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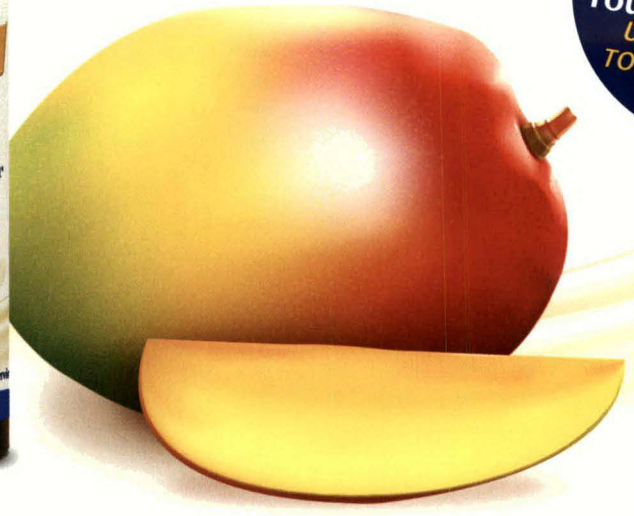

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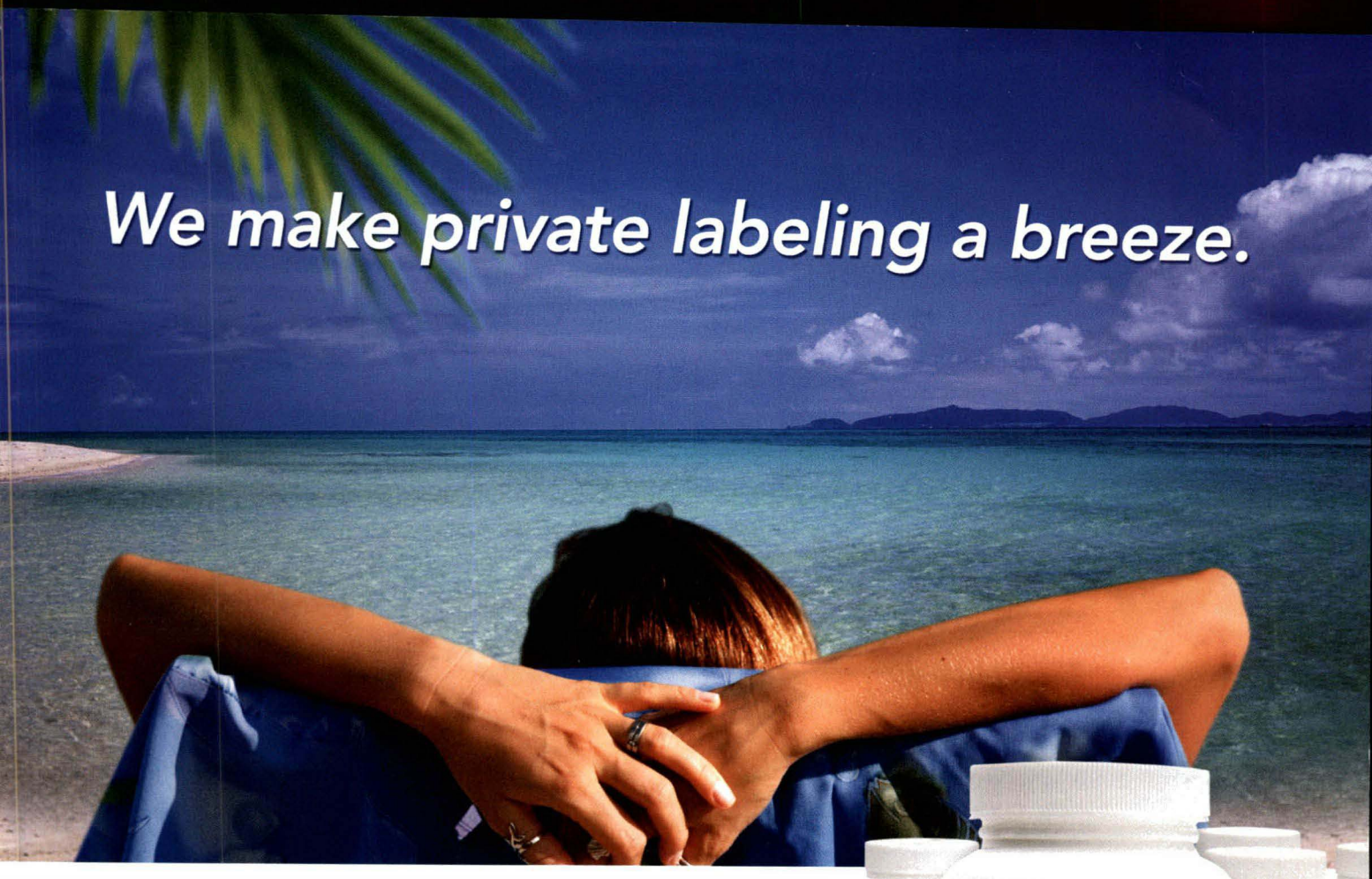

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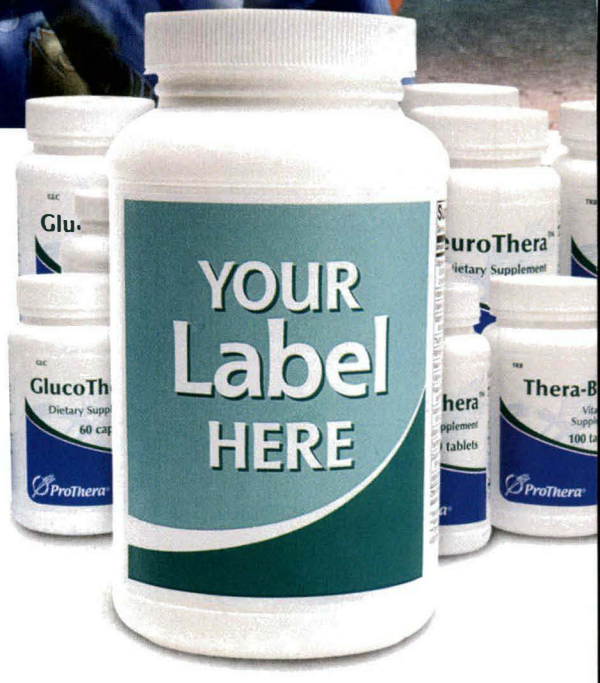

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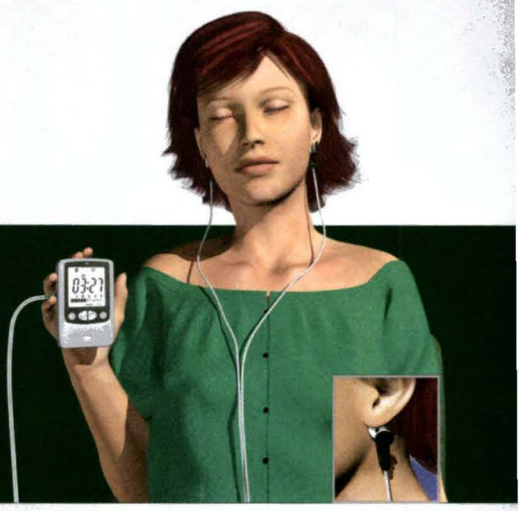

