such massive quantities?

MR: They have access to it, but they don't use it. I talked to one of the scientists at the organic center and said, "To my knowledge, this thallium could be coming in through the manure through the certification process." The scientist, who did not ever return my request for the information he promised to send me, said, "The certification process strictly prohibits the use of any manures that test for toxic heavy metals." I asked, "What agency did the testing and would you show me a copy of the report?" I haven't seen one. Then he backed up and said, "Well, I think that's what it was in Washington [state], because that is where most of my experience is." And I said, "Was testing done for toxic metals in Washington?" He said, "I'll have to get back to you on that." And I said, "Let's get back to California for a minute. Do you know if any testing has been done here?" He said, "You know, I'll have to get back to you on that." I was on the phone with two other scientists who were his buddies, and they were sitting there very quietly. I just said, "I look forward to getting that information." I emailed him twice and voice mailed him once and said, "You know, Duke, I haven't ever received that information you said you would send me," and I copied his two colleagues. Nobody ever got back to me.

Environmental Burden

MR: The coal-ash industry produces more than 100 million tons a year in the U.S. In terms of thallium production, I found a study indicating that in 1987 that figure was about 28 tons per year. Ernie found a newer study at least five years old reporting 2,000 to 5,000 tons annually, compared to 28 tons in 1987.

EH: We already know that China is pumping immeasurable quantities of toxic metals around the world through the jet stream [with coal ash levels estimated at 2.5 billion tons a year]. They have no regulation on their coal-generated electrical power plants.

MR: What we don't know is the synergism of thallium with other heavy metals, like mercury. Mercury is also found heavily in coal-ash. Mercury is found extensively in fish, but nobody has been looking for thallium in fish. There could be a harmful synergism of activity between these two heavy metals that exceeds the toxic effect of either one alone.

NF: But there is also an adverse synergism in conditions like Lyme, because thallium is attracted to myelin. Fatty tissue sequesters both lipophilic toxins and Lyme spirochetes.

What Remains to Be Done?

EH: No one has been watching this magnification occurring. The link between thallium and the food chain was reported in Czechoslovakia 10 years ago, but no one did lab testing to confirm the presence of thallium in the human population. We stumbled on a couple of the dots that had not been connected. Using Doctor's Data and Curtis & Tompkins laboratories, we funded an initial pilot sample to explore thallium levels in the food chain and make the clinical connection.

MR: What else needs to be done that has not yet done? Another dimension of this story is how much thallium is contained in flesh foods from animals whose feed consisted of grains grown on coal-ash, gypsum fertilizer or high-thallium manure. That means testing chicken, beef, and fish, as well as baby food. Clearly more testing is needed on all aspects of these exposures, both human and agricultural.

Discussion

This article presents an overview of preliminary findings in a study of toxic metals in foods produced and/or sold in Marin and Sonoma Counties, California.[1] Although this is a pilot study, the authors consider the implications significant enough to warrant making the findings available.

The findings suggest a number of possible next steps by either federal or non-government watch dog agencies:

- Further verification of findings presented to date
- Determination of the source(s) of heavy metals in the farm-to-retail channel
- Identification of the process by which these metals might accumulate in consumer products, particularly in products such as baby food consumed by vulnerable populations
- Consider possible near- and long-term remediation strategies for affected consumers and farmers

Heavy metals were detected in both organically-certified and non-organically-certified foods. Due to the number of tests conducted to date, more testing will be required before a clearer picture emerges regarding the nature and source of heavy metals in the food supply.

No conclusions are made in this document regarding the presence or absence of toxic heavy metals in food beyond the

continued on page 74 ➤

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data presented. This study has also not demonstrated that there is a difference between the presence or absence of toxic heavy metals in organically-certified vs. non-certified foods. Finally, this study has not yet conclusively identified the source or sources of toxic heavy metals. The information presented in this research needs to be further evaluated, verified, and duplicated.

Michael Rosenbaum, MD

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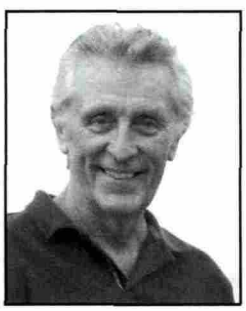

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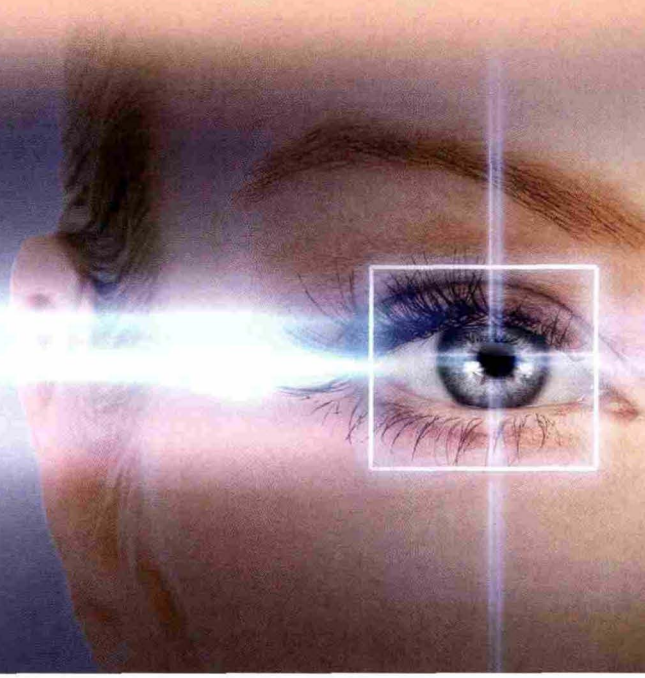

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Lyme Disease: Prevalence, Diagnosis, and Comprehensive Treatment

by David I. Minkoff, MD

A recent autopsy on a 5300-year-old mummy revealed the presence of the bacterium that, in modern times, is known to cause Lyme disease. Suffice it to say that Lyme disease and ticks have coexisted for thousands of years.

In 1909, a Swedish dermatologist, Arvid Afzelius, presented his research into an expanding ringlike lesion, erythema migrans (EM), that would later be a hallmark of Lyme disease. By 1921, he suggested that the disease might be transmitted by the *Ixodes scapularis* tick, better known as the deer tick.

By the 1940s, people were receiving house calls from their family physicians for signs of a similar tick-borne illness that usually often started with a ringlike rash and then developed into multisystem problems. In the same decade, spirochete-type organisms were found in skin samples, which led to the use of penicillin as a treatment.

Fast-forward to the 1970s, when children and adults in Lyme and East Haddam, Connecticut, presented with crippling joint inflammation, headaches, paralysis, and severe chronic fatigue; 25% of them reported having had an EM rash.

In 1981, a scientist studying Rocky Mountain spotted fever (also caused by a tick bite), Willy Burgdorfer, PhD, MD, definitively made the connection between the adult deer tick, *Ixodes dammini* (originally referred to as *I. scapularis*), and the thin, spiral-shaped Lyme-disease-causing bacterium that it carried, which would in 1982 be named *Borrelia burgdorferi* in his honor.

Conclusive proof that *B. burgdorferi* causes Lyme disease was unveiled in 1984, when spirochetes were cultured from the blood of people with the EM rash, from rash lesions, and from the cerebrospinal fluid (CSF) of a patient with meningoencephalitis who had an EM rash.

The Centers for Disease Control and Prevention (CDC) began surveillance for Lyme disease in 1982, and the US Council of State and Territorial Epidemiologists (CSTE) designated Lyme as a nationally notifiable disease in 1991. In 2012, Lyme disease was included as one of the top 10 notifiable diseases by the CDC.

Lyme Disease

Lyme disease can be a devastating illness, one that masquerades as, among others, multiple sclerosis, rheumatoid arthritis, lupus, and brain cancer. It can cause meningitis, congestive heart failure (CHF), depression, schizophrenia, and a range of other neurological disorders.

In fact, 93% of those with chronic fatigue syndrome (CFS) and most of those with fibromyalgia have Lyme, a disease which was linked to 4,396,900 officially diagnosed cases in the US between 1982 and 2012, and that is according to the restrictive surveillance criteria established by the CDC.

If we use a broader, more diagnostically appropriate definition, then that would take our estimated number of cumulative US cases up to 30 to 36 million, according to Daniel Kinderlehrer, MD. In terms of global spread, the World Health Organization (WHO) states that Lyme disease "is now the most common tick-borne disease in the Northern Hemisphere."

Today we also know that there are 5 subspecies of *B. burgdorferi*, over 100 strains in the US, and 300 strains worldwide. According to the International Lyme and Associated Diseases Society (ILADS), bacterial "diversity is thought to contribute to its ability to evade the immune system and antibiotic therapy, leading to chronic infection." In addition, the bacterium has 21 plasmids, 3 times more plasmids than any other known bacterium.

This species diversity and genetic repertoire vitally contribute to *B. burgdorferi*'s antigenic variability and its antibiotic resistance. On top of this, there are related *Borrelia* species that also cause Lyme disease in North America, including *B. bissettii*. Other related Lyme-causing species outside North America include *B. garinii*, *B. afzelii*, and *B. spielmanii*.

Of note, there are other related species that cause different tick-borne diseases, notably *B. miyamotoi* from Japan, a bacterium that causes borrelia miyamotoi disease (BMD), a tick-borne infection that can inflict even more severe symptoms than those of Lyme disease.

In addition to bacterial species and plasmid-caused genetic diversity, there are several different ticks known to carry *Borrelia*; namely, deer ticks, the Western black-legged tick (*Ixodes pacificus*), *Ixodes angustus* (no common name), the Lone Star tick (*Amblyomma americanum*), and the brown dog tick (*Rhipicephalus sanguineus*).

The Rocky Mountain wood tick (*Dermacentor andersoni*) is not believed to carry Lyme; however, this nasty critter does transmit Rocky Mountain spotted fever, tularemia, Colorado tick fever, and tick paralysis. Likewise, its biting cousin, the American dog tick (*Dermacentor variabilis*), also transmits Rocky Mountain spotted fever and tularemia.

In terms of tick carriers, in addition to deer, experts now also believe that

infected ticks are hitching a free ride via approximately 100 species of migrating birds as well as chipmunks, foxes, hedgehogs, rabbits, sheep, voles, and the white-footed mouse.

How do the Lyme–disease carrying ticks pass on the disease? After latching on, the deer (or other) tick takes a blood meal and, in so doing, transmits the Lyme–disease causing spirochetes to the bloodstream. The tick must remain attached for as long as two to three days in order to take a complete meal – it is able to transmit the spirochetes during this time.

Our Approach to Chronic Disease

Before we get to our approach to Lyme disease, let's take a look at what I refer to as the three causes of illness; to wit:

1. **Nutritional deficiency**: through suboptimal diets and compromised metabolisms, we are typically deficient in many micronutrients and some macronutrients.
2. **Toxicity**: we are all exposed to chemicals, heavy metals, pesticides, and other toxins throughout our lives.
3. **Allergy**: the body is mobilizing immune, inflammatory, and allergic responses to agents that it should not be reacting to.

Along with the three causes of illness are seven basic assumptions with which my team and I approach all patients visiting our center:

- **Every patient is toxic**: the body has a cumulative toxic burden that has been building for a lifetime.
- **Every patient is deficient**: the body is missing nutrients and functions.
- **Most patients are allergic**: most patients have a level of sensitivities, intolerances and allergies.
- Correcting 1, 2, and 3 will result in significant improvements in most, if not all, patients.
- Without intravenous (IV) nutrients, our efforts don't work very well.
- Modalities such as PEMF (pulsed electromagnetic field therapy), stem cells, ozone, and homeopathics move healing along faster.
- Without some form of autonomic testing, our approach will not produce the results we would like.

In addition to these foundational causes and basic assumptions, we find some combination of the following body-load problem areas in patients with chronic conditions, some of which are touched on above:

1. **Genetic problems**; e.g., methylation defects.
2. **Nutritional deficiencies**; e.g., essential amino acids (EAAs), essential fatty acids (EFAs), vitamins, and minerals.
3. **Toxic load**: chemicals, vaccine residue, heavy metals, pesticides, electromagnetic field (EMF) radiation, prescription drugs.
4. **Coinfections**: viral, bacterial, parasitic, fungal.
5. **Hormonal deficiencies**.
6. **Dental problems**; e.g., root–canal treated teeth.

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7. **Gut issues**; e.g., toxic gut.
8. **Allergies**.
9. **Autoimmunity**.

Our Approach to Lyme Disease

While acute, recently diagnosed Lyme disease often responds well to antibiotics, chronic Lyme disease – patients were bitten years before and have developed multiple problems and coinfections – is not very responsive to antibiotics, antifungals, and antiparasitics, and so we take a much more comprehensive approach.

In fact, we have found that good clinical outcomes only occur when nutritional deficiencies, electromagnetic pollution, toxic load, gut dysbiosis, immune dysfunction, coinfections, and hormonal imbalances are addressed.

When patients come to our center, Lyme disease has already disseminated to multiple organ systems and is often marked by arthritic, emotional, and neurological symptoms.

A few of the many observations that we have been able to make in our experience with patients presenting with chronic Lyme disease are:

- Patients with early disseminated or late-stage disease usually have strong serological activity, although seroreactivity alone cannot be used as a marker of active disease in the absence of other signs and symptoms.
- Lyme antibodies often persist for months or years following successfully treated or untreated infection. Western blot must be used if the Lyme IgG/IgM antibody serology is equivocal or positive.
- Lyme has immune-blocking secreted factors, such as nagalase (which blocks GcMAF, globulin component macrophage activating factor).
- Patients with chronic Lyme and who have root–canal treated teeth must have the failed tooth/teeth removed.
- Lyme patients always have some combination of coinfections that we look for, including (but not limited to): *Ehrlichia, Babesia, Bartonella, Rickettsia, Spirocheta*, Epstein-Barr virus (EBV), cytomegalovirus (CMV), herpes simplex virus, herpes type 6 and 7, varicella-zoster virus (VZV), human papillomavirus (HPV), *Candida*, MARCoNS (multiple antibiotic resistant coagulase negative staphylococci), *Mycoplasma*, and *Chlamydia*.

Over the years, we have been able to establish what I refer to as our "Mainstays of Treatment," modalities that are the foundation of our treatment protocols for patients with chronic Lyme disease, which include:

- **Ozone** (intravenous [IV] and HOCATT [hyperthermic ozone and carbonic acid transdermal therapy]);
- **Argentyn 23** silver hydrosol;
- **Kaqun** oxygenated water;
- **Herbals** (Monastery of Herbs, Nutrimedix);
- **PEMF** therapy and **MAS Mat** (pulsed magnetic field) therapy.
- **Nutritional Reconstitution** with Perfect Amino, BodyHealth Complete+ Detox.

Prior to, and in addition to, these treatment cores, we conduct: a careful and comprehensive medical exam, autonomic reflex testing (ART) with direct resonance testing and darkfield microscopy, neural therapy scar treatment and autoimmune disease treatment (if needed), and ALCAT food-allergy testing (if needed). We provide a dental referral (if needed) and carry out extensive laboratory tests to uncover toxicities and deficiencies.

We focus on gut restoration, hormone balancing, and metal detoxification (when ready). We recommend: an IV Myers cocktail plus glutathione, oral supplements (BodyHealth Complete + Detox, BodyHealth PerfectAmino, vitamin D, iodine, NanoGreens, magnesium), and a Paleo diet.

Conclusion

Lyme disease is often not diagnosed or is confused with the symptoms of the many comorbidities and coinfections with which it is associated and, thus, misdiagnosed. While patients with chronic Lyme disease often begin their healing journey filled with pain, despair, and confusion, a comprehensive workup and diagnostic battery are critical to uncover each patient's very specific clinical problems and deficiencies. A complete Lyme disease treatment program – one focused on correcting the core problems of nutritional deficiency, toxicity, and allergy/immunity – will not only offer patients health and freedom from the shackles of this multipronged and devastating disease but can also offer something infinitely more valuable: hope and a brand new life.

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Dr. Minkoff's wife became ill in 1995, and her physicians couldn't find what was wrong. Not accepting their "no hope" conclusion, Dr. Minkoff went on a search to help her, which led him out of emergency medicine into complementary and alternative medicine to find the answers. In the process he gained expertise in biological medicine, heavy metal detoxification, anti-aging medicine, hormone replacement therapy, functional medicine, energy medicine, neural and prolotherapy, homeopathy, and optimum nutrition. He studied under the masters in each of these disciplines until he became an expert in his own right. The answers he found were soon in demand when others learned of his wife's return to good health. In response to this, he and his wife, Sue Minkoff, RN, established Lifeworks Wellness Center in 1997, and it quickly became one of the most comprehensive complementary and alternative medicine clinics in the US. The demand for the products and protocols he discovered became a catalyst for founding BodyHealth in 2000, a cutting-edge nutritional products company. Dr. Minkoff is an avid athlete and has completed 41 Ironman triathlons. To keep his fitness maximal, he lives the lifestyle that he teaches, and tries to set an example for others so that they can enjoy a life free of pain and full of energy.

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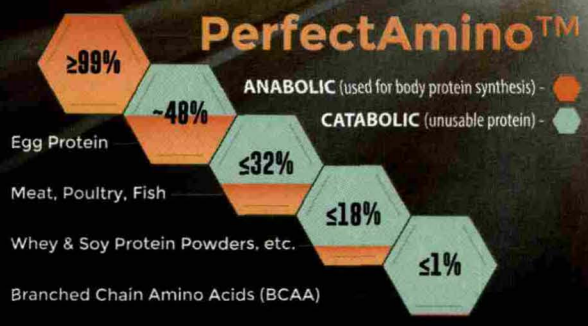

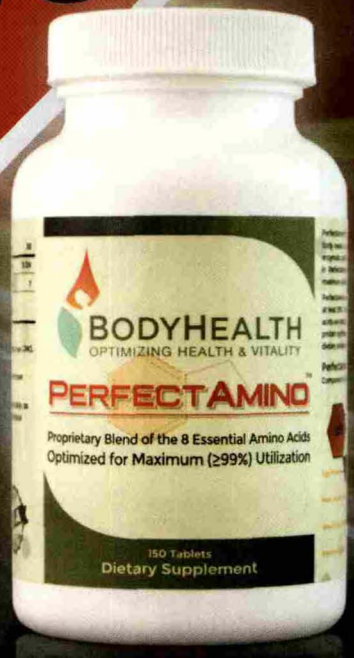

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Field Control Therapy (FCT) and its Successful Approach to Causes of Diseases in Women

by Savely Yurkovsky, MD

This approach focuses on addressing women's health at its fundamental level, as in men or children – by addressing the exact causes responsible for the loss of health. The main means to accomplish this are: bioresonance testing in order to noninvasively determine these causes, from the internal organs themselves, and causative homeopathy to remove these morbid causes from the body. Obviously, addressing bad diet and electromagnetic pollution also leads to the reduction of these corresponding morbid causes of disease. Both bioresonance testing and homeopathy act primarily through biophysical means, the most fundamental level of human physiology. The presented cases serve to illustrate the fruitfulness of this approach, which overall significantly reduces the number of other tests and treatments.

Case of Resolved Ovarian Cyst and Cancelled Potential Surgery

A young woman experienced severe pain in her left ovary for 1 week. She also complained of low energy and frequent gastrointestinal pains with diarrhea for months. Due to the severity of her ovarian pain and an ultrasound demonstrating an ovarian cyst of considerable size, her ob-gyn recommended its surgical removal,

unless the pain or cyst significantly reduced shortly.

Bioresonance Muscle Testing

This indicated systemic morbid effects of candidiasis and parasitosis, which were at least partly sustained by residues of antibiotics in the gut. Her ovaries, thyroid, and adrenal glands as well as lymphatic system tested as energetically weakened, too.

FCT Homeopathic Treatment, and Addressing Dietary and Electromagnetic Morbid Factors

The patient received proper remedies to address all of the identified causes of her systemic illness, including the malfunctioning organs. She also received electromagnetic stress-reducing technology (Memon), as well as the advice to cut out all of her regular sweets and alcohol rounds on weekends.

Follow-Up Visit Some 2 Weeks Later

The ovarian pain was completely gone; the patient felt more energetic and much better overall, even while continuing her regular sweets and alcohol regimen. The follow-up ultrasound report read that her left ovarian cyst was no longer present.

A Case of Hypothyroidism, Low Platelet Count, Chronic Fatigue and Other Medical Problems

A postmenopausal woman presented with autoimmune-induced Hashimoto's hypothyroidism and low platelet count, chronic fatigue and severe fluid retention, multiple food allergies, and gastrointestinal problems. She was treated for years with integrative medicine and medicated with Armour Thyroid 120 mg daily, reducing her severe fatigue, and bioidentical hormones, which helped her menopausal symptoms. She also consumed many supplements

FCT Bioresonance Muscle Testing, Homeopathic Treatment, and Overall Clinical Course

This woman's body, as in all chronically ill people, resembled a warehouse of toxic pollutants and infections, with all being zapped or electrocuted in addition by our daily environment. Just a few pollutants were severe mercury toxicity, lead, cadmium, and other toxic metals, pesticides, and herbicides. She carried multiple parasites and *Candida* species, influenza and Epstein-Barr viral infections, as well as Lyme and coinfections. Toxic residues of antibiotics were also present and addressed. She also reported significant improvement after significantly reducing her exposure to computers and using electromagnetic stress-reducing devices (i.e., Memon). She stated that she benefited specifically from parting with one source of such exposures, her hybrid car, following my advice based on bioresonance testing.

After the administration of specific antiparasitic homeopathic remedies or sometimes homeopathics to just strengthen her immune and endocrine systems, she would e-mail us photos confirming her exorcism from "wildlife" – numerous worms. Besides her energy level being completely restored, she managed to enjoy it with her thyroid hormone being discontinued while her thyroid blood tests have normalized for the first time in 35 years. In just as many years, her platelet count became normal, too. Likewise, her sex hormone replacement therapy was painlessly discontinued, as her normalized physiology started rejecting these as evidenced by the developed side effects and bioresonance testing.

A Case of Uterine Fibroids with Prolonged and Heavy Periods, Hypothyroidism, Fatigue, and Absent Sex Drive

FCT Bioresonance Testing, Homeopathic Treatment and Clinical Course

A woman in her 30s had the aforementioned problems plus very painful menstrual cramps necessitating pain killers, and excessive weight. She was managed on Synthroid and birth control pills and advised to have a hysterectomy. She was found to have multiple environmental chemicals, parasites, yeast infections, mercury toxicity, and viral infections, all having multisystemic effects, including her ovaries, endometrium, and thyroid. While the homeopathic treatment addressed these findings, she was also advised to remove her mercury fillings and replace her Synthroid with Armour Thyroid as suggested by bioresonance testing.

Since the installment of Memon in her house to address excessive EMF stress, her detoxification process seemed to move much faster. In the end, her energy level and sex drive were completely restored; the excessive weight came off; her very painful, heavy, and prolonged periods ceased; while both the birth control pill and pain killers were discontinued.

Conclusion

It is simple: either we get rid of causes of disease or these causes get rid of us. Anything in between is not good territory, either. ◆

Savely Yurkovsky, MD, graduated from II 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 has demonstrated numerous documented reversals, in a variety of chronic diseases.

His book, *Biological, Chemical, and Nuclear Warfare Protecting Yourself and Your Loved Ones: 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 (bioterrorism) 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. Dr. Yurkovsky's seminars on DVD, devoted to autism, other brain disorders, and Lyme disease, serve as a virtual step-by-step textbook classics explaining the fundamental nature of all chronic diseases (www.yurkovsky.com). 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 health practitioners' training can be made through information provided in the FCT ad on page 80 in this issue.

Fat and Breast Cancer Risk

by Jacob Schor, ND, FABNO

Scientific thinking about cancer occasionally goes through dramatic shifts in understanding. If we don't keep up with the research, we can end up left standing holding a trick-or-treat bag of old wives' tales and sounding ignorant.

High intakes of fat were once thought to cause breast cancer. This is no longer believed to be true. We should learn something important from this shift in thinking.

The first mention of this "fat causes breast cancer" idea was back in 1950, when Silverstone and Tannenbaum reported that the more fat they fed to mice, the more likely the mice were to get breast cancer.[1] This idea hung around for a quarter of a century but took off in 1975 when a paper by Armstrong and Doll caught our attention. They had plotted cancer incidence and mortality rates for a list of countries and compared these data to a range of dietary habits. The breast cancer graph was striking. The higher a country's per capita consumption of animal fat, the higher the risk for breast cancer appeared.[2] The graph's plot was nearly a straight line.

Then in 1978, Miller et al. made a convincing argument based on a case-controlled study of either 40 or 400 cases of breast cancer (sources conflict). Using recall questionnaires about diet, the researchers claimed that increased total dietary fat was associated with greater risk for breast cancer.[3] In Miller's data the association between breast cancer and fat did not quite reach statistical significance, but the idea that dietary fat caused breast cancer was considered proven. In the words of the authors, "Reasons why a weak association might have been anticipated are discussed, and it is concluded that in reality the association is stronger. Furthermore, its consistency with other evidence, both experimental and international, suggests that it is causal."

Taking Miller's study as proof, the Committee on Diet Nutrition and Cancer, a division of the National Research Council, came out recommending that Americans reduce fat consumption from an average of 40% of daily calories to 30% in 1982.[4] In 1984, the National Cancer Institute followed suit and adopted these recommendations into nationwide public policy. From that point on, this hypothesis was true.

In hindsight, this is so interesting. Everyone assumed that cancer was going to be an easy nut to crack, that it had a simple solution. If we declare a war on cancer, some smart scientists would be able to figure it out. The mindset was that cancer was like an infectious disease, that we could identify the causative agent and find a fix.

Even before the NCI had launched the public campaign to reduce fat consumption, research had already cast doubts on this "eating fat causes cancer" theory. Graham et al. reported in 1982 that after comparing the diets of 2024 breast cancer patients with that of 1463 controls without cancers, they had found no differences in fat consumption between those with cancer and those without.[5]

What followed was a back-and-forth, one study after another trying to prove the theory. Howe et al., who had pulled together a meta-analysis of 12 studies, countered Graham in 1990. These 12 individual studies had not shown a significant association between eating fat and breast cancer, but the combined data did. Howe's analysis also indicated that the more fruit and vegetables eaten, the lower a woman's breast cancer risk; this led to a famous conclusion: "If these dietary associations represent causality, the attributable risk (i.e., the percentage of breast cancers that might be prevented by dietary modification) in the North American population is estimated to be 24% for postmenopausal women and 16% for premenopausal women."[6]

We used this conclusion for many years to justify how we told patients to eat. Some doctors don't seem to have gotten the update that Howe's conclusions are no longer believed true.

There was a fault in Howe's methodology; the only accurate way to compare diets is when total calories are held constant, what is referred to as *isocaloric*. Eating enough calories to gain weight or eating so few as to lose weight has a greater impact on cancer risk than what foods a person actually eats. When these data were subjected to the necessary isocaloric calculations, the fat and cancer association became negligible when calculated for a 10% difference in total calories derived from fats.[7]

Sides were taken in this debate over whether fat affected risk of breast cancer, case-control studies being held up by one side or the other trying to prove that they were right. In the end, the real lesson seems to be that case-control

studies have inherent weaknesses that made it nearly impossible to prove the truth. The deciding data had to come from prospective studies.

Prospective studies are less prone to error than the earlier case-control studies that relied on unbiased selection of participants, and honesty, clarity of memory, and accuracy by all participants in completing food questionnaires that were often retrospective.

Phillips and Snowdon reported on breast cancer mortality during a 21-year period among Seventh-day Adventists in 1983 and found no significant trend toward increasing risk for breast cancer with greater meat consumption.[8]

Mills et al. after examining these same data reported no association between meat, milk, or egg consumption and breast cancer death. Oddly enough, women who adopted a vegetarian diet early in life were at higher risk of death from breast cancer.[9]

Willet et al. analyzed data from the Nurses' Health Study cohort which included 89,538 nurses in the US that was published in 1987. They found a trend toward a decreased risk of breast cancer for women who ate the most fat, a nonsignificant 18% decrease.[10]

Researchers have continued to monitor this Nurses' Health Study cohort. Holmes et al. published an updated analysis in 2014, 34 years after the start of the study. They reported that 1529 of the original group had died from breast cancer; the same nonsignificant trend persisted toward higher fat and lower risk for death from breast cancer (top vs. bottom quintile hazard ratio [HR] 0.85; 95 % CI 0.72, 1.01; p trend = 0.05).[11]

Half a dozen prospective studies were published from 1989 to 1993, and in none of these trials did the association between total fat and breast cancer reach statistical significance.

Willett: Nurses' Health Study; 1992[12]
Howe: Canadian study; 1991[13]
Graham: New York State Cohort; 1992[14]
Kushi: Iowa cohort; 1992[15]
Van den Brandt: Dutch Health Study; 1993[16]
Mills: Adventists' Health Study; 1989[17]

A 1996 meta-analysis by Hunter et al. combined the data from all six of these cohorts plus an additional Swedish study (Wolk) creating a database of 4980 cancer cases from studies that included a total of 337,819 women.[18] When women in the highest quintile of energy-adjusted total fat intake were compared with women in the lowest quintile, the relative risk of breast cancer was 1.05 (CI 0.94 to 1.16). There was no evidence that risk for breast cancer varied significantly with fat intake.[19]

That Swedish study by Wolk et al. is of interest in light of a recent study using PREDIMED data (that we will come back to later) which reported that eating extra-virgin olive oil (EVOO) was associated with lower breast cancer risk. Wolk's group analyzed diet data from 61,471 Swedish women of whom 674 had breast cancer occur. No significant association was seen for total fat intake and risk, but type of fat seemed to matter. Monounsaturated fat, as in olive oil, lowered risk of breast cancer, while polyunsaturated fat was associated with higher relative risk. Still, total fat eaten made no difference, but each 10 g of additional monounsaturated fats consumed a day was associated with a 55 % decrease in relative risk of breast cancer while each 5 g increase in polyunsaturated fat was associated with a 69% increase in relative risk.

Based on these more recent prospective study results, epidemiologists and researchers pretty much abandoned this idea: we no longer need to tell cancer patients to decrease fat.

Unfortunately, neither the public nor many health professionals have caught onto this change in thinking.

Our reliance on case-control trials to answer complex questions related to diet and cancer would appear to be misplaced. The more subtle the difference we are trying to detect in our population, the more likely that small errors in methodology will compound and hide the actual change differences so slight that the researchers in all honesty may have been unaware of them. If you doubt this, go and read about the "Pepsi vs. Coke taste test" campaign in Malcolm Gladwell's book *Blink*.

Risk for breast cancer is now thought to be related to some combination of total calories, basal metabolic index (BMI)/obesity, changes in weight, insulin resistance, and IGF-1 effects. In other words, dietary risk for breast cancer is attributed to everything but fat in the diet.

Silverstone and Tannenbaum, the originators of the fat and breast cancer theory, were well aware that caloric restriction lowered incidence of cancer and had studied whether intermittent fasting would decrease breast cancer in mice (caloric restriction worked but intermittent fasting didn't).[20]

How tall people grow to be is a good approximation for how well fed they were during childhood. Height appears to be closely correlated with breast cancer risk.

There are several notable prospective trials on diet and breast cancer that deserve mention.

The Women's Healthy Eating and Living (WHEL) study is one of them. Between 1995 and 2000, 3088 women who had been diagnosed and treated for breast cancer were split into a diet intervention group and a comparison group and then followed until 2006. The women in the experimental group were asked to follow a diet that consisted of 5 vegetable servings plus 16 oz of vegetable juice, 3 fruit servings, 30 g of fiber, and fat intake lowered to 15% to 20% of caloric intake.[21] Over the follow-up, 16.7% of the women in the diet group vs. 16.9% of the women in the control group developed invasive breast cancer. Rates of death were close: 10.1% in the diet group vs. 10.3% in the control group. These differences were not significant [22]

Here is something interesting; the women who were most active at the start of the study had a 53% lower mortality risk, compared with the less-active women, and those women who followed exercise guidelines given to everyone in the study had a 35% lower mortality risk.[23] These later differences

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are significant, both statistically and clinically.

Harvard Professor Willard Willet, PhD, lectured at the National Cancer Institute annual Cancer Prevention Symposium in 2012. At that point, this fat and breast cancer theory was already history. In Willett's words, "There was never any strong evidence for this idea, but it was repeated so often that it became dogma in the 1980s and 1990s ... the hypothesis that the percentage of calories from fat in the diet is an important determinant of cancer risk, at least during midlife and later, is not supported by the data."[24]

That phrase is worth remembering, not just for this fat business, but for other assumptions that we think are true: "It was repeated so often that it became dogma."

Another specific study that needs mention is the Women's Intervention Nutrition Study (WINS); this may have been the largest and most ambitious nutritional intervention study ever attempted.

Between February 1994 and January 2001, 2437 women were randomly assigned to one of two groups in a 40:60 ratio, either a dietary intervention group or control group.[25] This trial's initiation was 2 years before Hunter et al.'s meta-analysis. In hindsight we might question the wisdom in continuing this effort.