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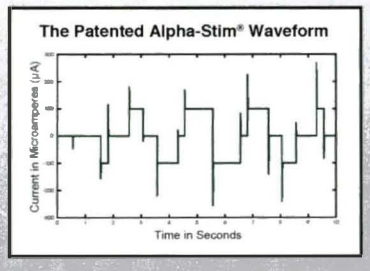

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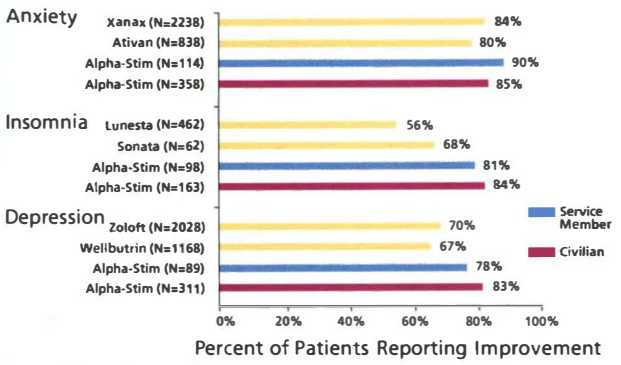

Patients who reported a positive response according to WebMD Drug Surveys, and Alpha-Stim Service Member and civilian surveys. Alpha-Stim Data from 2011 Military Service Member Survey (N=152) and Alpha-Stim Patient Survey (N=1,745). Conducted by Larry Price, PhD, Associate Dean of Research and Professor of Psychometrics and Statistics, Texas State University. Pharmaceutical Survey Data from www.WebMD.com/drugs. Accessed on October 28, 2011.

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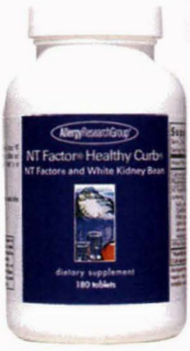

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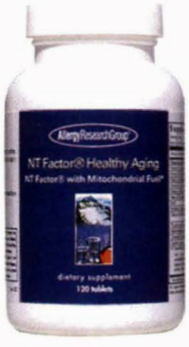

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1. Ellithorpe RR, Settineri R, et al. Functional Foods in Health and Disease 2011; 8:245-254.
2. Seidman M, Khan MJ, et al. Otolaryngol Head Neck Surg 2002; 127: 138-144.
3. Nicolson GL, Ellithorpe R, Settiner R. Journal of IiME 2009; 3(1): 39-48.
4. Nicolson GL, Ellithorpe R, et al. J Am Nutraceut Assoc. 2010;13(1):10-14.

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From the Publisher

Is Testosterone Therapy Contraindicated in Men with Heart Disease?

At the December 2013 A4M meeting in Las Vegas, Abraham Morgentaler, MD, associate clinical professor of urology at Harvard Medical School, lectured on the use of testosterone therapy in men. His title suggested a measure of optimism: "Testosterone Therapy: Panacea, Scourge or the Next Big Thing in Medicine?" Testosterone prescriptions have surged in the last several years, due in no small part to the large advertising budgets of pharmaceutical companies. Testosterone offers improvement in sexual functioning, enhancement in lean muscle mass, and mellowing of grouchy tempers – what men would not wants these benefits? Although testosterone is restricted by the DEA, requiring a controlled prescription, doctors have been freely prescribing the hormone, which worries the critics. Too many prescriptions are being made without

continued on page 8 ➤

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Letter from the Publisher

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laboratory evaluation, presumably to men who are not testosterone deficient. The serum testosterone reference level is remarkably broad (250–1200 ng/dl); most men test "normal." However, physicians who support anti-aging medicine believe that men having testosterone deficiency symptoms with serum levels below 500 ng/dl are testosterone deficient even if the tests results lie in the normal range. Hence, the prescribing of testosterone has almost become obligatory in anti-aging clinics – what reasons are there for not prescribing testosterone? In a widely publicized *PLoS One* study reported on January 29, 2014, the increased risk for developing a heart attack in men with heart disease may be a contraindication for prescribing testosterone.

Morgentaler was skeptical of the study results. When interviewed by *USA Today*, he said, "It's possible that the men's heart attacks in this study were caused by their underlying medical problems, not by testosterone. ... Most heart attacks occurred in the first 90 days after a prescription is written. It's unlikely that heart attacks could develop in such a short period of time."

A drug company, AbbVie, maker of AndroGel, stated that testosterone has been found to improve health and lower the risk of death. Long-term use of testosterone has been found to lower cholesterol, blood sugar, and blood pressure. However, a cardiologist spokesman, Steven Nissen, MD, at the Cleveland Clinic, thought that the testosterone drug manufacturers should now be obligated to conduct rigorous clinical trials to determine if testosterone increases heart risks.

The *PLoS One* report is not based on a clinical study; it is a statistical analysis of a large health-care database of men with and without heart disease who have been given new prescriptions of testosterone in comparison with Cialis. The authors tabulate cardiac events in the two groups through diagnostic codes found in the electronic medical records (EMR). Approximately 56,000 men were identified who were given new prescriptions of testosterone versus 167,000 men who were given new Cialis prescriptions. All men were studied to determine age, medical condition, and medications in use. Patients were separated into four groups based on being either younger or older than 65 and having heart disease or not. In each of the groups, the incidence of nonfatal heart attacks was determined for the year prior to the prescription of the drug and then for the 3-month period following the prescription of the drug. As expected, the incidence of heart attacks in the year prior to prescription of testosterone or Cialis was similar between the two groups. However, in the group treated with testosterone over age 65 who had a history of heart disease, the rate ratio (RR) of heart attack was nearly double in the testosterone group compared with the Cialis group. There was a modest

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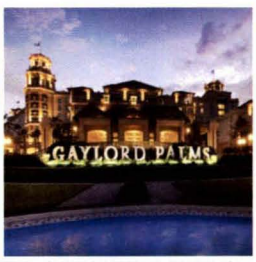

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1) Enhanced glutathione levels in blood and buccal cells by oral glutathione supplementation. J.P. Richie. Presented at Experimental Biology, April 22, 2013.