The WINS diet attempted to drop dietary fat down to 15% of daily calories. Twelve months into the study, participants in the diet group had dropped their daily fat from 51.3 g/day to 33.3 g/day. A 2006 interim follow-up reported that women in the low-fat diet group had lost 6 pounds. At that point, 9.8% of the women in the diet group had experienced a relapse or new breast cancer compared to 12.4% in the control group. These differences had not reached statistical significance.[26]

A final summary of data from this WINS cohort was presented at the San Antonio Breast Cancer Symposium in December 2014. This conference report has not been published in the peer-reviewed journals yet. According to Rowan Chlebowski, after more than 15 years of follow-up, the low-fat WINS intervention was effective only at improving survival among women with hormone receptor-negative tumors. In women with estrogen receptor (ER)-negative tumors, a 36% statistically significant reduction in deaths was seen with the dietary intervention. The benefit was even greater – a 54% reduction in deaths – among women whose tumors were negative for both estrogen and progesterone receptors (PR).[27]

Yet there was no overall survival benefit in the group as a whole; mortality rates were 17.0% in the low-fat groups and 13.6% in the control group, a nonsignificant difference. For the 478 estrogen-negative patients, the differences were significant, with the low-fat group surviving 13.6 years compared with 11.7 years (HR = 0.64, p = .045). For the 362 women with ER- and PR-negative cancers, survival times were even better, 14.0 years (HR = 0.46, p = .006).[28]

Between the results from the WINS and the WHEL trials, the researchers have failed to prove that the dietary interventions that they instituted after breast cancer diagnosis improved prognosis. These subgroups of ER-negative women may prove to be more responsive.[29]

Was it the low-fat WINS diet or something else that accounts for the benefit in this subgroup of women? At the end of the study, women on the low-fat diet had lost 5% of their body weight. The perceived benefits may just be due to this weight loss.[30]

Exercise and weight loss certainly improve breast cancer survival.[31] Gaining weight after treatment is associated with greater risk of recurrence.[32] Weight gain is significantly associated with increased risk of triple negative breast cancer. Obesity is strongly associated with ER-negative and PR-negative breast cancer incidence in women less than 50 years old.[33] Perhaps the perceived benefit is only secondary to obese women losing weight. Weight loss certainly may have more effect on ER and PR negative breast cancers: "The detrimental relationship between body size and breast cancer recurrence may be more pronounced among women with estrogen receptor (ER)/progesterone receptor (PR)-negative breast cancer."[34]

In June 2014, Vitolins reported on a pilot study of obese women who were survivors of double-negative breast cancer and who through diet lost an average of 14 pounds in just 12 weeks. The long-term impact of this intervention is still unknown, but obviously these researchers are hoping that it proves useful.[35]

ER-negative tumors may respond differently to other dietary interventions than ER-positive tumors do. A May 2015 paper reported that low HDL cholesterol was correlated with worse prognosis in triple-negative breast cancer. TNBC patients are more likely to have elevated blood sugar than the women diagnosed with other types of breast cancer.[36] Weight loss would be more likely to improve glucose control and conceivably cancer prognosis than being on a low-fat diet.

A 2014 study that compared 12 months on a low-carbohydrate diet (n = 59) vs. a low-fat diet (n = 60) reported that the low-carb diet was superior at achieving weight loss and increased HDL.[37]

There may be another good reason to hesitate encouraging women to limit fat consumption, at least when it comes to EVOO. Two recent studies suggest that high intakes of EVOO may provide protection, in particular against hormone receptor-negative cancers.

In 2014 Spanish researchers analyzing data from the EpiGEICAM cohort reported that a Mediterranean-style diet pattern was associated with lower risk of breast cancer, especially in contrast to a Western-style diet.

EpiGEICAM researchers compared dietary data from 1017 breast cancer cases with a similar number of matched controls. Adherence to the Western dietary pattern was associated with a higher risk of breast cancer (OR 1.46; 95% CI 1.06–2.01), especially in premenopausal women (OR = 1.75; 95% CI 1.14–2.67). In contrast, the Mediterranean pattern was related to a lower risk (OR 0.56; 95% CI 0.40–0.79). The protective effect of the Mediterranean pattern was stronger for triple-negative tumors (OR = 0.32; 95% CI 0.15–0.66). [38]

A recently published analysis from the PREDIMED trial also suggests that adherence to a Mediterranean-style diet and in particular consumption of EVOO is associated with lower risk of breast cancer. In this prospective trial, 1476 participants were assigned to a Mediterranean diet supplemented with EVOO, 1285 to a Mediterranean diet supplemented with mixed nuts, and 1391 to a control diet in which participants received dietary counseling encouraging a low-fat diet.

Participants in the two intervention groups were given either a liter of free EVOO each week or free mixed nuts (30 g/d) according to their group. In the primary analysis, adding either nuts or EVOO significantly reduced risk of cardiovascular events (that is, dying of a stroke or heart attack).[39] EVOO addition to the diet was associated with a 68% decrease in breast cancer diagnosis over the 4.8-year study. Adding nuts was associated with a 41% drop. [40]

Rather than attempting to control or limit fat consumption, it may be more prudent for women to strive to increase EVOO and nut consumption.

Two groups of researchers have recently been debating about dairy fats, in particular butter, and whether these fats are associated with increased risk.

In May 2013, a paper by Candyce Kroenke et al. argued that high intake of dairy fat is associated with worse breast cancer survival because of the estrogenic hormones derived from these foods. These researchers had analyzed data from 1893 women in the Life After Cancer Epidemiology (LACE) study diagnosed with early-stage invasive breast cancer, of which 349 had a recurrence and 372 died, 189 from breast cancer. Those women consuming larger amounts of high-fat dairy exhibited a trend toward higher breast cancer mortality ≥1.0 servings/day: HR = 1.49 (CI = 1.00 to 2.24, p = .05).[41]

In response to Kroenke's paper, Zucchetto et al. analyzed data already in their possession from an Italian cohort of 1453 women who had been diagnosed with breast cancer and had been enrolled in a case-control study. Among this group there had been 503 deaths, 398 from breast cancer. Zucchetto found no association between dairy consumption and all-cause or breast-cancer mortality. (FYI: Overall mortality was lower with greater cheese consumption [all-cause HR for ≥1 servings/day vs. <0.5 serving/day = 0.74, 95% CI = 0.56 to 0.99]).[42]

Kroenke et al. hypothesized that the differences in their findings from those of the Italians are due to possible differences in Italian dairy farming practices that might lower estrogen content of Italian milk products, though they offered no specific details to what these differences were or evidence that these milks differ. [43]

These are again case-control studies, and we need to stop trusting these kinds of studies when it comes to cancer and diet; they don't work.

The first lesson from this review is that it is time to abandon the old hypothesis that high fat consumption leads to breast cancer. Continuing to let patients believe in this disproven idea may dissuade them from eating more nuts or olive oil, two foods that many still avoid because they are high fat. Given the pronounced benefits seen in prospective studies, avoiding these foods should now be considered detrimental to health.

The second lesson we need to learn from this story is that we need to look more closely at the type of evidence that we are relying on to make decisions. In particular, case-control studies have not provided reliable conclusions. In general, well-done randomized, prospective studies outweigh the case-control studies when it comes to cancer and diet research.

Publication of a study in a peer-reviewed journal does not mean that the conclusions reached are true. We remember the many past predictions based on epidemiological data which suggested that specific nutrients would be cancer preventive and how badly the prospective trials failed.[44–48]

We naturopathic physicians take pride in and enjoy being on the leading edge of nutritional science. Our leading position as early adopters does come with an added ethical accountability; when the science changes, we are responsible for spreading the word. We do not want our patients or the public whom we've put made such an effort to educate to continue on a misdirected path.

Bottom line: A diet to prevent breast cancer should probably be a lower-carbohydrate version of a Mediterranean-style diet, with special emphasis on high EVOO and nut intake and perhaps less butter.

A low-fat diet may still prove useful in certain subgroups of breast cancer patients, in particular double- or triple-negative cancers, but the evidence supporting this idea has not been published yet, and possible confounders may void the perceived benefit.

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Fat and Breast Cancer Risk

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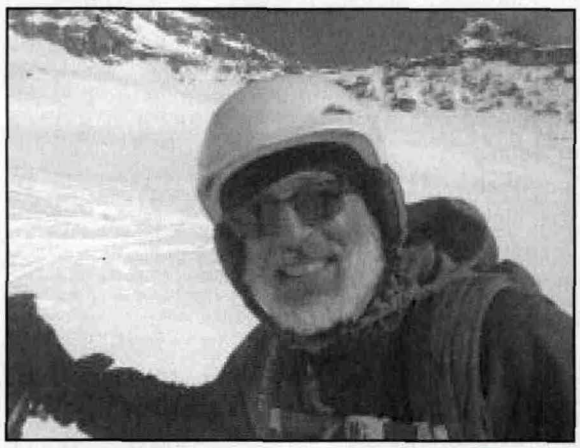

Jacob Schor, ND, FABNO, has practiced as a naturopathic physician in Denver, Colorado, with his wife, Rena Bloom, ND, since they graduated from National College of Naturopathic Medicine in 1991. He was humbled in 2008 when presented with the Vis Award by the American Association of Naturopathic Physicians (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*.

Letter to the Editor

The Death of Dr. Nicholas Gonzales

I learned with sadness about the death of Dr. Nicholas Gonzales, a leading physician in alternative cancer for whom I have great respect. A few years ago, we participated in a seminar together on pancreatic cancer in London. This is another tragedy among so many others over the past decades, with leading doctors who died from disease or suddenly from heart failure, but supposedly in good health, like Dr. N. Gonzales. Are we sure that he was healthy as the medical system says we are healthy? In fact, every day, people die like that while under medical supervision and check-ups; in fact, this is totally wrong, since medical checkups only say everything is normal, but this is only one face of the reality.

We are overly concerned with declared disease and how to treat disease, but too often we neglect preventative measures for ourselves, such as checking up on other alternative diagnostics, having a better diet, taking supplements, and drinking organic vegetable juices. Often we forget or are neglectful while giving advice to our patients. Was Dr. Gonzales eating healthful foods and taking supplements such as coenzyme Q10, garlic, potassium, omega-3s, SOD, and glutathione, for example? Wondering if he had, would he have died from heart failure? Did he ever have an iridology checkup or a Vega computerized electromagnetic field scan or a bioelectrometer test with a terrain assessment? An alkaline and oxidized terrain favors cardiovascular disease, for example. Another diagnostic can be performed with a live blood analysis test that can show many useful types of information such as thrombi in the blood, oxidized fat particles, or platelet or red cell aggregation.

What was the dietary style of Dr. N. Gonzales? Several of my colleagues in Portugal and Europe died from cardiac arrest, but they were too busy, living under high stress, eating just regular food. A few years ago, a doctor whom I knew died while lecturing at one of the integrative and alternative medicine congresses hosted by American Biologics, where I was participating. This was a shock for all the participants. Incidentally, he was lecturing on oxidative stress and antioxidants. Most alternative doctors do not take care of themselves or even take prevention as part of their job or profession. They have no rules in their lives and even neglect a healthful way of eating. One of my colleagues and friends from England died of heart attack the same morning that he arrived by ship in Lisbon to visit me, but I know that he was eating every kind of commercially available food, particularly meat in excess. Another doctor, one of my assistants, died from a heart attack during a flight between Lisbon and Paris. He was only 53 years old, but was not doing anything in terms of prevention or a healthful lifestyle to take care of himself. He was also smoking. And I haven't even mentioned the ones who died from cancer.

So again, the question is whether we are really doing something for ourselves and not just for our patients. Being a physician of alternative medicine or cancer doesn't mean that one is following the principals of naturopathy and believes that he should eat better food and look after himself. One consultant, a PhD from the US whom I knew very well from meeting on several occasions at congresses, was always ➤

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lecturing about liver detox, antioxidants, diet; to my surprise I discovered him eating fried eggs and bacon at breakfast, so you see here we have a problem to define this misconception.

Since I first met Dr. B. Jensen in 1962 in Los Angeles, I have followed what I believe is good for my health, the same as for my patients. Every day I take about 30 capsules of a mixture of vitamins, enzymes, omega-3s, supplements such as coenzyme Q10, and magnesium, plus 30 ml of enzyme yeast cells that also contain a high level of natural coenzyme Q10, glutathione, and most everything that the body needs. It keeps your blood more fluid and richer, with better oxygen circulation. Beyond my rules in the way of eating and nutrition, for the last three decades I have regularly run, jogged, swum, cycled, and even have been in few triathlon competitions, although now that I am a youthful 73 years old, I have reduced my activity. I only go swimming and jogging now about 4 to 5 times per week, but during the summer I swim 1 hour per day in the ocean. Exercise is good for the heart, it attracts more oxygen, and keeps your brain alert. The Mediterranean diet is most important in preventing cancer and especially heart disease. In fact, this is our diet in Portugal, with a large intake of fresh fish, fresh vegetables, and large quantity of cold-pressed 100% virgin olive oil. This is not only the food of the native people of Crete, but also Portugal, although the new generation goes for hamburger, french fries, and other fast foods.

One of my former colleagues and friends in Portugal, who was not only a medical doctor with a very brilliant mind but an alternative doctor as well, was found dead in his hotel room in Istanbul Turkey, while he was participating in a conference. He was only 48 years old and died from heart failure. He never worried about or took care of himself. So you see, the tragedy of Dr. Gonzales was not an isolated incident. It is time to realize that these same naturopaths, physicians of alternative medicine or cancer prevention, had better not only believe in what they do professionally, but as a lifestyle. From the beginning I realized that nature, a nutritionally sound diet, and exercise are our best medicine and this is what the body needs. Today with increasing stress and environmental pollution, we really need to look carefully at our own health by taking supplements, undergoing detox, and regularly drinking organic vegetable juice as I personally do, several days per week. I will not even present further examples of colleagues who foolishly died because of not having any principles and practicing a healthful way of eating in their personal lives. Of course, I myself hopefully plan to be active on life's stage for many more years to come, and will continue to treat my patients, teach, and write books and many more informative articles.

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Response to Lodi's Article on the Lack of Oxalate Dangers in the Green Smoothie Diet

In response to the inaccurate, unscientific article by Lodi on oxalates, I will make the following point-by-point responses:[1]

1. Cartoons about Popeye.

I will not use any cartoons in my response. Anyone interested in cartoons should immediately stop reading this article and start reading their local paper's comic section.

2. Inaccurate references.

The tone for accuracy of the author is set in the very first paragraph of his article in which his first reference, 23, has nothing to do with my green smoothie article, which is reference 24. A better reference would actually be 2 from my article.[2] When the clock strikes 13, the accuracy of the other 12 hours of the clock is in serious question.

3. Inaccuracy about the contribution of endogenous production to total oxalate load.

Lodi states that 80% to 90% of oxalates in the body are endogenously produced. Unfortunately, the best scientific study refutes his assertion. According to Holmes et al., who did extremely well-controlled studies on every aspect of oxalate metabolism and have published 41 scientific articles on oxalates in the peer-reviewed literature, the mean dietary oxalate contribution to total oxalate in the diet is 52.6 % on a *high*-oxalate diet, which was defined as a diet of 250 mg oxalate per day. The person drinking a green smoothie with 2 cups of raw spinach ingests *1312 mg of oxalates*, or over 5 times the level of what Holmes considers a high-oxalate diet, just in the spinach consumption alone and over 26 times the amount of oxalates in a low oxalate diet (50 mg per day).[4] The estimated human production of oxalates is 40 mg per day.[3] On a green smoothie diet with 2 cups of spinach, the diet in normal humans contains 33 times the endogenous human production of oxalates just based on the spinach alone.

All of Lodi's assertions about the benefits of a vegetarian diet are meaningless, since there is no single vegetarian diet; there are as many vegetarian diets as there are vegetarians.

4. Inaccuracy about the availability of calcium and magnesium in spinach.

Lodi states that "every plant, green and otherwise (including spinach) has abundant magnesium and calcium and potassium." Unfortunately, none of the calcium in spinach or other high-oxalate plants is bioavailable, since it is strongly bound to oxalates. Furthermore, the average oxalate value of spinach is 7.5 times its calcium content, making spinach a very poor choice for someone to maintain adequate calcium stores.[5] According to Kohmani, who added a good deal of spinach (similar to the diet of a person ingesting a daily green smoothie or a large daily spinach salad) to the diet of rats to determine its effects:

> If to a diet of meat, peas, carrots and sweet potatoes, relatively low in calcium but permitting good though not maximum growth and bone formation, spinach is added to the extent of about 8% to supply 60% of the calcium, a high percentage of deaths occurs among rats fed between the age of 21 and 90 days. Reproduction is impossible. The bones are extremely low in calcium, tooth structure is disorganized and dentine poorly calcified. Spinach not only supplies no available calcium but renders unavailable considerable of that of the other foods. Considerable of the oxalate appears in the urine, much more in the feces.[5]

5. Lodi argues that his patients haven't complained about kidney stones while drinking a lot of green smoothies, so oxalates must not be problematic.

Lodi's contention that his patients on a high-oxalate diet don't have kidney stones is anecdotal. He presents no data from active chart review of his patients to determine if questions about kidney stones were ever asked. Furthermore, it is doubtful that his patients would have even have connected their diet with their kidney stones. I have had numerous seminars on the connection between oxalates and kidney stones, and it is common to get feedback from the audience members that they had kidney stones shortly after starting either a diet including a spinach green smoothie or a large spinach salad on a regular basis. Since these comments were not even solicited, it is likely that even a larger number of individuals may have experienced kidney stones but were shy to voice their experiences. A neurologist friend attributes his recent severely disabling stroke to the dietary changes encouraged by his wife that placed him on a daily green spinach smoothie for a considerable time.

Furthermore, Lodi seems to think that a lack of kidney stones indicates a lack of oxalate problems. However, oxalates may form in virtually every organ of the body, including the eyes, vulva, lymph nodes, liver, testes, skin, bones, gums, thyroid gland, heart, arteries, and muscles.[6,7] Oxalates may occur in these other organs without appearing in the urinary tract at all and in individuals without genetic hyperoxalurias. Oxalates have been implicated in heart disease, stroke,

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Response to Lodi's Article

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vulvodynia, and autism.[7–10] Women of childbearing age need to be especially careful of the spinach green smoothie diet because of the autism–oxalate connection and the negative effects of spinach containing oxalates on fertility.[5] Inmates in the state prisons in Illinois were encouraged by the Weston A. Price Foundation to file a lawsuit against the state because of their deteriorating health due to a high amount of soy protein in the prison diet.[11] Soy protein ties with spinach as the highest-oxalate food.[4] Oxalates are especially toxic to the endothelial cells of the arteries, leading to atherosclerosis.[12] Oxalate crystals are concentrated in the atherosclerotic lesions.[7] Such lesions have commonly been overlooked by the use of stains of atherosclerotic lesions that make the oxalate crystals difficult to visualize. The relatives of people consuming the green smoothie diet would only know of their loved ones' oxalate deposits throughout their organs on the day of their autopsies which employed pathological examinations that can detect oxalates.

Primary genetic hyperoxaluria is not the major cause of kidney stones in adults, since 80% of individuals died of this disorder before age 20 and it is so rare that it could not possibly be the cause of most cases of oxalate kidney stones.[13] However, a genetic polymorphism present in up to 20% of Caucasian groups called P11L codes for a protein with 3 times less activity of alanine–glyoxylate aminotransferase (AGT) than the predominant normal activity polymorphism, leading to excessive endogenous production of oxalates.[14] This substantial group of individuals would be even more susceptible to the harm of a high-oxalate diet. Kidney stones were rampant in the UK during the world wars when rhubarb, another high-oxalate food, was recommended as a substitute for other low-oxalate but unavailable vegetables.[13]

In summary, those who do not care for their health can eat or drink whatever they want. But they should realize that their diets are fad-based and/or based on quasi-religious ("feasts" as part of the "awakening," according to Lodi) reasons, not based on hard scientific evidence. Furthermore, they should be aware that their diet may kill them.[15] The green smoothie fad will go down in medical history with the AMA journal allowing cigarette advertising with physician endorsements and the use of mercury-containing teething powder for babies as one of the greatest health follies in a considerable time.

William Shaw, PhD

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Gaby Editorial: "Another Drug That We Don't Need"

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to measure for people who have difficulty sleeping at night. However, during the course of the study, "entrainment" – which involves urine tests that measure biochemical correlates of circadian rhythm – was added as a coprimary end point. Subsequently, entrainment was listed as the sole primary end point, and total nighttime sleep was eliminated as an end point. Finally, one month before the study results were released, a new coprimary end point was added: a measure of response defined as a "significant improvement ... in key clinical measures." Vanda also massaged the data in several other ways in order to reach the conclusion that its drug is effective.

So, here we have a drug company spending enormous amounts of money to try to convince people to spend enormous amounts of money on a drug that may not work very well, and which may be no more effective than a low-cost over-the-counter supplement. One wonders how they can sleep at night.

Alan R. Gaby, MD

Notes

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The Corruption of Scientific Literature

review by Ira L. Goodman, MD, FACS, ABIHM, FAARM

Doctoring Data: How to Sort out Medical Advice from Medical Nonsense, by Malcolm Kendrick, MD
Columbus Publishing Ltd.; Monmouthshire, UK
© 2014; softcover; $14.99; 279 pp.

Statistical manipulation, biased thought leaders, financial influences, and clever marketing techniques all conspire to make today's so-called medical literature nothing more than pulp fiction.

Dr. Kendrick practices in the UK, is an original member of the Centre for Evidence-Based Medicine in Oxford as well as THINCS (The International Network of Cholesterol Skeptics), and has authored *The Cholesterol Hoax* as well as this book.

His long-term interest in epidemiology as well as his many publications in the *BMJ* and similar journals make him an authority on medical statistics.

The book, although at times dry, is humorous as well as enlightening on number of fronts. Some of the tactics that Big Pharma uses in regard to manipulating study results are spelled out in clear detail and are one reason why Dr. Marcia Angell, a former editor of the *New England Journal of Medicine* for 20 years, said: "It is simply no longer possible to believe much of the clinical research that is published, or to rely on the judgment of trusted physicians or authoritative medical guidelines. I take no pleasure in this conclusion, which I reached slowly and reluctantly over my 2 decades as an editor of the NEJM."

Kendrick points out the following ways that Pharma gets the results it wants from clinical studies:

- conduct a trial of its drug against a treatment known to be inferior
- conduct a trial of its drug against too low a dose of the competitor
- conduct a trial of its drug against too high a dose of the competitor, making it seem less toxic
- conduct trials too small to show differences from competitors
- use multiple end points and select only the favorable end points for publication
- use multicenter trials and select only favorable centers for publication
- use subgroup analysis and select only favorable groups for publication
- use relative risk instead of absolute risk, NNT, and NNH statistics to prove efficacy but use absolute risk to prove safety.

The excellent book *Bad Pharma* by Ben Goldacre talks about many other manipulations intended to deceive and overall is a better read than Kendrick's book, although the latter explains statistical concepts better.

I especially liked Kendrick's proposed statement to current medical students: " Dear Medical Student: About 80% of what you are about to be taught is based on no clinical evidence whatsoever. Of the rest, about 50% is so biased that you should ignore it. Of the remaining 10% about 50% will be proven wrong in the future."

There is a reasonable effort at explaining relative vs. absolute risk as well as number needed to treat (NNT) and the pitfalls of some of these measurements. I think that both Norton Hadler and Gilbert Welch do a better job of this in their books, but overall Kendrick is successful at pointing out how dangerous medical treatment can be and that most medical "facts" are really just pulled out of thin air with almost no evidence. He also points out that all-cause mortality should be the preferred end point, and if it's not mentioned in a study, you can be sure that the drug made no impact on it, no matter what the relative mortality results showed for a specific end point such as death from MI. The book proves the first law of statistics: "Given enough statistics, you can prove anything."

My take on this book:

I completely agree with most of Kendrick's conclusions about the shameful manipulation of statistics used to sell drugs. Some of us may remember a time when drugs were discovered. Now they are sold and marketed, and the Pharma budgets show it. Medical literature from 50 or 60 years ago is much clearer without the promotion so prevalent in current journals. It should be noticed that in any other field except medicine, literature refers to fiction. Unfortunately, it appears that our "literature" is 90% fiction currently. As physicians, we rely on reputable journals to distill the vast universe of medical research into the most clinically relevant and vetted material, since most of us don't have the time to do that. In reality, what gets published is based on financial relationships not fully disclosed and unverified data. You must be very critical in your reading and knowledgeable about medical statistics in order to separate the wheat from the chaff. ◆

Robert A. Anderson's Inspirational Memoir

review by Jule Klotter

Stories of Healing – A Family Doctor's Journal, by Robert A. Anderson, MD
Lorian Press, 2204 E. Grand Ave., Everett, Washington 98201
© 2011; softbound; 168 pp.; $18.95.

Stories of Healing – A Family Doctor's Journal is Robert A. Anderson's memoir about patients who affected the way he practiced medicine. This is a book of heart, wisdom and humility by a family physician, now retired, who loved his work. In each short chapter, Dr. Anderson recounts stories about patients who helped him grow from a conventional doctor to a physician who became open to alternatives. He came to respect the importance of nutrients and proper nutrition and the effects of environmental exposures. He also developed a strong appreciation for the roles of mind and emotions in health and illness. Dr. Anderson is founding president of the American Board of Integrative Holistic Medicine (1996). Long-time *Townsend Letter* readers will remember his mind-body research column "Psychoneuroimmunoendocrinology Review and Commentary," published from 1996 to 2010.

"I trust these stories from my journal will stimulate you to think for yourself, make your own observations, and find what works."

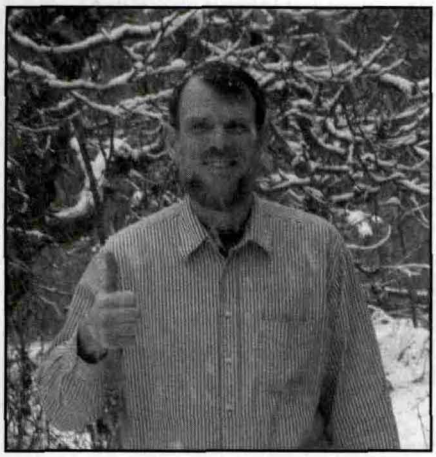
In his memoir, Dr. Anderson recounts cases in which nutrient supplementation was instrumental in healing numerous conditions, including gingivosis, osteoporosis, type 2 diabetes, skin conditions, shingles, and cardiovascular disease. He came to understand "that many damaged tissues in the body are in a state of flux and that adequate nutrients can push the equation toward reversal of disease." Dr. Anderson first became aware of the healing power of nutrients when a 40-year-old patient with atrial fibrillation responded to magnesium administered by another doctor. Conventional treatment, prescribed by Dr. Anderson, had failed to help the man; but a slow intravenous injection of magnesium (2 grams) restored his heartbeat to normal within 15 minutes. That experience convinced Dr. Anderson to order magnesium for all of his patients who showed signs of a heart attack upon hospital admission. Although the magnesium did not always help, Dr. Anderson says, "Survival of my heart attack patients was far above average." Magnesium's pronounced effect on heart rhythm also propelled Dr. Anderson to study nutrition.

"Imagination, especially evoked when one is in the relaxed state of mind, is a largely untapped resource in the matrix of healing and maintaining health."

Sometimes, the key to healing is to remove specific foods from the diet. Dr. Anderson tells the story of a 32-year-old woman with rheumatoid arthritis who was "slowly and inexorably getting worse" despite medication. The woman had a childhood history of cow's milk allergy; and, "on a hunch," Dr. Anderson asked her to avoid all foods that contained cow's milk for 14 days. By day 11, the woman was free of pain and joint swelling. A challenge test of three glasses of milk per day saw a resurgence of symptoms on day 4, convincing her to maintain a dairy-free diet. "Joan's experience confirmed for me what physicians espousing different medical principles (Clinical Ecologists) have long taught – that *any organ of the body can be the target for an allergic or sensitivity reaction,*" he writes. "... I also learned again that the human body often manifests an amazing capacity for self-healing. In her case, *the rheumatoid arthritis joint changes reversed themselves.*"

Dr. Anderson's experiences with patients pushed him to look beyond his conventional medicine training. The case of a young woman who developed thrombophlebitis after a kitchen remodel with off-gassing particle board highlighted the effects of environmental chemicals. A woman with chronic diarrhea showed him that releasing intense feelings can resolve functional problems. With other patients, he learned about the power of imagination to heal. Each patient who pushed him beyond the comfort zone of his previous training sent him on a journey to see if known science could support the result he observed.

"Healing presents itself with many faces. There is no one road, no right or wrong, sometimes not even any conventional logic at all," Dr. Anderson writes. "It behooves us all to pay attention, make observations, wrestle with making sense of them, and share them with those ready to listen." *Stories of Healing* inspires readers to learn from their experiences. I highly recommend it to practitioners and patients alike. ◆



NEW COLUMN

Ask Dr. J

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

This is a new column being offered by the *Townsend Letter*. The theme relies on a quote that may or may not have been uttered by Albert Einstein: "Everything should be made as simple as possible, but not simpler."

I go to seminars, read books, and read articles in magazines wherein everyone seems to know what is best for patients with whatever disease is being written or talked about. Also, there will be many and sometimes many, many therapeutic options that will most definitely work in these cases. I am always amazed at what I could possibly try clinically and many times disappointed with the results of the "treatment of the month." Every therapy works sometimes. The true skill in our professions is to know when that sometime is! One secret given to me by Eric Gordon, MD, is to treat the individual in front of you. This will help to tease out the correct therapeutic option(s) for each and every individual whom you see in your clinic. I will attempt here in this column to give clinically simple, individualistic therapeutic choices that pack a powerful punch for various clinical conditions.

So, let's begin with the "me" of 33 years ago after transferring up to National College of Naturopathic Medicine from Pacific College of Naturopathic Medicine in California, which had just gone bankrupt. I was 31 years old and had just come back from Petersburg, Alaska, where I had worked in the freezers of a halibut/salmon processing plant. I had worked 55 out of 60 days and 45 of those consecutively, all of them 12-hour days. It was tough being a naturopathic student back then: no real financial options to speak of if you didn't have rich parents.

I had enough money to pay for school and kind of live. I thought I knew what a healthful diet was but realize now that I was early in my dietary evolution. Potatoes were cheap, and I ate every manageable type of potato dish: baked, mashed, stir-fried, steamed and mixed with water in a blender to form a stock for soups, and so on. In the second quarter at NCNM, I started developing some severe GI signs and symptoms. I had debilitating bouts of epigastric pain/malaise, which had started the semester before as hit-and-miss periods of abdominal pain/malaise that slowly increased in occurrence and severity, and were now occurring 1 or 2 days per week. They appeared to start after meals but not after any consistent meal. I was also becoming bloated after almost every meal, and my stools were becoming irregular and extremely odiferous. I also had two bouts of black, tarry stools. I even signed up for health insurance for the only time in my adult life until Obamacare made me! I was beginning to become a tad frantic. Also, I forgot to mention that I was eating these fantastic fish/meat stews for lunch and dinner at a great little restaurant in Petersburg all summer that most days had – you may already have guessed it – potatoes in them.

During this time at NCNM, there was a resurgence in the eclectic naturopaths of the past, including Drs. Bastyr, Scott, and Dick. They had used a radionics machine to scan samples of blood sent in to them on filter paper to determine that person's food intolerances. I had my blood sample scanned and, voilà, I was allergic to potatoes, of course, plus regular salt (but not sea salt) and grains and eggs combined. I stopped all the above immediately (I haven't had a potato in 33 years and go to PA meetings!). My abdominal pain was almost immediately 90% better. I then started looking at what I was eating with a stronger microscope, and of course I was eating cheese with regular salt. When I switched over to cheese with sea salt, no more abdominal pain! When it works sometimes, it's too good to be true!

Next, let's look at two cases in which simpler interventions paid huge dividends.

Patient #1 is a 34-year-old female with an 8-year-old son and 4-year-old daughter. She states that she never recovered completely from the birth of her daughter. Her fatigue has become almost unbearable. She wakes up exhausted and somehow makes it through the day to come home, make dinner, try to talk to her husband and kids, and fall asleep. She has multiple other hypothyroid symptoms and signs, but for her the worst was the 80 pounds that she had gained since her daughter's birth. She rates the stress of her work life a 12 out of 10. Her TSH was 2.5, total T4 6.2, and free T4 0.99, all within normal limits, although TSH is high normal and T4 and free T4 are within normal limits but at the low end of the optimal ranges . Her cholesterol and LDL were mildly elevated but no other lab values were amiss. She had been offered antianxiety drugs and had refused and came to see me as, of course, a last resort.

I live in the mountains of Northeastern California, where many people are struggling in our corporate kleptocracy. If I order lab tests, insurance will not cover them. I need to rely on what I have learned in my practice, talking to friends, reading magazines like the *Townsend Letter*, and the many seminars that I attend. Thus, I try to follow what my mother always told me when I was having issues: she didn't raise a fool.

Different people have various names for the following enzymes. I will use what I have read from the National Academy

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of Hypothyroidism. They list three types of deiodinase enzymes. D1 converts T4 to T3 throughout the body but is not a significant determinant of pituitary T4 to T3 conversion. D2 is responsible for pituitary conversion of T4 to T3. D3 changes T4 to reverse T3, and the pituitary does not contain D3. Reverse T3 acts as a competitive inhibitor of T3 by blocking T3 from binding to its nuclear receptor and thus blocking its metabolic effects by reducing cellular metabolism throughout the body. Reverse T3 also suppresses D1, which slows T4 to T3 conversion and blocks T3 and T4 uptake into the cell. This sounds even worse than the possibilities for our next president!

Let's take a small deviation from our patient story. Why would our bodies have the potential to make a destructive molecule like reverse T3? Let's go back 1000 years to what was Germany (my mother was 100% German). There were no Safeways or Whole Foods back then. Sometimes the fall harvest was mediocre to minimal. This meant a lean winter, foodwise. There are many initiators of reverse T3, but physical or emotional stress or both are huge reasons for its formation. In January 1015, a person who had very little to eat would definitely be under both types of stress. Having a reverse T3 molecule to slow their metabolism and to slow the loss of whatever weight they put on during the fall harvest would have a been a huge benefit. Unfortunately, we have way too many physical, emotional, and spiritual stressors in our lives today and much too easy access to empty calories at Safeway and Whole Foods. This stress/empty-food cycle creates a catch-22 that most people are unable to escape from.

I first talked to this patient about the stress in her work life. I asked her who/what/where/why/when questions. We reached the conclusion that she needed to quit her job, which she actually did do. Luckily, she almost instantaneously found another job. Now, I don't believe in accidents, never have, never will. I thought that she might repeat the same vicious, emotional rollercoaster in her new job. In my last article (November 2015), I talked about using my handouts for Limbic Breathing and the neurolinguistic programming exercise Breath of Life (which is all about building new ways of reacting in your brain so that you don't fall back into old dysfunctional patterns of relationships with other people). Both handouts help people manage their stressful lives. I taught her how to practice both, explaining to her that she needed tools to help her be successful in her interactions in the work world and truthfully in her life in general.

I also used my NAET (Nambudripad's Allergy Elimination Techniques) training and checked her for food intolerances. She was positive for milk, nuts 1 (peanuts and walnuts), and sugar. As happens so many times with our patients, she was hooked on ice cream, peanut butter, and sweet treats. I treated her with NAET for each of those foods. I was taught that NAET totally eliminates the problems those foods create in your body; practically, I find otherwise. I tell people that I have decreased their intolerance to those foods, and it is up to them to find out what amount and how often they can tolerate these reactive foods. Doing the NAET treatments also helps to decrease the cravings that people will have for those foods, which then assists them in regulating their uncontrollable urges for them!