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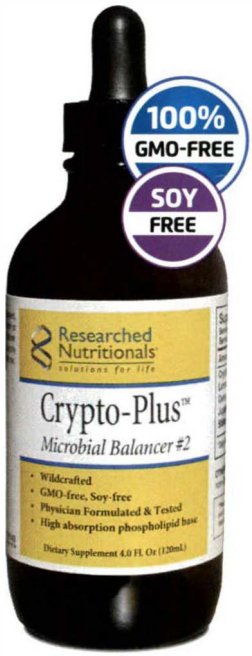

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IN THIS ISSUE April 2014 | #369

Best of Naturopathic Medicine 2015

The *Townsend Letter* is pleased to announce our seventh Best of Naturopathic Medicine competition. Naturopathic students, faculty, researchers, and practitioners are invited to submit research papers, reviews, and articles. Selected papers will be published in our February/March 2015 issue. The author of the winning paper will be awarded $850. Runner-up papers will be published and authors will receive an honorarium.

Papers submitted should be 1500 to 3500 words and referenced. Author guidelines are available at the *Townsend Letter* website: www.townsendletter.com. Papers should be submitted digitally, preferably as a Microsoft Word document. Papers authored by multiple writers are acceptable; the lead author should be an ND graduate or candidate of an accredited four-year naturopathic school. Papers submitted for the competition may not be submitted to other publications or have previously been published. All entries must be submitted by October 31, 2014.

Send papers to editorial@townsendletter.com. The subject line should read: "Paper for Best of Naturopathic Medicine 2015."

ON THE COVER: Managing Type 2 Diabetes (42); Solid Food for Babies (75); Insulin Resistance (59); Healthy Aging (70); Small Changes, Big Difference (81)

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Letter from the Publisher
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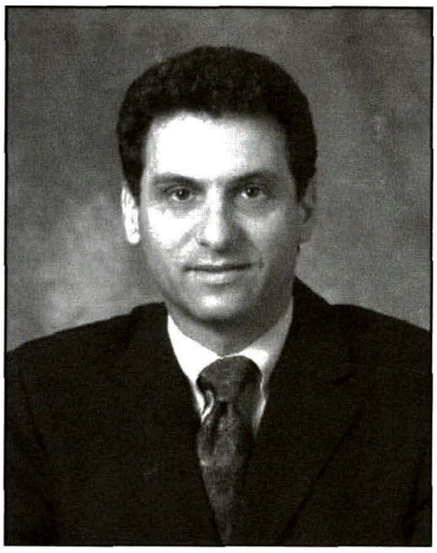
increase in the RR of heart attack in the group treated with testosterone under age 65 who had a history of heart disease. In comparison, in the Cialis group there was only a modest increase in the RR of heart attack in the men with a history of heart disease both for men above and under age 65.

While the statistics for this study were robustly made with an additional arcane statistical marker known as the ratio of rate ratio (RRR), the case numbers are remarkably low. In the testosterone-treated group, 37 men developed myocardial infarcts in the year prior to receiving testosterone and 20 men developed heart attacks 3 months after being treated. In other words, this study's significance hinges on the observation that 20 men over age 65 in a group of 7000 men treated with testosterone developed an MI within 3 months. If there had only been 9 men who had developed a heart attack in this testosterone-treated group, there would have been no statistical difference – the RR and the RRR would have been identical to the Cialis-treated group. So we are talking about the difference between 20 men versus 9 men equaling 11 men, from a group of 7000 – this is the entire basis for the conclusion that testosterone treatment in men over age 65 with a history of heart disease leads to an increased risk for developing a heart attack.

In other words, 9 men of a group of 7000 would be the reason that we should begin to restrict the prescribing of testosterone to treat low testosterone and the anti-aging process. Does this make sense? We are talking about the incidence of 1 heart attack in 350 men who are over age 65 and have a history of heart disease. I don't think that 1:350 is a good justification to bar testosterone therapy.

It should also be noted that this is a study involving men using unspecified testosterone treatment – oral testosterone treatment is not metabolized well by the liver. There is no discussion about measuring testosterone levels; was testosterone being administered inadequately or excessively? Presumably, the majority of these



Abraham Morgentaler, MD

men were under treatment with numerous medications, but minimal or no nutritional supplementation; minimal or no lifestyle, dietary, and exercise intervention; and minimal or no complementary therapies. Anti-aging physicians do not prescribe testosterone without supporting the patient fully. The chief cardiovascular concerns of testosterone prescribing are the increased risk of thrombosis presumably secondary to a relative increase in red blood cell production, and excessive metabolic breakdown of testosterone to dihydrotestosterone (DHT) and estrogen. It would be prudent for the anti-aging physician to screen and monitor patients over age 65 for heart disease. The patient should be advised of testosterone's possible increased cardiac risk. However, there is little justification to contraindicate the use of testosterone in all cardiac patients.

Morgentaler examined the 2013 *JAMA* study that found an increase in myocardial events and strokes in men using testosterone therapy. At the A4M Las Vegas meeting, he disputed the reported increased risk of events in the testosterone group compared with placebo. Morgentaler tallied the actual number of events in the testosterone group compared with the untreated group. The number of events in the placebo group was actually higher than in the testosterone group. Hence the conclusion of the study was wrong. Morgentaler approached the authors with his data review, and they agreed that, based on the number of events, the testosterone group did not have an increased risk for developing a cardiovascular event. However, when Morgentaler contacted *JAMA*, the editorial board was unwilling to retract the study. Morgentaler further noted that other studies have shown that patients with the lowest testosterone levels have the highest incidence of heart disease and mortality.

No, testosterone is not contraindicated in patients with heart disease.

Introducing Baby to Solid Foods

It has been a truism that babies should be breast-fed and not introduced to solid foods until they are at least 6 months old – even better if they are older; potentially highly allergenic foods such as peanuts, eggs, and dairy should be avoided until 1 year of age. However, such thinking may be flawed and actually contribute to the development of allergy and atopic disorders. In this issue of the *Townsend Letter*, Kimberly Sanders, ND, and Jacob Schor, ND, review the recent studies that have examined what happens to infants introduced to solid foods at a much earlier age – 6 months, even 4 months. The results are surprising. Many of the infants introduced to solid foods at 6 months of age or younger have a lower incidence of IgE and IgG allergy. There appears to be a "sweet spot" of delaying solid foods until 4 months, limiting the diet to only breast-feeding up to then. Introducing solid foods between 4 and 6 months of age limits the development of allergic antibodies

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compared with delaying introduction of solid foods to an older age.

There appears to be a remarkable parallel to the introduction of solid foods at an early age and the observation that infants exposed to "dirt" in their home environments have a lower incidence of allergenic disorders compared with children restricted to "ultraclean" environments. Pediatric studies comparing infants in poorer socioeconomic communities in Russia with infants in more affluent cities in Finland show a marked reduction in allergenic disorder. The researchers hypothesize that an early exposure to dirt, animals, and other allergens enables an adaptive response by the immune system, lessening the development of allergic disorders.

Sanders and Schor discuss how the early introduction of milk plays a role in the development of type 1 diabetes mellitus. For solid foods, it appears that introduction earlier than 4 months or later than 6 months both increased risk for developing diabetes.

Do You Think You Know All About Insulin Resistance?