In her case, she just wanted to stay away from them completely. It's too bad that magic doesn't work for every patient, but here it did. In the first month, her stress went from a 12 to a 5, in her own words her energy doubled, and she dropped 10 pounds. Over the course of the next year, she lost 50 pounds and found herself with the energy of her teenage years.

Two last notes on this case: First I was taught (in some forgotten conference) that food intolerances can also activate D3 and increase reverse T3 and create the illusion of hypothyroidism with normal T4 and TSH values. For this patient, both managing her stress and cutting out her intolerant foods dampened her D3 and as a result her reverse T3.

Second I want to reinforce the need to eat photon-rich food that works optimally for your unique biochemistry. I ask patients, how many times per year do they actually consume food? They're usually a little mathematically challenged, so I help them. I use the example of 3 meals and 2 snacks per day which is 365 × 5, or 1825, times per year (1830 in a leap year). They then begin to understand the magnitude of eating suboptimal, photon-poor food so many times per year. Watching the light switch on in their eyes never ceases to amaze me!

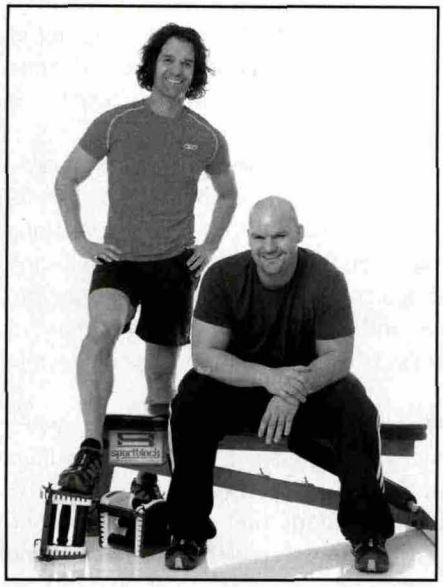
Patient #2 is a 48-year-old postmenopausal woman. She has what I have termed the "duck" syndrome. For me, it if walks like a duck, quacks like a duck, and looks like a duck, it's a duck, no matter what the lab values. I have a "Hypothyroid Signs and Symptoms" handout for patients to fill out, and she circled 50 out of 60 possibilities on it. I have never had anyone else even come close! Her TSH value was quite low, 1.6. Her local doctor refused to even think about giving her thyroid hormone with such a low value, especially as her T4 was within normal limits at 5.1. (Although we know that optimally 6.0 would be the low normal!). Unlike the former patient, she has a great job, wonderful husband, and loving, adult children. She was, however, also severely depressed.

I wish I could more easily and more often lock into that subconscious mind/spirit that has all the answers. For some reason, I was looking over my notes for Datis Kharrazian's "Mastering the Thyroid" seminar. I came across something that he had said: low dopamine leads to increased prolactin, which artificially decreases TSH.

So, I started digging a bit deeper: "Tell me more about your depression." She seemed to be detached from her depression and almost trying to find someone to blame for it. She also had severe compliance issues. She would find a supplement that would possibly help her and take it for a short period of time, then stop and then start another one. Despite her fatigue, she was also easily annoyed, according to her husband, who accompanied her. She also had a total lack of energy and drive and felt overwhelmed by life. These are fairly solid symptoms of dopamine deficiency.

I placed her on a supplement to increase her dopamine and also a high-dose fish oil because omega-3 fats are MAO inhibitors and can raise dopamine levels approximately 40% by themselves. For 2 weeks, there was little improvement. At 3 months she retook my thyroid questionnaire and now only circled 10 items. She now feels as if she can actually enjoy her loving family.

In this monthly column, I will attempt to share some of my eclectic knowledge gained over the last almost-40 years, which mirrors the wonderful Grateful Dead line in "Truckin'," "What a long, strange trip it's been"! Please send in some of your more challenging cases for my feedback. Not every letter will end up in the *Townsend Letter*; however, every letter will receive an answer from me. I look forward to hearing from you! ◆



Exercise is Medicine

by Jade Teta, ND, CSCS, and Keoni Teta, ND, LAc, CSCS
jade@metaboliceffect.com | keoni@metaboliceffect.com

Weight Management in Menopause

Keoni and I typically write more scientifically referenced columns for the *Townsend Letter*, but in this one we are going to keep it clinical.

We have a very good track record in dealing with weight gain around the time of menopause. So much so that we developed an online program that has literally helped thousands of menopausal women figure this thing out.

This column gives a overview of our approach to practitioners who have been struggling with this issue in their practice.

Background and Protocol Rationale

Estrogen and progesterone, while lower in the fat-burning hierarchy compared with insulin and cortisol or thyroid and adrenaline, nevertheless do affect a woman's fat-burning metabolism.

Estrogen is an insulin sensitizing hormone and a hormone that controls the negative impact of cortisol. Progesterone opposes the action of estrogen on insulin, but works together with estrogen in controlling the negative impact of cortisol.

Why is this important? Because insulin and cortisol are a bad hormonal combination for fat loss. These two hormones, when combined in high amounts over long periods, push the female physiology toward storing fat when calories are high (as opposed to building muscle) and reducing the amount of fat burned when calories are low (burning muscle instead). This is a bad combination for any woman, but a menopausal woman is affected to a much greater extent.

Since insulin and cortisol may be the primary culprits in female belly-fat storage, the transition into menopause often results in fat gain, especially around the middle.

An Approach to Fixing the Issue

Patients are far more carbohydrate reactive and stress sensitive after menopause. Which means that the carbohydrates they once ate without affecting their waistlines may now be too much and do just that.

Likewise, the stressful exercise and lack of sleep that they could tolerate in their younger years, while still remaining lean, will now start to show on their waists.

To deal with these hormonal impacts requires a far more insulin-centered approach than a caloric one. In other words, whereas a lower-calorie diet may have been enough in their younger days, they may now need to watch their starch and sugar intake as well.

Food Prescription

At menopause, it may no longer be just refined sugars that are the issue. You may want to counsel regulation of *all* foods that have potential insulin-promoting action. This includes many foods that are regarded as "healthful."

Whole-grain breads, sweet fruits, dairy foods, and starchy vegetables, which may have once been a central part of their lean diet, may now be working against them. Reducing these foods while simultaneously increasing low-starch vegetables, low-sugar fruits (berries, apples, and pears), and protein foods has been a very simple approach for us in dealing with menopausal weight gain and belly fat. It also reduces many of the associated risk factors (i.e., BP, HgA1C, triglycerides, etc.).

How to Exercise

Exercise too must be approached differently. Cortisol is produced during intense exercise and long-duration exercise. This includes long-duration jogging or running and high-intensity interval training (HIIT), metabolic conditioning, or weight training.

However, intense exercise that is short also raises growth-promoting hormones such as HGH and testosterone, and these hormones work with cortisol to burn fat and build, or at least maintain, muscle.

Long-duration exercise works differently. It has a different hormonal impact, and it may exacerbate the negative effects of cortisol because it raises cortisol without the balancing action

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Exercise is Medicine

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of the growth hormones. And raising cortisol this way during menopause, a time when the female physiology is far more susceptible to the negative impact of cortisol, can frequently cause more issues than it solves for weight gain.

For this reason, we prescribe shorter intense exercise. We have seen it be more beneficial and tolerable compared with long-duration moderate-intensity exercise.

Cortisol can also be controlled and lowered nicely by relaxing activities. These include leisure walking (to be distinguished from power walking), restorative yoga (to be distinguished from intense yoga), and tai chi, as well as massage, sauna, and other restorative nonexercise practices.

All of this is important because the dominant message sent to menopausal women, from the typical nutritionists and doctors, as well as the mainstream press, runs completely counter to all we just covered. The message is to do more jogging and power walking, not less. They are instructed to eat more grains and dairy and less protein. And they are rarely told to *lift* weights or educated on the benefits of rest and recovery-centered activities

Together, a lower insulin-promoting diet and a smarter stress-inducing exercising regime can make a huge difference. Remember, the menopausal physiology is more carbohydrate reactive (estrogen is no longer there to help offset insulin) and more stress sensitive (estrogen and progesterone are not there to dampen cortisol's negative effect).

The changes to diet, exercise, and lifestyle can help combat menopause weight gain. Here are the changes that we recommend:

1. Leisure walk daily 1 hour per day (it lowers cortisol). Preferably do it in a nature setting (it lowers cortisol even more). A study out of Japan published in the *Journal of Physiological Anthropology* in March 2007 showed some very interesting metabolic effects of walking, especially when done in a natural environment.
2. Weight-train intensely at least 1 time per week, preferably 3. These sessions should be short. Shoot for less than 60 minutes or even better, less than 30. They work great along with walking too. Studies demonstrating this were published in 2000 out of the *Journal of Clinical Endocrinology and Metabolism* (85[2]) and in the March 2004 issue of the *American Journal of Physiology, Endocrinology and Metabolism* (286).
3. Drastically increase nonstarchy vegetable intake while cutting back on starchy foods, grains, and dairy (this does not mean not to eat these foods, just eat less).
4. Raise protein intake with foods that are mostly protein (fish, chicken, etc.) versus mostly starch or fat (beans and nuts have some protein but *far* more starch and fat). To help, consider a protein powder replacement shake 1 or 2 times per day.
5. Build in restorative and relaxing activity. A concept we call "rest-based living." Sleep, nap, physical affection, laughter, massage (even self-massage such as foam rolling), sauna, restorative yoga, and tai chi are all great.

I know that many practitioners will want to know, what about supplements and HRT? Sure, they can work, but not like the above recommendations. We have found that prescribing supplements or hormones without getting the lifestyle stuff above is a lot like trying to clean up a spill on your kitchen floor with a Dixie cup instead of a mop. It won't do nearly the job you want it to.

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Calendar

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

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

FEBRUARY 3-5: 1st INTERNATIONAL SYMPOSIUM OF THE CANCER RESEARCH CENTER in Toulouse, France. CONTACT: www.toulouse-onco-week.org

FEBRUARY 4-6: CARDIOMETABOLIC ADVANCED PRACTICE MODULE – Prevention of Chronic Metabolic and Cardiovascular Disorders in Atlanta, Georgia. CONTACT: www.functionalmedicine.org/Cardiometabolic

FEBRUARY 6: THE BRAIN – NUTRITIONAL PERSPECTIVES AND CONSIDERATIONS in Ft. Lauderdale, Florida. CONTACT: www.facebook.com/BioticsResearch.

FEBRUARY 7-9: IMMUNE ADVANCED PRACTICE MODULE – The Many Faces of Immune Dysregulation and Chronic Inflammation in Atlanta, Georgia CONTACT: www.functionalmedicine.org/Immune

FEBRUARY 13-14: 2016 NWNPC CONVENTION: Food as Medicine in Portland, Oregon. CONTACT: foodasmedicineinstitute.com/2016-symposium-ce/

FEBRUARY 19-21: LDN 2016 CONFERENCE in Orlando, Florida. CONTACT: www.ldn2016.com/townsend/

FEBRUARY 24-27: INTEGRATIVE HEALTHCARE SYMPOSIUM ANNUAL CONFERENCE in Midtown, New York. CONTACT: ihsymposium.com/annual-conference/

MARCH 1-3 & 8-10: INCLINIC PRECEPTORSHIP BIOIDENTICAL HORMONES with Erika Schwartz, MD in New York City, New York. CONTACT: dkingman@drerika.com; drerika.com/content/speaking-and-events

MARCH 3-6: BHRT SYMPSOIUM in San Francisco, California. CONTACT: www.a4m.com/bhrt-symposium-san-francisco-march-2016.html

MARCH 4-6: ENVIRONMENTAL HEALTH SYMPOSIUM ANNUAL CONFERENCE in San Diego, California. CONTACT: www.EnvironmentalHealthSymposium.com

MARCH 5: AUTOIMMUNITY-THE HPA CONNECTION, IODINE AND THYROID in Englewood, Colorado. CONTACT: www.facebook.com/BioticsResearch.

MARCH 5-6: 4th ANNUAL WOMEN IN BALANCE SYMPOSIUM in Portland, Oregon. CONTACT: womeninbalance.org/4th-annual-women-in-balance-conference/

MARCH 11-12: INTERNATIONAL ACADEMY OF ORAL MEDICINE AND TOXICOLOGY (IAOMT) SPRING CONFERENCE in Orlando, Florida. CE credits. CONTACT: iaomt.org/events/2015-annual-meeting/

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Environmental Medicine Update

by Marianne Marchese, ND
www.drmarchese.com

Genetic Polymorphisms and Women's Health

Introduction

A single nucleotide polymorphism (SNP) is a common genetic change seen in people. A SNP represents a difference in a single DNA building block, which is called a nucleotide. It is a substitution of one base for another. SNPs occur throughout a person's DNA, and these variations are found in the DNA between genes.[1] When SNPs occur within a gene or in an area near a gene, they may play a role in the development of disease by affecting the gene's function. Researchers have found SNPs that predict an individual's response to certain drugs, susceptibility to environmental toxins, and risk of developing diseases.[1] SNPs are different than genetic mutations in DNA that cause disease. Disease-causing mutations occur within a gene's coding or regulatory regions. Disease-causing mutations affect the function of the protein encoded by the gene. SNPs are not necessarily located within genes, and they may not always affect the way a protein functions, but they correspond to the risk for getting a certain disease.[2] Some SNPs, however, do affect protein function correlating with a disease. They may change the amino acid sequence of the gene's protein product or change the timing, location, or level of gene expression.[2] There are numerous SNPs located throughout the body. Several occur in estrogen metabolism genes that are linked to increased risk for estrogen-driven conditions in women. This discussion of the link between single nucleotide polymorphisms and women's health conditions will focus on the liver biotransformation pathways and the MTHFR gene. There are of course many more SNPs that affect estrogen metabolism and many other conditions linked to SNPs than what are discussed here. This is merely an introduction to the link between SNPs in genes and women's health conditions.

The Liver

Some SNPs affect the liver's biotransformation pathways in humans. The liver is important in protecting us from potentially toxic chemical exposures. This protective ability stems from the expression of enzymes whose function is to catalyze the oxidation, reduction, and hydrolysis reactions (phase I metabolism) and/or conjugation reactions (phase II metabolism) of functional groups on drug and chemical molecules. One of the major enzyme systems that determines the liver's ability to deal with drugs and chemicals is the cytochrome P450 enzymes. These enzymes are located in several places in the body but predominately in the liver. They are responsible for phase I biotransformation or metabolism. Other enzyme systems include dehydrogenases, oxidases, esterases, reductases, and a number of conjugating enzyme systems including glucuronosyltransferases, sulfotransferases, and glutathione S-transferases. These are responsible for phase II liver biotransformation.[3] There are over 50 human genes coding for the various phase I cytochrome P450 (CYP) enzymes. There are several CYP isoforms that are of particular importance due to their involvement in metabolism of drugs, hormones, and other exogenous substances including environmental toxicants. These include CYP1A1, CYP1A2, CYP1B1, CYP3A4, CYP3A5, CYP2E1, CYP2E6, CYP2D6, CYP2C9, CYP2C19, and CYP2C8. Phase II conjugation reactions include glucuronidation, glutathione transferases, S-methylation, N-methylation, acetylation, sulfotransferases, thioltransferases, and glycination (amino acid conjugation).[4] Any of these may be polymorphic, affecting liver phase I and II biotransformation pathways.

Polymorphisms of cytochrome P450 enzymes were first described about 30 years ago when a small proportion of people given the antihypertensive drug debrisoquine had extreme falls in blood pressure which were related to abnormally high plasma drug concentrations.[5] It has since been found that debrisoquine and well over 70 other drugs are metabolized by the enzyme known as CYP2D6 in the liver. CYP2D6 metabolizes numerous medications. Population studies have shown that approximately 8% of Caucasians but less than 1% of Asians have a SNP of 2D6 and are poor metabolizers. As for phase II liver biotransformation pathways, the first polymorphism was

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described over 40 years ago for acetylation. It is now known that N-acetyltransferase (NAT) is controlled by two genes (NAT1 and NAT2), of which NAT2 A and B are responsible for clinically significant metabolic polymorphisms.[5] SNPs of liver phase I and phase II biotransformation pathways affect more than just drug metabolism. They are responsible for metabolizing environmental chemicals and hormones such as estrogen. SNPs can be linked to disease especially related to women's hormonal health.

Women's Health

Many women's health conditions have been linked to specific SNPs of cytochrome P450 enzymes and conjugation reactions as well as MTHFR gene function. Several laboratories are now offering tests that look for these genetic variations that may either explain a patient's health condition or determine her risk for developing disease. Polymorphisms occur in several areas of the body, not just the liver. As a simple introduction to correlating SNPs to disease, the link between four common women's health conditions and a few estrogen-metabolizing gene polymorphisms is described. This is by no means a complete review.

Endometriosis

Endometriosis is a common disease, causing menstrual pain and infertility. It is a multifactorial condition with links to estrogen metabolism and environmental toxicants. Studies correlating the role of polymorphisms are mixed, with newer studies starting to make connections. The glutathione S-transferases (GSTs) are a family of enzymes responsible for the metabolism of xenobiotics and carcinogens in phase II liver biotransformation. GSTM1, one member of the GST family, is important in the detoxification of the toxicants and oxidative stress product during ovulation. GSTM1 gene polymorphism is associated with endometriosis. A significant excess of the GSTM null genotype (gene deletion) is also seen among women with endometriosis.[6] The GSTM1 null genotype is related to an increased susceptibility to endometriosis. The GSTM1 gene polymorphism likely contributes to the pathogenesis of endometriosis.

Endometriosis is an estrogen-dependent condition that can be influenced by defective signaling in the estrogen pathway. Estrogen metabolizing polymorphisms can be associated with defective hormonal signaling, leading to disease. A recent study linked polymorphism of CYP19A1 to endometriosis.[7] CYP19A1 is found in the endoplasmic reticulum and catalyzes the last steps of estrogen biosynthesis. Mutations in this gene can result in either increased or decreased aromatase activity. A 2014 study looked at 500 women with endometriosis and 500 women without the condition and found CYP2C19 associated with endometriosis.[8] Some studies report conflicting information on the link between SNPs and endometriosis. An older 2001 study showed no link to GSTM1 null genotype alone but did find a link to endometrioses if a woman had both GSTM1 null and a CYP1A1 polymorphism.[9] CYP1A1 is another phase I cytochrome P450 enzyme responsible for estrogen metabolism.

PCOS

Polycystic ovary syndrome (PCOS) is a very common condition affecting thousands of women. It's a leading cause of infertility and a complex multifactorial disorder involving a number of genetic and environmental factors. CYP1A1 encodes a phase I cytochrome P450 enzyme involved in the oxidative metabolism of estrogens. Emerging evidence suggests that common functional polymorphisms in the CYP1A1 gene increase susceptibility to PCOS, but individually published results are inconclusive. However, a recent meta-analysis published in 2013 looked at five case-control studies with a total of 1036 subjects, including 521 PCOS cases and 515 healthy controls. The meta-analysis indicates that the CYP1A1 polymorphism may contribute to increasing susceptibility to PCOS among the general female population in Turkey and India.[10]

Methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms have recently been linked to several health conditions. It has also become common for practitioners to test patients for MTHFR polymorphisms. The MTHFR gene provides instructions for making the methylenetetrahydrofolate reductase enzyme, which plays a role in processing amino acids, the building blocks of proteins. Methylenetetrahydrofolate reductase is important for a chemical reaction involving forms of the vitamin folate. A 2015 study set out to determine if there is an association of C677T and A1298C polymorphisms of MTHFR gene with the susceptibility to PCOS. Blood samples of 115 PCOS patients and 58 fertile non-PCOS women were collected for DNA extraction. The results show that the MTHFR gene C677T polymorphism is associated with PCOS. The A1298C polymorphism of the MTHFR gene is not associated with the occurrence of PCOS. Also, the study determined the folate level in red blood cells is lower in PCOS patients, for whom folate should be supplemented.[11]

Fibroids

Uterine leiomyomas (fibroids) are a common estrogen-dependent condition. It has been suspected that SNPs in genes involved in estrogen metabolism might play a role in the development of fibroids. Liver phase I enzymes CYP1A1 and CYP1B1, along with phase II COMT and GST pathways, are mostly responsible for estrogen metabolism in the liver. The results of a 2015 meta-analysis suggest that CYP1A1 polymorphism is significantly associated with uterine leiomyoma risk. [12] In 2014 a group of researchers evaluated all the estrogen metabolism enzyme gene polymorphisms and risk of developing fibroids. The genetic polymorphisms in COMT, CYP1A1, and Ala119Ser loci in CYP1B1 were risk factors for uterine leiomyoma development. However, Leucine432Valine locus in CYB1B1 may be a protective factor.[13]

This is an important distinction to note when testing patients for SNPs. Many labs simply report that the COMT or CYP1B1 is positive for a SNP but don't report where on the

gene loci. This study broke down CYP1B1 and tested several gene loci and found that one was a risk factor for developing fibroids and another was protective. A 2015 study also found Leucine432Valine SNP in the gene encoding cytochrome CYP1B1 possibly protective against the formation of uterine fibroids.[14]

The COMT liver phase II biotransformation pathway is not the only phase II pathway linked to the formation of uterine fibroids. The GST gene polymorphisms play a role as well. Although less often studied, it appears that there is a link to uterine fibroids and GSTT1 null polymorphism in the Iranian population. The null genotype significantly increased the susceptibility to uterine leiomyoma compared with individuals carrying the present genotype.[15]

Breast Cancer

This is the area with perhaps the most research linking estrogen-metabolizing gene polymorphisms and an estrogen-dependent condition. The CYP3A4 is a major enzyme catalyzing the metabolism of both endogenous and exogenous agents that may play a role in the development of cancer. It is responsible for metabolizing hormones and the majority of pharmaceutical medication. Studies show a link between CYP3A4 polymorphism and an increased risk for breast cancer as well as taxane toxicity in breast cancer patients undergoing chemotherapy using taxanes.[16,17] A recent meta-analysis indicated that the GSTM1 and GSTP1 polymorphisms might significantly contribute to breast cancer susceptibility in Asian populations, especially East Asian.[18]

Genetic polymorphisms of CYP1B1 and 1A1 are also associated with breast cancer in Caucasian women.[19,20] An interesting study published in *Environmental Health* linked SNPs of CYP1A1, CYP17, and COMT and levels of serum perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) to increased risk of breast cancer.[21] These are known estrogen-disrupting chemicals and used in the manufacturing of Gore-Tex and Teflon products, and they contaminate drinking water.

The MTHFR enzyme is essential for DNA synthesis and DNA methylation, and its gene polymorphisms have been linked to several health conditions as previously mentioned. Several studies have investigated the association between the MTHFR polymorphism and breast cancer risk, but the results have been inconclusive. However, 2014 meta-analysis of 22 case-control studies found that MTHFR C677T polymorphism was significantly associated with breast cancer risk in the Chinese population. Meanwhile, MTHFR A1298C polymorphism was not associated with breast cancer risk in the Chinese population.[22] More research in this area is currently under way.

Summary

Single nucleotide polymorphisms (SNPs), a common genetic change seen in people, were first described over 40 years ago in relation to impairment in drug metabolism. More recently, links have been made between SNPs and the development of disease. Both patients and practitioners are testing for SNP gene polymorphisms in an attempt to explain a current health condition or determine the risk for developing a disease. Gene polymorphisms occur throughout the body, and several SNPs of estrogen metabolism and the link to women's health conditions were described here. Many studies are conflicting in the area of SNPs' correlating to disease, but there is enough research making a positive association to find the information useful. Clearly more research needs to be done in the area, including valid methods to assist the functioning of gene polymorphism as a means to prevent diseases linked to that SNP.

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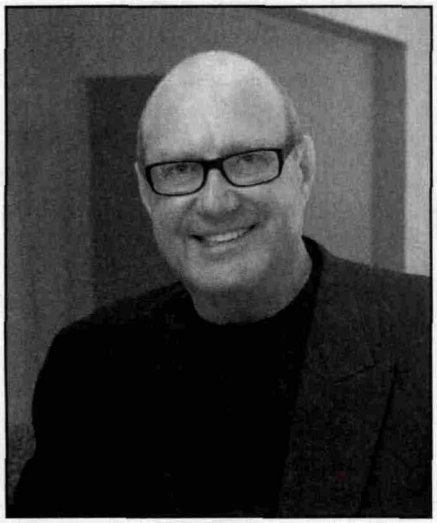

Monthly Miracles

by Michael Gerber, MD, HMD
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Nevada Homeopathic and Integrative Medical Association Fall 2015 Conference

William Clearfield, DO; Reno, Nevada: Hormone Myths vs. Scientific Evidence: Making the Case for Bioidentical Hormone Replacement as the 'Standard of Care'

We are very pleased to have Dr. Clearfield join our community of integrative physicians in Reno. He is a graduate of the College of Osteopathic Medicine and Surgery in Des Moines, Iowa, in 1978 and a native of Pennsylvania with an extensive background in Medical Acupuncture from UCLA and Diplomat of the American Board of Medical Acupuncture as well as the American Board of Family Practice and American Board of Anti-Aging/Regenerative Medicine.

Dr. Clearfield presented three lectures for us: Battlefield Acupuncture, Rapid Auriculotherapy Technique for Pain Reduction, Thyroid Optimization, and the Case for Bioidentical Hormones. All were excellent and in keeping with *Townsend Letter* February/March theme. I will review his bioidentical lecture. Because of the extensive nature of his documentation on these themes, I strongly recommend that you get a high-quality video of the lecture from us (nevadahomeopathy@gmail.com).

Myth: No Credible Evidence Exists on the Value of Bioidentical Hormones

- Current evidence does not support the use of testosterone in older men with low testosterone levels.
- Evidence of the value of testosterone as an anti-aging therapy does not exist.
- Current evidence fails to support the efficacy of HGH as an anti-aging therapy.
- The long-term use of estrogens with or without progestins causes more risks than benefits.
- DHEA as an anti-aging supplement shows neither meaningful benefit nor serious adverse effects.
- No evidence of long term changes in therapeutic dose of "anti-aging hormones."
- From the Executive summary of the AMA House of Delegates 2009 Annual Meeting Council on Science and the Public Health Report. The use of hormones for "anti-aging": A review of efficacy and safety.
- Mayo Clinic: No evidence currently suggests that custom CBHT formulations offer clinically relevant benefits.[1]
- Auburn University School of Pharmacy: Pharmacists compounding bioidentical hormone therapy are ill informed regarding the lack of scientific underpinning associated with the efficacy and safety of the practice of bioidentical hormone therapy.
- Most medical organizations have in essence refuted the bioidentical hormone therapy claims as unsubstantiated.[2]
- American Association of Clinical Endocrinologists: For women who cannot control severe vasomotor symptoms. Lifestyle changes should be implemented first.[3]
  - Pharmacologic therapy.
  - Antidepressants Venlafaxine (Effexor)
  - Antidepressants intolerant
  - Clonidine (Catapress)
  - Megestrol (synthetic progesterone)
  - Gabapentin
- Serum thyrotropin (TSH) is single best screening test for primary thyroid dysfunction for the vast majority of outpatient clinical situations.
- Standard treatment is replacement with levothyroxine. The decision to treat subclinical hypothyroidism should be tailored to the individual patient.
- Any treatment other than T4 (i.e., Synthroid or generic equivalent) is outside the realm of medicine.[4]
- There is no evidence to support using desiccated (natural) thyroid hormone in preference to L-thyroxine monotherapy in the treatment of hypothyroidism.
- Desiccated thyroid hormone should not be used for the treatment of hypothyroidism.
- Desiccated thyroid Recommendation 22.4 was a unanimous expert opinion.[5]

Dr. Clearfield Rebuts These Myths

Negative Influences Preventing Conversion of T4 to T3: Factors influencing the conversion of T4 to T3 include advanced age, excessive goitrogen consumption, gluten sensitivity, infectious disease, adrenal insufficiency, iodine deficiency, stress, medications, chemotherapy or radiation exposure, toxin exposure, extreme exercise, inflammation,

low iron, and low testosterone. I like to remember that there are no T4 receptors in the human body, only T3.

Desiccated Thyroid Hormone Replacement

When 50 mcg of T4 were replaced by 12.5 mcg of T3 cognitive performance, mood and depressions improved with no adverse effects with the combination.

In a double-blind, crossover study of a porcine thyroid extract vs. levothyroxine, the authors concluded that the desiccated extract caused more weight loss, and 50% felt better on the desiccated thyroid extract. Conversion factor for TSH found in this study: 100 mcg T4 = 88 mg of thyroid extract.[6,7]

Desiccated thyroid replacement and brain function studies showed improved memory, cognitive function, and decreased neurodegenerative diseases, including dementia and improved mood and schizoaffective disorders.[8,9]

Desiccated Thyroid Replacement and Heart Disease

Desiccated thyroid replacement lowers blood pressure and improves cholesterol, metabolic syndrome, and insulin resistance.[10,11] Optimizing thyroid improves lipids, CHF, homocysteine, arterial stiffness, and endothelial dysfunction.[12] After heart attacks, it normalizes the QT interval and improves CRP. Low T3 is the strongest independent predictor of cardiac death.[13]

Dr. Mark Star reminds us in his letter in the August/September 2013 *Townsend Letter* of the mountain of evidence from Broda Barnes, MD, PhD, in his book *Hypothyroidism, the Unsuspected Illness*, published in 1976. His 22-year study was of 1569 patients who took desiccated thyroid for a minimum of 2 years study. When compared with the Framingham Study, his patients should have had 72 heart attacks; only 4 occurred. In my column in that same issue, I cited 119 scientific articles gleaned from Dr. Kent Holtorf's publications showing that TSH and T4 levels were very poor predictors of thyroid sufficiency.

Myth: Current evidence does not support the use of testosterone in older men with low testosterone levels.[14]

Facts: Testosterone and Heart Disease

Low testosterone levels are associated with increased mortality, atherosclerosis, and incident coronary artery disease.

Mortality is reduced by one half in testosterone-deficient men treated with testosterone therapy compared with untreated men.

Exercise capacity is increased with testosterone treatment vs. placebo in men with known heart disease (angina, heart failure).

There is uniform improvement in CV risk factors (fat mass, waist circumference, insulin resistance) with testosterone therapy vs. placebo.[15]

Testosterone and Heart Disease Study Retracted

"People find it hard to believe that *JAMA* would publish a study in which the percentages of men who suffered an adverse event was lower by half in men who received testosterone than untreated men, yet results were reported as if the opposite were true" writes Andre Grey, professor of endocrinology at Tufts University. The Vigen article was also condemned by 160 leading testosterone researchers and 29 medical societies from around the world calling for retraction of the study following revelation of the data errors, asserting that the magnitude and quality of the errors rendered the study "no longer credible."[15] The study also included 100 women.

Myth: Testosterone causes prostate cancer.

This myth was based on one report from 1941. The authors found no relationship of testosterone, DHT, or estradiol to prostate cancer. There were no reports of prostate cancer in men treated with testosterone after radical prostatectomy and there were benefits from head to toe when hypogonadism was treated[16]. In a study of 1023 patients with up to 17 years testosterone hormone replacement therapy there was no increase in the risk of prostate cancer.[17] Testosterone replacement therapy appears to have little effect on prostate tissue androgen levels and cellular function and causes no significant adverse effects on increasing prostate cancer risk or benign prostatic hyperplasia. In fact it should be recognized that prostate cancer becomes more prevalent exactly at the time in a man's life when testosterone levels decline.[18–20]

Myth: Testosterone causes "'roid rage."

Reality: Higher-testosterone men are more sociable and gregarious, had more energy and showed less aggression.[21,22]

Testosterone has antidepressant effects in depressed patients, especially those with hypogonadism and also produces significant gains in lean mass, strength, and aerobic endurance with significant reductions in whole-body and trunk fat in older men.[23]

Myth: Current evidence fails to support the efficacy of HGH as an anti-aging therapy.

GH therapy for GH-deficient men reverses an early atherosclerotic change; namely, the increased thickness of the intima media of the common carotid artery and the carotid bifurcation in 11 GH deficient-men.[24] It decreased oxidative stress by 50% and increases thyroid and androgen activities, but decreases cortisol.[25,26]

All mortality with GH use decreased post MI by minimum 300%.[27]

GH supplementation improves quality of life, nutrition, and cardiovascular risk during hemodialysis in a randomized trial.[28]

HGH administered vs. placebo: 12 men with IGF-1 values < 350 were given .03 mg of biosynthetic HGH per kilogram of body weight SQ 3x/wk. They had and 8.8% increase in lean body mass, 14.4 % decrease in adipose tissue mass, 1.6 % increase in average lumbar vertebral

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bone density, and 7.1 % increase in skin thickness. The nontreatment group had no significant change.[29]

Myth: The long-term use of estrogens with or without progestins cause more risks than benefits.

2002 WHI Study—"HRT" is Dangerous!

Premarin (conjugated equine estrogens) alone given to older postmenopausal women caused adverse effects in the first year (strokes, blood clots).

Oral estrogens cause blood clots, transdermal estradiol does not. Adding Provera (medroxyprogesterone acetate) caused more adverse effects (breast cancers, heart attacks, and dementia). Provera increases breast cancer and vascular inflammation, progesterone does neither. Thousands of lawsuits are pending: drug companies are running a legal-protection propaganda campaign to paint all "hormones" as equally dangerous!

Myth: Estrogen causes cancer.

In a study of 80,377 postmenopausal women showed no increase or decrease in breast cancer in women on estradiol and progesterone. Estradiol plus medroxyprogesterone acetate had a 69% increased risk of breast cancer. Progestins are not progesterone.[30]

In the E3N-EPIC Study of 55,000 women with an 8 year follow up showed that transdermal estradiol alone increased breast cancer risk by 1.2%, estradiol plus progesterone decreased risk to 0.9% and estradiol plus progestins increased risk to 1.4%.[31]

Estradiol Restoration

- Protects against heart disease, dementia, and osteoporosis.
- Improves insulin sensitivity – prevents diabetes.
- Eliminates hot flashes, restores sleep.
- Restores cognitive function and mood
- Maintains thickness, fullness of skin and hair.
- Maintains genital/pelvic health, helps with vaginal lubrication, incontinence and bladder infections.
- Protects against colon cancer and macular degeneration.
- Prevents the oxidation of LDL
- Improves lipid profile.
- Reduces lipoprotein(a).
- Improves endothelial function.
- Reduces plaque formation.
- Improves insulin sensitivity.