Insulin resistance is just another way of talking about metabolic syndrome and prediabetes, right? That middle-aged individual with a paunch has insulin resistance, but surely that svelte younger woman couldn't, right? If the blood glucose and hemoglobin A1c are normal, then there's no need to worry about insulin resistance, right? Sorry; all of the previous statements are wrong. Individuals with metabolic syndrome are insulin resistant, but some insulin-resistant individuals don't have metabolic syndrome – for example, the trim woman might be insulin resistant. We should worry about insulin resistance even if the glucose and hemoglobin A1c are normal, because eventually insulin resistance will progress to glucose intolerance and, perhaps, diabetes.

Filomena Trindade, MD, MPH, examines in this issue the continuum of insulin resistance, glucose intolerance, prediabetes, and diabetes. Trindade's hypothesis is not for lazy patients *or doctors*. A fasting blood glucose of above 100 mg/dl is diagnostic for prediabetes – there are many patients and doctors whose fasting blood glucose is above 100 mg/dl. Trindade dismisses the idea that prediabetes is not a disease. She asserts that it clearly increases the risk of sustaining a cardiovascular event and developing frank diabetes. Trindade prefers the fasting blood glucose to be 87 mg/dL – the target for those who are seeking not to have glucose intolerance; ideally Trindade prefers patients to have a fasting blood glucose of 81 mg/dl and a hemoglobin A1c of 5.4%. Admittedly, these numbers are difficult to achieve – essentially impossible without a patient and doctor committed to diet, exercise, nutritional supplementation, and lifestyle changes. However, Trindade thinks that without assessing the level of insulin resistance, one cannot effectively diagnose or treat the patient. The svelte female may not have glucose intolerance or prediabetes, but she might have insulin resistance. Determining her insulin resistance may not only prevent diabetes and cardiovascular disease but also play a long-term role in preventing cancer and neurodegenerative disease.

Jonathan Collin, MD

Notes

1. Finkle, WD, Greenland S, Ridgeway, GK, et al. Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men. *PLoS One*. 2014; doi:10.1371/journal.pone.0085805.
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Sierra Integrative Medical Center Offers Advanced Training Program

Sierra Integrative Medical Center (SIMC; Reno, NV) is responding to the many requests that it receives from general practitioners and specialists for advanced training in groundbreaking alternative treatment therapies. Throughout 2013, SIMC medical director Dr. Bruce Fong has spoken on his successful treatment modalities for patients suffering from Lyme disease and other autoimmune disorders. Dr. Sean Devlin of SIMC has lectured throughout the US on alternative cancer treatment and pain management. SIMC is excited to offer its expertise to physicians wishing to expand their treatment options, through an advanced training program at its Reno medical center.

Effective treatment for difficult cases of chronic degenerative diseases is hard to find. Medical centers are turning to alternative therapies to support and enhance traditional allopathic treatment plans, but trained practitioners are rare. SIMC routinely treats patients suffering from chronic fatigue syndrome, Lyme disease, multiple sclerosis, and other neurodegenerative and chronic infectious diseases. This year, SIMC is expanding options for patients nationwide by instructing physicians in specialties such as integrative oncology, nutrition, alternative medicine, Chinese herbal medicine, acupuncture, and homeopathic remedies. Also to be reviewed in SIMC physician training are front-office protocols, legal paperwork, and billing procedures.

Fong notes, "At Sierra Integrative Medical Center, we think of our treatment plans as embracing the best of the West and East. Now we have a format for sharing our experience with other practitioners. This is good news for patients and physicians who have felt limited by pharmaceutical

Sierra Integrative Medical Center physicians Ann Barnet, MD; Bruce Fong, DO, HMD; and Sean Devlin, DO, HMD

prescriptions and insurance formularies as the primary source of care."

SIMC deals primarily with long-term degenerative and chronic diseases. Treatment plans are based on identifying root causes. SIMC sees many patients with similar symptoms, allowing staff to more readily properly diagnose and treat neurodegenerative and chronic infectious diseases. SIMC is now training physicians to recognize early indicators and red flags that staff has come to know through many years of focused care. "In my lectures and traveling throughout the US, I see many docs who feel they have exhausted treatment options within the allopathic community. By providing training, new doors are open for reinvigorating careers and improving patient health and overall well-being," observes Devlin.

Learn more about Sierra Integrative by visiting www.SierraIntegrative.com or call 775-828-5388. Physicians can inquire about training options by requesting an interview appointment with Fong or Devlin at 775-828-5388.

Sierra Integrative Medical Center (SIMC) optimizes health service by drawing from all schools of medicine. SIMC utilizes scientifically proven conventional treatments in combination with alternative therapies that are designed to strengthen the body so that it can heal itself.

Services are designed to provide a holistic healing approach with a broad range of healing modalities, including but not limited to homeopathy, natural and biological medicines, behavioral medicine, nutritional therapies, orthomolecular integration, and neurotherapy.

If you have a specific request, please contact SIMC to discuss your health treatment, career development, or wellness plan.

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Shorts

briefed by Jule Klotter
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Avandia

Doctors can once again prescribe Avandia and other rosiglitazone-containing diabetes medications to patients without having to enroll them in the US Food and Drug Administration's Rosiglitazone Risk Evaluation and Mitigation Strategy (REMS) program. Avandia use was restricted to patients who did not respond to other diabetes medications in 2010, following the recommendation of a FDA expert panel. Clinical evidence, including an independent meta-analysis of placebo-controlled, randomized studies, showed that patients who used rosiglitazone, an insulin sensitizer, were more likely to have a heart attack or other cardiovascular event.

A new FDA expert panel, convened in 2013, used REMS data and a reanalysis of the Rosiglitazone Evaluated for Cardiovascular Outcomes & Regulation of Glycemia in Diabetes (RECORD) clinical trial as the basis for reversing most of the 2010 restrictions. The RECORD study, funded by GlaxoSmithKline and published in the *Lancet* (June 20, 2009), has been the subject of much criticism. The open-label study investigated cardiovascular outcomes and rosiglitazone (Avandia) use. It compared patients using rosiglitazone in combination with metformin or a sulfonylurea with patients using a combination of metformin and sulfonylurea, the approved treatment for type 2 diabetes. The study's authors did notice an increased risk of heart failure and fractures in rosiglitazone users, especially in women. They did not, however, find an increased risk of cardiovascular events, stating in their conclusion: "Although the data are inconclusive about any possible effect on myocardial infarction, rosiglitazone does not increase the risk of overall cardiovascular morbidity or mortality compared with standard glucose-lowering drugs." The accuracy of this conclusion, however, is questionable; both the study's design and execution are flawed.

Because RECORD was an open-label study, participating doctors, patients, and manufacturer GlaxoSmithKline researchers knew who was taking which combination. Data could be easily manipulated. During a partial examination of the study's data, FDA reviewer Dr. Thomas Marciniak identified "a dozen instances in which people taking Avandia appeared to suffer serious heart problems that were not counted in the study's tally of adverse events," according to a *New York Times* article by Gardiner Harris (July 9, 2010). Such findings raise serious questions about the study's quality.