Myth: Estradiol replacement increases risk of clots.

Transdermal estradiol does not increase risk of venous thromboembolism like oral estradiol and is cardioprotective with decreased risk of heart attack and type 2 diabetes. Micronized progesterone reduces risk of type 2 diabetes and does not increase risk for venous thromboembolism and reduces blood pressure.

Internal carotid artery lumen widens by 22.4% when patients administered estradiol >6 months.[32,33]

Benefits of estradiol plus progesterone (natural) therapy: It is safe and effective in young postmenopausal women. It counteracts climacteric symptoms, osteoporotic fractures, diabetes, and prevents long-term degenerative diseases and cognitive impairment. Natural progesterone has a positive cognitive effect and no increase in breast cancer. Transdermal estrogen and natural progesterone have significant advantages.[34]

Estrogen Dominance

- Allergies
- Autoimmune diseases
- Anxiety, moodiness
- PMS
- Bloating, fluid retention
- Fibrocystic breasts
- Heavy periods
- Endometriosis
- Breast cancer
- Ovarian cancer
- Uterine cancer
- Gallstones

Progesterone is the only effective treatment for estrogen dominance.

Progesterone vs. Breast Cancer

- Progesterone cream applied to the breast reduces proliferation.[35-37]
- Estradiol is carcinogenic in breast cell cultures unless progesterone is present.[38]
- Normal breast cells proliferate after estradiol treatment, but become quiescent when progesterone is added.[39]
- Estradiol upregulates cancer-promoting gene bcl-2, progesterone downregulates it.[40]

Progesterone and Stroke

1. Progesterone inhibits ischemic brain injury.
2. Progesterone reduces infarct volume and improves functional deficits following cerebral ischemic event.
3. Dose: 8 mg/kg progesterone gave the best clinical results.[41-43]

Fact: Patent drugs are not equivalent to human hormones. Patent drugs are not human hormones. Synthetic estrogens are not estrogen and progestogens are not progesterone. Hormones are not drugs.

Conventional HRT is really HST: hormone substitution therapy! Estradiol substitutes: conjugated equine estrogens (CEE = Premarin) and ethinyl estradiol (in birth control pills all are called "estrogen." Progesterone substitutes: medroxyprogesterone acetate (MPA – Provera) and 30+ other "progestins" – all are called "progesterone." Testosterone substitute: methyltestosterone is also a patented drug and not a human hormone. Most docs don't know the difference! Human hormones cannot be patented, no profits.

Oral Estrogens are Dangerous

First-pass effect on the liver increases CRP, increases clotting factors, blood clots, strokes, heart attacks in the first year. Transdermal estradiol mimics normal production and does not increase blood clotting.[44]

Ethinyl estradiol in birth control pills cannot be inactivated by normal oxidation, does not interact with estrogen receptor beta, and is 12,000 to 60,000 times more potent than estradiol. Ethinyl estradiol is thrombogenic, with a twofold increased risk of deep vein thrombosis and pulmonary emboli.

Conjugated equine estrogens contain at least 10 estrogens, only three are human; also contain horse androgens and progestins.[45]

Provera vs. Progesterone

Scientific studies show that:

Provera	Progesterone
• Causes birth defects	• Maintains pregnancy
• Can cause depression	• Improves mood
• Insomnia, irritability	• Improves sleep
• Fluid retention	• Is diuretic
• Raises blood sugar	• Has no effect on blood sugar
• Counteracts estrogen-induced arterial dilation	• Maintains estrogen-induced arterial dilation
• Worsens lipid profile	• Improves lipid profile
• Causes heart attacks	• No increase in CVD
• Increases estrogenic stimulation of breasts	• Reduces estrogenic stimulation of breasts
• Causes breast cancer	• Prevents breast cancer

Myth: Testosterone is for males only.

Testosterone is the most abundant active sex steroid in women throughout the female lifespan.[46] It helps maintain muscle and bone strength, restores sex drive and libido, improves overall feeling of wellbeing, and reduces "bad" cholesterol. Testosterone deficiency leads to dry eyes, pale faces and thinning of inner third of eyebrows.

Testosterone is essential for women's physical and mental health and wellbeing. Androgen deficiency in pre- and postmenopausal women and aging men can manifest as dysphoric mood (anxiety, irritability, and depression), sexual dysfunction, urinary complaints, incontinence, physical fatigue, hot flashes, rheumatoid complaints, pain, breast pain, bone loss, muscle loss and changes in cognition, memory loss and insomnia.[47]

More Myths: Testosterone and Women

Myth: Testosterone masculinizes females. **Fact**: Testosterone does not have a masculinizing effect on females.[48]

Myth: Testosterone causes hoarseness and voice changes. **Fact**: There is no evidence that testosterone causes hoarseness or irreversible vocal chord changes in women.[49]

Myth: Testosterone causes hair loss. **Fact**: Testosterone increases hair growth in women.[50]

Myth: Testosterone causes liver damage. **Fact**: Nonoral testosterone does not adversely affect the liver or clotting factors.[51]

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Myth: Testosterone replacement increases the risk of breast cancer. **Fact**: In a study of 1268 pre- and postmenopausal women given testosterone treatment, the control group without testosterone had more than double the risk of breast cancer.[52]

Myth: DHEA as an anti-aging supplement shows neither meaningful benefit nor serious adverse effects. **Fact**: DHEA protects against cortisol catabolism and decreases visceral and subcutaneous fat in elderly persons. It reduced LDL and improved bone density. Supplementation relieved fatigue, dry eyes, and skin. It has been shown to regulate mood, supports the immune system, and improves insulin sensitivity.[53,54]

DHEA reduces atherosclerotic plaques and inhibits platelet aggregation (similar to aspirin), free radical formation, and nuclear factor kappa B dependent transcription. It improves sexual function, skin tone, and vulvar vaginal atrophy in postmenopause with no systemic effects.[55–58]

Low levels of DHEA are associated with all-cause mortality, cardiovascular mortality, immune dysfunction, autoimmune disease, cancer, hypertension, cardiovascular disease, depression and loss of well-being, low libido, erectile dysfunction, and osteoporosis.[59] DHEA at 50 mg per day increase testosterone (60%) and estrogen (40%) in women, not men with no adverse effects.[60] 7-Keto-DHEA gives weight loss without side effects (Kalman), improves immune function and is useful in Raynaud's and autoimmune diseases.[61]

Myth: Vitamin D is a vitamin.

1. 1000 IU per day is more than enough.
2. Most people in the USA get adequate amounts.
3. Extreme caution is needed not to produce toxicity of this fat-soluble vitamin.
4. 15 minutes in the sun per day produces adequate vitamin D.
5. The only function of vitamin D is calcium regulation. All you need is a balanced diet.
6. Vitamin D does not prevent cancer.
7. Vitamin D does not prevent autoimmune disease.
8. Vitamin D does not prevent heart attacks and heart disease.
9. The cause of clinical influenza is the influenza virus transmitted from the sick to the well.
10. The best way to prevent influenza is the vaccine.
11. Vitamin D and sports performance? Ridiculous.

Facts: Vitamin D Deficiency in US

Vitamin D deficiency is found in all age groups from children to the elderly. US: Very low 25 (OH)D = calcidiol <20 ng/ml 36% aged 18–29. 42% in African American women aged 15–49, 41% of outpatients ages 49 to 83, 57% of inpatients in Europe from 28% to 100% of healthy adults.[62]

Dr. Clearfield also visited vitamin D deficiency in infectious disease and cardiovascular disease. **Fact**: Vitamin D is effective preventing and aborting the spread of influenza. Calcitriol induces production of human cathelicidin (LL-37) a polypeptide antimicrobial. LL-37 can fight bacterial and viral infections.[63–66] Vitamin D acts as an immune system modulator. It prevents excessive expression of inflammatory cytokines and increases the oxidative burst potential of macrophages and dramatically stimulates the expression of potent antimicrobial peptides, which exist in neutrophils, monocytes, natural killer cells, and in epithelial cells lining the respiratory tract.[67]

Myth: Melatonin is only for sleep.

Fact: Melatonin manages circadian rhythm of our inner clock and controls sleep wake cycle. Low melatonin is associated with Alzheimer's, cardiovascular disease, insulin resistance, cancer, and infectious disease.

Fact: Melatonin is a potent free radical scavenger.

- more effective than glutathione or vitamin E.
- protects lipids, protein, DNA and works against the prooxidation effect of iron.
- protects DNA, mitochondria from injury
- protects against ionizing radiation.
- aids reperfusion of ischemic tissue.
- inhibits tumor growth.
- counteracts stress induced immunosuppression.
- increases CD4 cells, natural killer cells, activates cytokine system.
- decreases pro-inflammatory cytokines.
- increases immune function in winter counteracting environmental stressors.[68]
- potent analgesic effects in a dose-dependent manner, effective in fibromyalgia, irritable bowel syndrome, and migraine.[69]

Melatonin and Cancer

Melatonin inhibits tumor growth in humans and has antimitotic activity, downregulates activity of receptors with decreased estrogen binding to cells in breast cancer with enhanced immune response, free radical scavenging, and antiangiogenesis properties. It improves outcomes in glioblastoma, malignant melanoma, and breast cancer. When used in conjunction with chemotherapy and radiation, it protects against chemo/radiation toxicity. Large doses were used, 20 to 700 mg/day.

370 patients with advanced solid CA were given 20 mg of melatonin orally at bedtime. In at the study of chemotherapy vs. chemo/radiation, there was a significant regression rate and survival in the combination group.[70]

In 10 adjunctive or sole treatment studies of melatonin and solid tumors (1992–2003), melatonin reduced the risk of death at 1 year.

Melatonin also protects against hypertension and B-amyloid formation, and stimulates neural stem cell proliferation in hypoxic states.

Dr. Clearfield suggests a low-dose melatonin lozenge 2 to 3 hours before sleep, 0.3 mg SL and combined ½ hour before bedtime with melatonin 3 to 30 mg, magnesium taurate 200 to 400 mg, and vitamin D 2000 to 5000 IU.

His lecture provided a wealth of invaluable information. There is much more great information from his lecture on the video.

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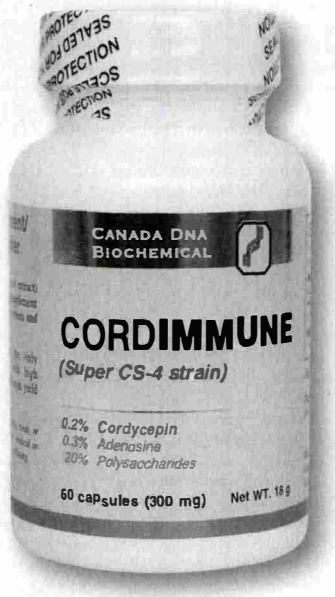

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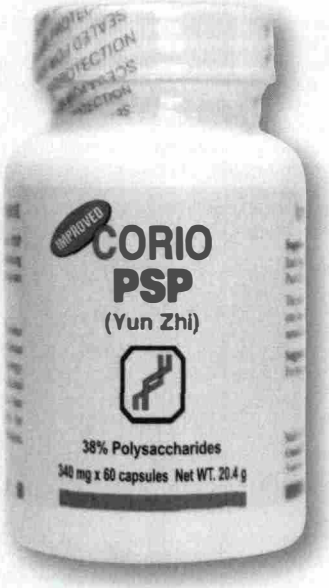

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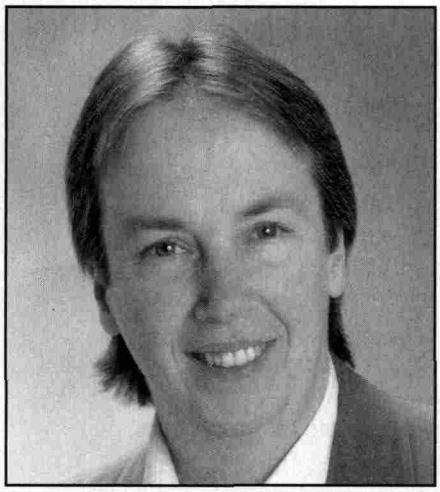

Women's Health Update

by Tori Hudson, ND and
womanstime@aol.com

Women's Health Treatment Protocols That I Count on

The following treatment plans are sample plans in my common approaches to these problems in women's health. Each individual woman's case has individual nuances, including past and current history, current medications, family history, stressors, lifestyle habits, and risk for future health problems that additionally guide the plan to include either more considerations or perhaps even simpler approaches than are listed below.

In addition, I chose to include proprietary product names for this column, due to trying to offer the most instructive approach. My disclosures are listed below:

Scientific advisory boards: Integrative Therapeutics, Nordic Naturals, Gaia Professional Solutions, Natural Health International, Nutritional Fundamentals for Health, Pharmaca Integrative Pharmacies; co-owner, Vitanica.

Endometriosis

Treatment plan addresses multiple mechanisms with documentation of being involved in etiology and/or progression of endometriosis:

- abnormalities in both cell-mediated and humoral components
- increased cytokine production
- decreased phagocytic activity
- increased protein called endo I (similar to haptoglobin)
- increased interleukin 6
- decrease NK cells
- compromised immune surveillance
- peritoneal fluid: high concentrations of cytokines, growth factors, and angiogenic factors
- once endometriosis lesions: secretion of pro-inflammatory molecules, lipid peroxidation
- oxidants are proposed to stimulate endometrial cell growth
- estrogen receptor issues

Comprehensive Sample Plan

- Diet: Increase omega-3; decrease omega 6 (low saturated fats diet); soy isoflavones most days; reduce inflammatory foods
- Curcuminoids; e.g., 750 mg of BCM-95 Curcumin, yielding a minimum of 500 mg curcuminoids per capsule; 1 capsule twice daily
- Pine bark; e.g., Pycnogenol 100 mg daily
- N-acetylcysteine 600 mg 3 times daily
- Melatonin 10 mg before bed daily
- Antioxidant combination product (e.g., Antioxidant Formula; Pure Encapsulations)
  - Per 1 capsule:
  - Vitamin A (as beta carotene) 10,000 IU (200% DV)
  - Vitamin E 100 IU (333% DV; as D-alpha-tocopherol succinate)
  - Riboflavin (B2) 25 mg (1471%DV)
  - Zinc (picolinate) 5 mg (33%DV)
  - Selenium (selenomethionine) 100 mcg (143% DV)
  - N-acetyl-L-cysteine (NAC) 100 mg
  - Milk thistle (*Silybum marianum*) extract (seed) 100 mg (standardized to contain 80% silymarin)
  - Mixed carotenoids 300 mcg (as alpha-carotene, zeaxanthin, cryptoxanthin, and lutein)
  - Ascorbyl palmitate (fat-soluble vitamin C) 100 mg

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Dose 2 capsules twice daily

- Concentrated fish oils with higher with specific doses of EPA/DHA
  E.g., EPA/DHA = approximately EPA 1200 mg/DHA 900 mg
- Consider: Oral micronized progesterone 200 mg before bed, days 15–26 in those with a regular monthly menstrual cycle
- Address acute pain issues as needed

Acute Dysmenorrhea

Sample Plan

- Ginger capsules 250 mg 4 times daily starting 2 days prior to menses and continuing for first 3 days of menses
- Niacin 100 mg every 2–3 hours
- Consider/ A combination herbal/nutrient product Cramp Bark Extra (Vitanica); 2 capsules every 3 hours during pain days (contains magnesium, calcium, B6, niacin, E, C, valerian, black cohosh, ginger, rutin)
- Valerian capsules
- Fenugreek 900 mg 3 times daily for first 3 days of menses
- Cinnamon 420 mg capsules; 2 capsules 3 times daily at onset of menses

Vulvovaginal Candidiasis

Sample Plans

Acute: Compounded boric acid capsule/suppositories: 600 mg twice daily for 3–10 days

Chronic:

- Boric acid capsule/suppositories: 600 mg twice daily for 1 month, then once daily during menses only, for 4 consecutive months
- Combination probiotic formulation specific for urogenital colonization: e.g., Fem Ecology (*L. rhamnosus, L. reuteri, L. salivarius, L. plantarum, L. acidophilus*); total 10 billion: 1 capsule daily for 4–6 months to assure colonization

Atrophic Vulva/Vagina

Sample Plan

- If vaginal symptoms only: compounded estriol 2 mg/g cream – insert ½ g nightly for 2 weeks then twice weekly maintenance
- If vulvar symptoms only: Compounded estriol 2 mg/g cream- apply ½ gram nightly for 2 weeks then twice weekly maintenance
- If both vulvovaginal symptoms, then compounded estriol 2 mg/g: insert ½ g and apply ½ g nightly for 2 weeks, then twice weekly maintenance

Urinary tract infections

Sample Plan

Acute

- e.g. CranStat Extra (Vitanica): 2 capsules every 2 hours for the first 2 days, then 2 capsules 3 times daily for 1 week

Chronic

- CranStat Extra (Vitanica): 2 capsules daily
- Mannose: 1–2 g daily
- Fem Ecology (Vitanica), urogenital specific probiotic combination: 1 capsule daily
- If postpartum, perimenopausal, or postmenopausal: add vaginal estrogen twice weekly; compounded estriol 2 mg/g – insert ½ g twice weekly

Bacterial Vaginosis

Sample Plan

Acute: V-Fresh Suppository (special vitamin C preparation with homeopathics; Vitanica); insert daily for 6 days; wait 1 week and repeat

Consider: vaginal prescription metronidazole gel .75 %; insert 1 applicator twice daily for 10 days

Chronic:

- Metronidazole gel 75 %; insert 1 applicator twice daily for 10 days then once per week for 6 months.
- Oral Fem Ecology (*L. acidophilus, L. rhamnosus, L. reuteri, L. plantarum, L. acidophilus, L. salivarius*) 10 billion per capsule; take 1 capsule daily for 4 months and insert once weekly for 6 months during the 6 months of once weekly metronidazole gel
- Avoid vaginal exposure to semen (to facilitate vaginal pH becoming acidic) and optimal to avoid oral sex for 6 months (to avoid mixing oral flora with vulvovaginal flora)
- Consider role of vitamin D deficiency, high starchy carb diet
- Consider using biofilm disruptors

Perimenopause/Menopause Hot Flashes/Night Sweats

Sample Plan

Mild:

1. Black cohosh standardized extract 40 mg/day or
2. Femenessence (Natural Health International): Macalife 2 capsules twice daily for perimenopause or Macapause 1 capsule twice daily for postmenopause

3. Women's Phase II (Vitanica; wild yam, burdock root, dong quai, licorice root, motherwort): 3 capsules twice daily or
4. Pycnogenol: 100 mg daily or
5. Estrovera (Metagenics; Siberian rhubarb): 1 tablet daily
6. Grapeseed extract 200 mg per day

Moderate to Severe:

One or two of the above, likely two.