Dr. Steven Nissen believes that the reanalysis of the flawed RECORD study was instigated by leadership of the FDA's Center for Drug Evaluation & Research (CDER), which is responsible for drug regulation. Nissen, Cleveland Clinic's Chairman of the Department of Cardiovascular Medicine, and colleague Kathy Wolski wrote the May 2007 meta-analysis that showed a 43% increase of heart attack in Avandia users. At the time, neither realized that the CDER and Avandia manufacturer GlaxoSmithKline (GSK) had found similar results in a 2005 study. "In Congressional testimony, CDER officials acknowledged that FDA statisticians had confirmed our findings, reporting a 40% increase in the risk of heart attack," Nissen states in an opinion article for *Forbes*. CDER and GSK agreed to conceal the hazard from practitioners and patients. Publication of the Nissen-Wolski meta-analysis made it impossible to continue hiding Avandia's cardiovascular risks. "In 2012, GSK pled guilty to criminal misconduct," Nissen writes, "related in part to concealing the hazards of Avandia and paid a $3 billion fine, one of the largest in US history."

A commentary in *Pharmacist's Letter/Prescriber's Letter* (January 2014) says, "... experts warn that reanalyzing a flawed study doesn't make it valid ... and other studies DO suggest Avandia increases CV risk." The publication suggests using pioglitazone, instead of rosiglitazone, if a glitazone is needed. Like rosiglitazone, however, pioglitazone increases the risks of weight gain, peripheral and macular edema, heart failure, and fractures. Pioglitazone has also been associated with increased risk of bladder cancer.

FDA to lift some *Avandia* (rosiglitazone) prescribing/dispensing restrictions. *Pharmacists Lett/Prescribers Lett.* Therapeutic Research Center; Stockton, CA. PL Detail-Document #300105. January 2014.

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Fructose Metabolism and Metabolic Syndrome

Fructose has been identified as a cause of metabolic syndrome and weight gain, according to animal research, epidemiological studies, and a few clinical experiments. This nonessential sugar is present in fruit, high-fructose corn syrup, and table sugar (sucrose). Until recently, the assumption has been that consuming large amounts of fructose directly leads to a greater risk of metabolic syndrome. However, the location of fructose metabolism (the organs in which the sugar breaks down) has an even greater effect on metabolic syndrome development, according to a 2012 experiment conducted by T. Ishimoto and colleagues.

Fructose is metabolized by fructokinase, an enzyme that has two isoforms: fructokinase A and fructokinase C. "Fructokinase C is expressed primarily in liver, intestine, and kidney and has high affinity for fructose, resulting in rapid metabolism and marked ATP depletion," the authors explain. "In contrast, fructokinase A is widely distributed [in these and other organs especially skeletal muscle], has low affinity for fructose, and has less dramatic effects on ATP levels."

The researchers developed mice that lacked the genetic ability to make fructokinase A and mice that were unable to make both A and C. Unlike wild-type mice, the mice that lacked both A and C (meaning that they did not metabolize fructose) failed to develop the symptoms of metabolic syndrome when fed high amounts of fructose. These mice excreted the fructose in their urine. The mice that produced just the C isoform, however, fared worse than the A-C knockout mice or the wild-type mice. At 25 weeks, these fructokinase A knockout mice had significantly higher epididymal fat mass, serum insulin, serum leptin, and intrahepatic triglycerides, and more severe hepatic steatosis than the wild-type mice. Even though fructokinase A does not have as strong an affinity for fructose as isoform C, A is found throughout the body, including skeletal muscle, and can break fructose down before it reaches the liver. The researchers say, "By reducing the amount of fructose for metabolism in the liver, fructokinase A protects against fructokinase C-mediated metabolic syndrome."

The presence of fructokinase A in skeletal muscle may help explain Luc Tappy's observation that plasma triglyceride concentrations do not increase in people with high fructose consumption who also exercise daily. He says, "For athletes, a high fructose intake may even be beneficial, as it has been shown that fructose can be metabolized during exercise, and increase performance."

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Jamun Fruit, Anthocyanins, and the Liver

Eugenia jambolana (jamun) fruit reduces liver injury due to cholestasis (obstructed liver bile flow), according to a 2012 study. When bile acid concentrations rise, free radical production and inflammation also increase, damaging and killing liver cells. Eventually, hepatic bile obstruction can cause hepatic fibrosis and cirrhosis. Ajay C. Donepudi and colleagues with the US Department of Agriculture chose Jamun fruit because of its use in Ayurvedic medicine and because of its high anthocyanin content. Anthocyanins are antioxidant compounds that give plants their blue, purple, and red colors. For this study, Donepudi and colleagues performed bile-duct ligation (obstructing bile flow) or sham surgery on male mice. Twenty-four hours later, the mice orally received the first of 10 daily treatments: a Jamun fruit pulp extract (100 mg/kg of body weight) or placebo. Twenty-four hours after the last treatment, researchers euthanized the mice and collected blood samples and the animals' livers. Mice in the ligation group had 10 times the serum ALT activity (indicating liver damage) seen in the sham surgery mice. Jamun fruit extract lowered the high serum ALT levels in bile duct ligation (BDL) mice by 60%. Collagen deposition (fibrosis formation) was also reduced in BDL mice treated with the extract. In addition, the extract decreased reactive oxygen substances, nitric oxide production, macrophage infiltration, and pro-inflammatory cytokine expression in BDL mice.

Jamun fruit is by no means the only rich source of anthocyanins. In 2006, USDA researchers screened over 100 common store-bought foods for anthocyanins, including fresh and dried fruits, vegetables, nuts, spices, breakfast cereals, baby foods, chocolate, and juices. Fresh chokeberries, elderberries, black raspberries, blueberries (particularly wild varieties), and black currants had the highest anthocyanin content among tested foods. Anthocyanins were rarely detected in processed foods, including breads, cereals, and baby foods.

Over 600 anthocyanins have been identified so far. Determining their bioavailability, health effects, and responses to processing is an ongoing project.

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Shorts

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Metabolic Syndrome, Gut Bacteria, and Probiotics

Feng-Ching Hsieh and colleagues in Taiwan have developed a strain of *Lactobacillus reuteri* GMNL-263 (Lr263) that decreases insulin resistance and lessens hepatic steatosis in rats on a high-fructose diet. High fructose consumption causes many symptoms of metabolic syndrome as well as increasing fat deposits in the liver in both rodents and humans. In this experiment, the researchers fed two groups of rats a high-fructose diet for 14 weeks; one group also received Lr263. A control group ate a standard diet (instead of high-fructose diet) without the probiotic. At study's end, serum glucose, insulin, leptin, C-peptide, glycated hemoglobin, GLP-1, liver injury markers, and lipid profile measures in serum and liver were significantly higher in high-fructose-fed rats, who did not receive the probiotic, compared with controls. In the Lr263 group, these same measures were similar to the control mice eating a standard diet.

Feng-Ching Hsieh and colleagues also tracked bacterial content in stool samples. Both groups on the high-fructose diet had an increase in clostridia (considered harmful), compared with controls. The Lr263 group, however, had a 2.5 ± 4.9% increase while the group without Lr263 had a 30.1 ± 5.9% increase in clostridia. As expected, the Lr263 group had considerably more lactobacilli than the control (35.4 ± 7.8); but the bifidobacterium level was also higher (26.7 ± 3.4%). Lactobacillus and bifidobacterium levels in the high-glucose group without Lr263 were similar to the control group's.

Lr263 is not the only probiotic to show therapeutic promise for treating type 2 diabetes and metabolic syndrome. Two review articles – one by K. Naydenov and colleagues and the other by Yong Zhang and Heping Zhang – cite research concerning imbalances in gut microflora that contribute to diabetes and obesity. Like Lr263, *Lactobacillus acidophilus* and *Lactobacillus casei* have shown antidiabetes effects, according to Naydenov et al. They propose that yogurt, containing lactobacilli and other beneficial bacteria, may be useful in treating diabetic and prediabetic conditions. (Consumers need to be aware that many commercial yogurts – especially those with sweeteners and gelatin or thickening agents – have few, if any, live probiotic bacteria.) In addition to yogurt and/or probiotics, Zhang and Zhang point out that some botanicals – such as berberine in *Coptis chinensis* – "have anti-diabetic effect through modulating microbiota composition. ... " What we eat – for good or bad – can change gastrointestinal microflora and, in turn, increase or decrease the risk of developing metabolic syndrome and diabetes.

Normally, the human gut contains as many as 1000 different microbial species that provide a large variety of metabolic and immune-enhancing services. Researchers are just beginning to understand the complex relationships between these microbes and our health. What if the microbes living within us, our own personal ecology, hold the key to preventing diabetes and other chronic illnesses?

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Silymarin and Hepatitis C

Silymarin, a collection of flavonolignans in milk thistle (*Silybum marianum*), shows antiviral and liver-protective effects in patients with hepatitis C, according to a 2011 Iranian pilot study led by Hamid Kalantari. Milk thistle has a long history as an herbal treatment for liver disorders. Kalantari and colleagues report that many people with chronic hepatitis C infection use milk thistle preparations in addition to or instead of ribavirin-interferon combination therapy, which is expensive and has adverse effects. Kalantari and colleagues decided to test a locally available commercial silymarin product (Goldaru Pharmaceutical Co.; Isfahan, Iran) for efficacy and safety.

Fifty-five people infected with hepatitis C virus, ages 10 to 67 years, took part in the prospective, self-controlled pilot study. Each patient took 630 mg of silymarin per day for 24 weeks. The researchers measured serum hepatitis C virus RNA, liver enzymes (ALT, AST), liver fibrosis markers, and patient well-being at baseline and after treatment. ALT and AST (which indicate liver injury) declined. Mean ALT before treatment was 108.7 and 70.3 at posttreatment ($p < 0.001$). Mean AST was 99.4 before treatment and 59.7 after treatment ($p = 0.004$). Nine patients showed no signs of the hepatitis C virus at treatment's end ($p = 0.004$). Liver fibrosis markers significantly improved in patients with fibrosis at baseline ($p = 0.015$). Quality of life, as measured by the Iranian version of a validated short-form healthy survey (SF-36), also significantly improved ($p < 0.001$).

In the study's discussion section, Kalantari and colleagues point out that their positive results contradict two earlier studies. A 2006 randomized, double-blind, placebo-controlled, crossover study involving patients with chronic hepatitis C, conducted by A. Gordon et al., found no significant effect on serum hepatitis C viral RNA, liver enzyme levels, quality of life, or psychological well-being. The Iranian researchers suggest that this lack of effect may be due to the small number of subjects and/or the study's design. A 2004 Egyptian double-blind study, led by M. D. Tanamly, also showed no significant improvement in liver enzyme levels, liver fibrosis markers, or viral RNA even though patients' symptoms and quality of life improved. In this case, Kalantari and colleagues cite patient genotype, study design, and/or the dose of silymarin as possible reasons for the negative results.

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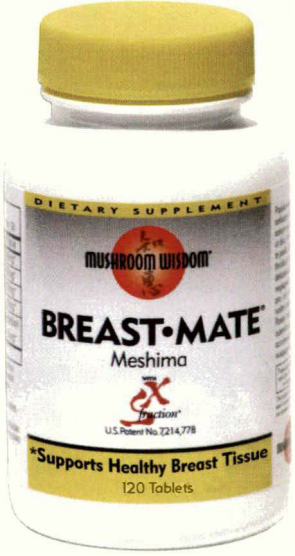

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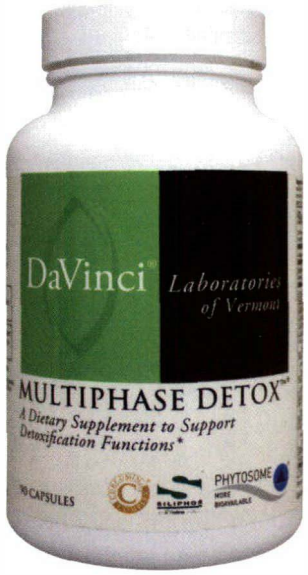

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Conflicting trial results are common when looking at botanicals because herb quality varies. Unlike the active ingredient in pharmaceutical medications, botanicals contain a variety of compounds that may act synergistically. Moreover, compound levels vary in different strains of the same herb. In the case of milk thistle, silymarin content in raw plant material can vary from season to season, depending upon growing conditions. Extraction and processing, which differ from company to company, also affect a botanical product's potency.

Given the interest in silymarin for treating hepatitis C, Kevin Anthony and colleagues assessed 45 commercially sold silymarin products for a recent study. They measured each product's silymarin content, antioxidant activity, and antiviral response to the hepatitis C virus. Total silymarin content varied greatly among the products and often did not match the content listed on the product label.

In general, total silymarin content directly corresponded to HCV antiviral activity and free radical scavenging and antioxidant activity, but there were several exceptions. One product, for example, with a total silymarin content of 248.5 ± 0.1 mg/gram tablet showed more viral inhibition (88 ± 8%) than a product with 274.3 ± 0.5 mg/gram tablet (46 ± 19% inhibition) and more than another product with 848.7 ± 1.1 mg of silymarin per tablet (76 ± 11% inhibition). '"Many of these products consist of a mixture of multiple extracts and/vitamins that also may contribute some biological activity in our assays," say the authors. Such mixtures complicate the process of assessing silymarin's affect. The analysis conducted by Anthony et al. gives practitioners and patients a starting point for choosing a silymarin product, but the real proof lies in clinical application.

Anthony K, Subramanya G, Uprichard S, Hammouda F, Saleh M. Antioxidant and anti-hepatitis C viral activities of commercial milk thistle food supplements. *Antioxidants*. 2013;2:23–26. Available at www.mdpi.com/journal/antioxidants. Accessed December 27, 2013.