Consider estrogen/progesterone combination; dose and delivery widely variable.

1. Average oral dose: estradiol 1 mg daily + oral micronized progesterone 100 mg daily in women with uterus
2. Average transdermal estrogen patch dose: 0.05 mg Vivelle-Dot generic – apply 1 patch every 3.5 days + oral micronized progesterone 100 mg nightly before bed in women with uterus

Premenstrual Syndrome

Sample Plan

Combination product (Women's Phase I; Vitanica: B6, calcium, chromium, kelp, chaste tree, St. John's wort, ginkgo, borage seed oil extract, vitamin E, magnesium, passion flower, dong quai, wild yam, dandelion leaf): 2 capsules twice daily throughout whole cycle

If premenstrual dysphoric disorder: use the above plus add Travacor (Neuroscience)

ASCUS HPV High Risk Positive
Sample Plan for 6–12 months

Indole-3-carbinol 200 mg/day (e.g., Indolplex; Integrative Therapeutics)

Coriolus versicolor

1500 mg twice daily (e.g., hot water extract from Nutritional Fundamentals for Health)

Folic acid

10 mg/day (L-methylfolate in select cases)

Oral green tea

1 capsule daily or 3 cups daily

4 months of the 6–12 months:

Green tea suppositories 150 mg of 15% extract compounded from compounding pharmacy only; insert twice daily

Consider: curcumin 150 mg suppositories in HPV 16, 18 cases (refer to published research study in women for dose and regimen)

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. ◆

Calendar

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

➤ *continued from page 96*

MARCH 12: ORGANIC ACIDS WORKSHOP FOR DISCOVERING UNDERLYING CAUSES OF CHRONIC ILLNESS with Kurt Woeller in Atlanta, Georgia. CONTACT: www.organicacidworkshop.com

MARCH 14-18: APPLYING FUNCTIONAL MEDICINE IN CLINICAL PRACTICE – 5 day foundational course in Phoenix, Arizona Also, **JUNE 6-10** in Austin, Texas and **SEPTEMBER 19-23** in Baltimore, Maryland. CONTACT: www.functionalmedicine.org/AFMCP

MARCH 16: WISDOM DAY 2016 in Washington, D.C. Precedes **39th Annual Psychotherapy Networker Symposium**. CONTACT: www.dcnn.pro/WisdomDay2016.en.html

MARCH 19-20: 2016 HOMEOPATHY SYMPOSIUM @ National College of Natural Medicine in Portland, Oregon. CONTACT: career-alumni.ncnm.edu/homeopathy/

MARCH 21-23: AMERICAN CENTER FOR INTEGRATIVE MEDICINE presents 13th ANNUAL NUTRITION & HEALTH CONFERENCE in Denver, Colorado. CONTACT: www.nutritionandhealthconf.org/

MARCH 31-APRIL 3: ADVANCED TOPICS IN ENVIRONMENTAL MEDICINE in Irving, Texas (near Dallas). Includes Dr. Alan McDaniel's 2-day Endocrinology course. CONTACT: American Academy of Environmental Medicine, 316-684-5500; www.aaemconference.com

APRIL 2: COULD METHYLATION BE THE HOLY GRAIL OF AGING GRACEFULLY? in Bethesda, Maryland. CONTACT: www.facebook.com/BioticsResearch.

APRIL 5-7 & 12-14: INCLINIC PRECEPTORSHIP BIOIDENTICAL HORMONES with Erika Schwartz, MD in New York City, New York. CONTACT: dkingman@drerika.com; drerika.com/content/speaking-and-events

APRIL 8-10: SOUTHWEST CONFERENCE IN BOTANICAL MEDICINE in Tempe, Arizona. Intensive with Donald Yance on new cancer drugs and synergistic natural medicines. CONTACT: 541-482-3016; www.botanicalmedicine.org

APRIL 8-10: 11th ANNUAL JOINT AMERICAN HOMEOPATHIC CONFERENCE – Ascending to New Heights: Reaching the Summit with Homeopathy in Westminster, Colorado (near Denver). CONTACT: www.homeopathycenter.org/2016-joint-american-homeopathic-conference

APRIL 9: HORMONES & CARDIOMETABOLIC FUNCTION – GETTING TO THE HEART OF THE MATTER in Charlotte, North Carolina. CONTACT: www.facebook.com/BioticsResearch.

APRIL 14-16: 14th ANNUAL INTEGRATIVE ONCOLOGY CONFERENCE @ Town & Country Resort in San Diego, California. CONTACT: www.bestanswerforcancer.org/annual-conference/2016-conference/

APRIL 14-17: 12th NATIONAL AYURVEDA MEDICAL ASSOCIATION CONFERENCE in Warwick, Rhode Island. CONTACT: www.ayurvedanama.org/?page=2016ConfOverview

APRIL 15-17: 60th NORTHWEST NATUROPATHIC PHYSICIANS CONVENTION – FOOD AS MEDICINE in Portland, Oregon. CONTACT: nwnpc.com

APRIL 15-17: SW COLLEGE OF NATUROPATHIC MEDICINE presents REGENERATIVE INJECTION THERAPY WORKSHOPS (Module 3): Lumbosacral Region & Pelvis in Tempe, Arizona. CONTACT: www.scnm.edu/RIT-WORKSHOPS

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

MAY 3-4 & 10-12: INCLINIC PRECEPTORSHIP BIOIDENTICAL HORMONES with Erika Schwartz, MD in New York City, New York. CONTACT: dkingman@drerika.com: drerika.com/content/speaking-and-events;

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

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

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

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

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

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

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

JUNE 7, 15 or 22: INCLINIC PRECEPTORSHIP HCG DIET by Erika Schwartz, MD in New York City, New York. CONTACT: dkingman@drerika.com; drerika.com/content/speaking-and events

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

JUNE 24-26: KLINGHARDT EUROPEAN NEURAL THERAPY & INJECTION TECHNIQUES in Kenmore, Washington. A transformative workshop: basic to advanced skills. CONTACT: 908-899-1650; info@klinghardtacademy.com; www.klinghardtacademy.com/Seminars-Workshops/Injection-Techniques-and-Skills-2016.html

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

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

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

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

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

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

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

SEPTEMBER 29-OCTOBER 2: 7th ANNUAL INTEGRATIVE MEDICINE FOR MENTAL HEALTH CONFERENCE in Reston, Virginia (near D.C.). CONTACT: www.immh2016.com/

OCTOBER 6-9: AMERICAN ACADEMY OF ENVIRONMENTAL MEDICINE ANNUAL MEETING – The Role of Mitochondria in Health & Disease in San Diego, California. CONTACT: AAEM, 316-684-5500; www.aaemconference.com

OCTOBER 22-23: 10th AUSTRALIAN HOMEOPATHIC MEDICINE CONFERENCE in Brisbane, Australia. CONTACT: www.homeopathyconference.com

OCTOBER 26-30: 10th ANNUAL MICROCURRENT CASE CONFERENCE in St. Pete Beach, Florida. CONTACT: microcurrent.info.

OCTOBER 28-30: DETOX ADVANCED PRACTICE MODULE – Biotransformation and *Toxicity* in Chicago, Illinois. Live Streaming Available. CONTACT: www.functionalmedicine.org/Detox

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Tackle Monday Morning Football-Fan-Fatigue with Nutrient Power Duo, Setria Glutathione and Cognizin Citicoline

Finding the playbook for a smooth Monday morning recovery after a football-fueled weekend is the greatest thing to happen to football season since fantasy lineups. Good news for fans of the game, Setria glutathione and Cognizin citicoline are the perfect post-tailgate teammates to ensure that fans feel recovered, refreshed, and ready to tackle the work week. Glutathione, the body's master antioxidant, can help aid in detoxification after too many beers and wings; while Citicoline, a naturally occurring brain booster, promotes mental clarity, recall, and alertness to block Monday morning mental fog. Both glutathione and citicoline are found naturally in the body but – according to published clinical research – each can be supplemented orally to increase the body's natural stores and give consumers an edge after a long weekend.

"Football fans tend to ingest unhealthy foods and excess alcohol on game day; this, combined with the natural stress of high-intensity games and insufficient sleep from late-night TV-watching, is a hard hit on the body," said Danielle Citrolo, registered pharmacist and manager of technical services for Kyowa Hakko USA. "Luckily, fans can aid their recovery and appear alert and refreshed to start the work week by supplementing with an antioxidant like Setria glutathione to eliminate toxic chemicals in the body, and Cognizin citicoline to improve mental alertness."

What Makes Glutathione a Winner?

Glutathione's many jobs include acting as the liver's main detox agent to fight oxidative stress and eliminate harmful toxins from the body; maintaining cell proteins; supporting immune health; and maintaining the healthy levels of vitamins C and E in the body.

According to a 6-month clinical trial, led by Dr. John P. Richie of Penn State University, Setria glutathione supplementation is proven to enhance body stores of glutathione; and the study results show that glutathione supplementation represents an effective intervention strategy to not only enhance body stores but also boost the body's immune function.[1]

Why You'll Score with Citicoline

Citicoline is a natural nutrient found in every cell of the body and is especially vital to boosting cognitive function. Citicoline is referred to by the scientific community as a "brain nutrient" because it aids the production of a critical building block in brain cells.

While the brain produces its own levels of citicoline naturally – to protect its cell membranes' integrity and help ward off disease – studies show that oral supplementation of citicoline allows for improved transport of critical nutrients and signal-sending neurotransmitters in the brain. Dr. Deborah Yurgelun-Todd, of the Brain Health Institute at University of Utah, recently published a study in *Food and Nutrition Sciences*, which found that by supplementing with Cognizin citicoline, study participants experienced improved memory recall and attention.[2]

About Setria Glutathione

Setria glutathione, manufactured by Kyowa Hakko Bio Co. Ltd., is a clinically studied form of glutathione that, when taken orally, has been shown to replenish the body's reserves, which may be depleted as a result of poor lifestyle choices, stress or natural aging. Called the "master antioxidant," glutathione helps protect cells in the body from the damaging effects of oxidative stress and toxins. Setria glutathione is manufactured through a patented fermentation and patent pending for increasing natural killer (NK) cell activity and is pure, vegetarian, and allergen-free. For more information about Setria glutathione, visit www.setriaglutathione.com.

About Cognizin Citicoline

Cognizin is a branded form of citicoline, a natural substance found in every cell of the body and especially vital to brain health. Citicoline is broken down during intestinal absorption and, after passing through the blood/brain barrier, is reconstituted in the brain as citicoline. Citicoline is a water-soluble compound that supplies precursors for the synthesis of phospholipids, including phosphatidylcholine, a major constituent of brain tissue; helps maintain normal levels of acetylcholine, a chemical that regulates memory and cognitive function; enhances communication between neurons, supports visual function, protects neural structures from free-radical damage, enhances metabolism and healthy brain activity, and helps sustain healthy cellular mitochondria for sustained energy. Cognizin is also highly stable, GRAS, ultrapure, and allergen free. For more information on Cognizin, visit http://www.cognizin.com.

About Kyowa Hakko USA Inc.

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, Pantesin pantethine, Setria glutathione, as well as sustamine L-alanyl-L-glutamine. For more information, visit www.kyowa-usa.com.

Notes

1. Richie JP Jr, Nichenametla S, Neidig W, et al. Randomized controlled trial of oral glutathione supplementation on body stores of glutathione. *Eur J Nutr*. Epub 2014 May 5. PubMed PMID: 24791752.
2. McGlade E et al. Improved attentional performance following Citicoline administration in healthy adult women. *Food Nutr Sci*. 2012;3:769–773.

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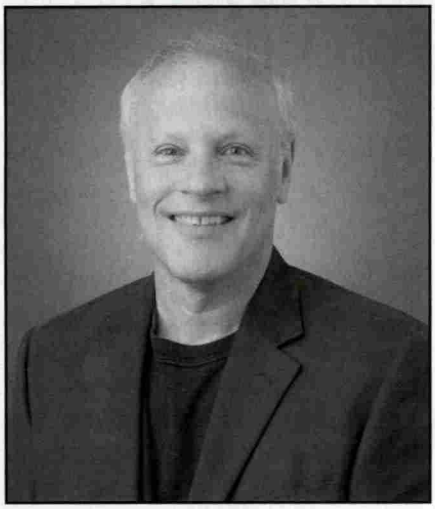

Another Drug that We Don't Need and Can't Afford

It seems like every time I watch television these days, there is a commercial depicting a middle-aged blind woman who is living a full life despite her blindness. However, because her eyes cannot perceive the normal daily cycle of light and darkness, she suffers from a circadian rhythm disorder known as non-24 sleep-wake disorder or, simply, non-24. People with non-24 have a circadian rhythm of about 24.5 hours, rather than the usual 24 hours, so their sleep-wake cycle is out of sync with the rotation of the earth. As a result, they often have difficulty sleeping at night and tend to need naps during the day.

But now there is a drug for people with non-24, and it only costs $281 per tablet ($102,565 for a 1-year supply). In January 2014, the US Food and Drug Administration (FDA) approved Hetlioz (tasimelteon), a melatonin receptor agonist, for the treatment of non-24. Since that time, Vanda Pharmaceuticals (which owns the patent for Hetlioz) has sponsored more than 11,000 ads on national television, as well as countless ads on the radio, designed to increase public awareness about non-24. The ads do not specifically mention Hetlioz (because Vanda knows that it has the only FDA-approved drug for non-24); rather, they invite the viewer to call a toll-free number or visit a website to "learn about the link between non-24 and blindness." The company does have to worry that patients (and insurance companies) might wonder whether melatonin, which costs 4000 times less than Hetlioz, is just as effective. However, Vanda must be heartened by the fact that FDA regulations prohibit melatonin manufacturers from telling people about research demonstrating that melatonin can reset circadian rhythms and improve sleep in blind people with non-24 sleep-wake disorder; or that prior to FDA approval of Hetlioz, melatonin was considered the treatment of choice for non-24.[1–3] Vanda also knows that even if melatonin distributors were allowed to use a structure-function claim such as "helps maintain a normal circadian rhythm," they would not have the budget for even one national ad, let alone 11,000 such ads.

Although all of the Hetlioz commercials are about blind people, Vanda knows that there aren't enough poorly sleeping blind folks in the US, even at $281 per tablet, to justify the cost of its massive ad blitz. Presumably, the company's main target audience is the millions of poorly sleeping sighted people who might identify themselves as having a similar circadian rhythm disorder. For reasons that are not clear, the FDA approved Hetlioz for all people with non-24, even though all of the clinical research on this drug was conducted in blind people. If insurance companies allowed themselves to be coerced into covering this drug for the hordes of phase-shift insomniacs, our insurance premiums and taxes would go up yet again. To help forestall this pending rip-off, the watchdog group Public Citizen filed a petition with the FDA several months ago, requesting that the approval and prescribing information for Hetlioz be limited to patients who are totally blind, since the drug has never been tested on sighted people.

Apart from the ridiculous price that Vanda is charging for its drug, there are serious questions about whether Hetlioz is effective enough to have warranted FDA approval. According to a report published by a financial analyst on TheStreet.com, an investigation into the clinical research on this drug revealed "a disturbingly large number of irregularities and red flags which should ring alarm bells for any investor."[4] One major irregularity was that the design of Vanda's phase III clinical trial was changed numerous times. Originally, the primary end point was the average total sleep time at night, a logical end point

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†Dr. Gersh is a Pure Encapsulations Medical Advisor. She has been retained as a consultant in advising Pure Encapsulations. She is compensated for this service.

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