Kalantari H, Shahshahan Z, Hejazi SM, Ghafghazi T, Sebghatolahi V. Effects of Silybum marianum on patients with chronic hepatitis C. *J Res Med Sci*. March 2011;16(3):287–290. Available at www.ncbi.nlm.nih.gov/pmc/articles/PMC3214335. Accessed December 31, 2013.

Sucralose

When sucralose, a synthetic organochlorine sweetener, became available in Canada in 1991, it was heralded as a new calorie-free sweetener with no negative biological effects. A detailed 52-page overview by Susan S. Schiffman and Kristina I. Rother indicates otherwise. The overview was partially funded by the National Institutes of Health and published in the *Journal of Toxicology & Environmental Health* (2013). Unlike other artificial sweeteners, sucralose is soluble in ethanol, methanol, and water, making it the sweetener of choice for thousands of low-calorie foods and drinks worldwide as well as pharmaceutical medications. Its biological effects have largely been ignored because manufacturers claim that virtually all of the chemical is excreted from the body intact.

In their overview, Schiffman and Rother discuss research pertaining to sucralose's effect on body weight, its alteration of gastrointestinal microflora, its effect on detoxification and possible interaction with therapeutic drugs, and questions about sucralose metabolite safety and toxicity. Metabolites have been detected in feces and urine from rats and from humans using thin-layer chromatography, but the identity and the safety of these metabolites is unknown. None of the research that Schiffman and Rother present is conclusive, but they do raise troubling questions.

The rationale for using a noncaloric artificial sweetener is weight reduction and blood sugar control for people with diabetes. Animal studies show that sucralose interacts with sweet taste receptors in the GI tract, the pancreas, and the hypothalamus. As a result, glucose transport and insulin secretion increase. How does this affect human weight? Schiffman and Rother found two studies in which sugar-sweetened drinks were replaced with sucralose-sweetened diet drinks: a 2-year study with adolescents and an 18-month study with children. The adolescent study found "no consistent reduction of weight gain," according to Schiffman and Rother. In the other study, the difference in total weight gain between children who drank artificially sweetened soda and children drinking sugar-sweetened soda was minimal – just 1 kilogram after 18 months. Schiffman and Rother found no long-term prospective weight studies involving sucralose use in adults. "Because [organochloride] compounds and artificial sweeteners have both been associated with weight gain, and because sucralose is a member of both categories, it is important to determine its effect on mechanisms that regulate body weight," state Schiffman and Rother.

Sucralose in the form of Splenda alters the bacterial composition of the gastrointestinal tract in rats, according to a 2008 study by Mohamed B. Abou-Donia and colleagues at Duke University Medical Center (Durham, NC). Splenda consists of sucralose, maltodextrin, and glucose. For 12 weeks, male Sprague-Dawley rats were given a daily dose of sucralose: 0 (vehicle control), 1.1, 3.3, 5.5, or 11 mg/kg of body weight. All dose levels were below the EU's Acceptable Daily Intake (ADI) of 15 mg/kg/day. (The US ADI is 5 mg/kg of body weight.) Researchers collected fecal samples during each week of treatment and for an additional 12-week follow-up. "Data showed that bacterial counts in the [gastrointestinal tract] from daily sucralose ingestion decreased progressively and monotonically in a methodical pattern during each successive week of sucralose treatment," write Schiffman and Rother. The numbers of lactobacilli, bifidobacteria, and other beneficial anaerobes declined significantly more than harmful bacteria such as enterobacteria. Three months after sucralose treatment ceased, the total number of beneficial anaerobes was still less than pretreatment levels. Does sucralose/Splenda have the same effect on human gut bacteria?

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As part of the same study, Abou-Donia and colleagues measured intestinal P-gp, CYP3A, and CYP2D activity. P-gp transports harmful chemicals out of intestinal cells and back into the lumen so that they can be excreted. Enzymes CYP3A and CYP2D metabolize drugs and other foreign chemicals. Activity levels of P-gp and the CYP enzymes did not change much when the rats were given 1.1 mg/kg of sucralose per day. All three increased with a dosage of 3.3 mg/kg/d sucralose, the equivalent of about two 12 oz servings (340 grams of sucralose) of diet soda for a 130-pound (58.9 kg) adult or one 12 oz serving for a 70-pound (31.8 kg) child. "CYP3A and CYP2D expression increased in a linear, dose-dependent manner as the dosage of sucralose increased from 3.3 to 5.5 to 11 mg/kg/d," report Schiffman and Rother. P-gp expression, however, "decreased significantly" at 11 mg/kg. Changes in P-gp and CYP expression were still evident at the end of the 12-week recovery period.

CYP3A and CYP2D take part in the breakdown of about 70% of all therapeutic medications. When the expression of these enzymes increases in response to sucralose, the bioavailability of some medications may decrease; the ramped-up CYP activity would break down the medications more quickly. "The finding by Abou-Donia et al. that the sucralose (delivered as Splenda) interacts with efflux and metabolizing proteins is consistent with an extensive scientific literature that indicates [organochlorine] compounds characteristically interact with CYP (and in some cases P-GP)," say Schiffman and Rother.

Sucralose manufacturer Tate & Lyle deems the Abou-Donia study "not credible" and the Schiffman and Rother overview as being based on "old, discredited" research, according to E. Watson. The article offers no specifics. I did find a rebuttal to the Abou-Donia study in *Regulatory Toxicology & Pharmacology* (October 2009): "Expert panel report on a study of Splenda in male rats." Its abstract claims the Abou-Donia study "was deficient in several critical areas." It, too, offers no specifics, and I could not access the full article. I wonder who declared the authors an "expert panel."

Abou-Donia MB, El-Masry EM, Abdel-Rahman AA, McLendon RE, Schiffman SS. Splenda alters gut microflora and increases intestinal P-glycoprotein and cytochrome P-450 in male rats. *J Toxicol Environ Health. Part A: Current Issues.* 2008;71(21). Available at www.ncbi.nlm.nih.gov/pubmed/18800291. Accessed January 25, 2014.

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Watson E. Tate & Lyle defends sucralose safety after researchers claim the sweetener is 'not biologically inert.' November 18, 2013. Available at www.foodnavigator-usa.com. Accessed January 29, 2014.

Supplements and Liver Injury

"Dietary supplements account for nearly 20 percent of drug-related liver injuries that turn up in hospitals, up from 7 percent a decade ago, according to an analysis by a national network of liver specialists," declared a December 21, 2013, *New York Times* article. Dietary supplements – vitamins, minerals, herbs, functional foods – cause 20% of liver injuries? The article, written by Anahad O'Connor, was based on new data from the Drug-Induced Liver Injury Network (DILIN) that tracks patients with liver damage from "certain drugs and alternative medicines." These data were presented at the November 2012 Liver Conference in Washington, DC. I was unable to find a published study with these data to see what drugs and supplements were included. However, a 2008 study from DILIN specifically states that liver injury due to acetaminophen, a primary cause of drug-induced liver injury, is not included.

The 2008 prospective study, led by Naga Chalasani, followed the first 300 patients with acute liver failure to enroll in DILIN for at least 6 months. The authors reported that a single prescription medication was linked to 73% of the patient injuries: "antimicrobials (45.5%) and central nervous system agents (15%) were the most common." Dietary supplements were associated with 9% of drug-induced liver injuries, and the remaining 18% of cases occurred in patients taking more than one drug/supplement. At the November conference, researchers said that supplements accounted for one-fifth of the 313 drug-related liver injuries reported to DILIN in 2010 to 2012. Weight-loss and muscle-building products are the biggest threats, according to O'Connor.

To illustrate the dangers of supplements, O'Connor presents a Texas high school student who "suffered severe liver damage after using a concentrated green tea extract he bought at a nutrition store as a 'fat burning' supplement. The damage was so extensive that he was put on the waiting list for a liver transplant." The actual case report, written by Dr. Shreena S. Patel and colleagues, appeared in *World Journal of Gastroenterology* (August 21, 2013). According to the case report, the young man was taking several products to lose weight: Nopal (cactus; 1 pill daily), Applied Nutrition Green Tea Fat Burner (2 pills/400 mg epigallocatechin-3-gallate [EGCG] daily), whey protein (3 times per week), and GNC Mega Men Sport (2 pills 3 times per week). He lost 56 pounds in 60 days – almost a pound a day. Rapid weight loss in itself (more than 4 pounds/week) can cause liver damage, according to *Harvard Health Letter*. Patel et al. did not mention this. "We are associating our patient's impending liver failure to his ingestion of green tea extract given the history taken, histological findings, and after literature review of all the products and ingredients ingested," said the authors. They relied solely on product labels to identify ingredients. The products themselves were not analyzed by a laboratory to identify contaminants or components not identified on the label. The authors assumed that green tea extract was the culprit because other reports have linked it to liver injury.

The catechins in green tea have shown therapeutic effects in animal and human trials for conditions such as cancer, metabolic syndrome and insulin resistance, and heart disease. The catechins have also *prevented* liver injury in research studies. An extract, however, is more

concentrated than drinking a cup or two of tea. More is not always better. In addition, some green tea extract products contain other ingredients that may interact in unexpected ways. When reports of liver damage in users of green tea extract arose, a US Pharmacopeia (USP) Dietary Supplement Information Expert Committee reviewed over 40 years of clinical case reports, published reviews, animal pharmacological and toxicological testing, and reports from adverse event systems in the US, Australia, UK, and Canada. "A total of 216 case reports on green tea products were analysed, including 34 reports concerning liver damage," according to the panel's report. "Twenty-seven reports pertaining to liver damage were categorized as possible causality and seven as probably causality." The panel found that adverse effects occurred more often when green tea extract is taken on an empty stomach. Green tea products should be consumed with food to lessen the risk of adverse effects. As a result of the review, the USP panel classified green tea extract as "Class A," meaning that no cautionary/warning labeling statement is required, according to "USP Update on the USP Green Tea Extract Monograph" (April 10, 2009).

Contrary to O'Connor's article that paints the entire category of dietary supplements as liver damaging, the category is much smaller. When liver damage arises from taking dietary supplements, those supplements are nearly always aimed at weight-loss and/or muscle-building products – some of which have been adulterated with steroids or pharmaceuticals. Forcing quick weight loss may also be a factor.

Chalasani N, Fontana RJ, Bonkovsky HL, et al. Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States [abstract]. *Gastroenterology*. December 2008;135(6):1924–1934. Available at www.gastrojournal.org/article/S0016-5085(08)01674-0/abstract. Accessed January 17, 2014.

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Sarma DN, Barrett ML, Chavez ML et al. Safety of green tea extracts: a systematic review by the US Pharmacopeia. *Drug Saf*. 2008;31(6):469–484. Available www.ncbi.nlm.nih.gov/pubmed/18484782. Accessed December 31, 2013.

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When the liver gets fatty. *Harvard Health Letter*. January 2011. Available at www.health.harvard.edu/newsletters/Harvard_Health_Letter/2011/January/when-the-liver-gets-fatty. Accessed January 22, 2014.

Séralini GM Corn Study Retracted

On November 28, 2013, Elsevier's *Food and Chemical Toxicology* retracted the 2012 article "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize," by biochemist and molecular biologist Gilles Eric Séralini and his research team at the University of Caen (France). The retraction came after more than a year of "growing pressure" from GM and Monsanto proponents, as documented in Jonathan Matthews's article "Smelling a ➤

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Corporate Rat" (December 11, 2012). A vicious campaign to discredit a GM study with negative results is not new, says Matthews. Matthews is founder and director of GMWatch. Monsanto's public relations army and allies that include GM scientists, the lobby group AgBioWorld, and sympathetic journalists have attacked and discredited other researchers who have reported problems with GM crops.

The GM proponents' primary criticisms were the small number of rats and the breed used in the Séralini study. The authors refuted these criticisms in a detailed response (See *Townsend Letter* Shorts, December 2013.) The breed, Sprague Dawley, is commonly used in toxicology studies; the same breed was used in a 2004 study that reported GM maize as safe. Significant abnormalities arose in some of the Séralini study treatment groups – even though only 10 rats were in each group. "Higher numbers of animals are only required in this type of safety [study] to avoid missing toxic effects (a 'false negative' result)," explains the European Network of Scientists for Social and Environmental Responsibility. Even with a small number of rats in each treatment group, toxic effects were significantly greater in these groups compared with untreated controls.

Rats that consumed GM maize and/or Roundup herbicide at half the minimal agricultural working dilution or less had more liver and kidney abnormalities than controls. They also developed more and larger tumors than controls. Unlike the 2004 study, which lasted only 13 weeks, the Séralini study lasted 2 years, the equivalent of a rat's average lifespan. The Séralini team pointed out, "The first large detectable tumors occurred at 4 and 7 months into the study in males and females respectively, underlining the inadequacy of the standard 90 day feeding trials for evaluating GM crop and food toxicity."

In an attempt to address critics, Séralini, as corresponding author, permitted A. Wallace Hayes, editor-in-chief of *Food and Chemical Toxicology*, access to the study's raw data. "Unequivocally, the Editor-in-Chief found no evidence of fraud or intentional misrepresentation of the data," according to the Elsevier press release, dated November 28, 2013. So why was the study retracted? Why was it erased from the journal's website? Not because the results were incorrect, according to the press release, but because they were inconclusive. Being inconclusive is not a legitimate reason to retract a journal article, according to Committee on Publication Ethics (COPE).

The European Network of Scientists for Social and Environmental Responsibility (ENSSER) has strongly criticized the decision to retract the 2012 study: "Uncertainty is inherent to science, as is the debate between conflicting explanations of findings. Openness of this debate and independent research to find the truth are crucial prerequisites for the survival of independent science." ENSSER is particularly disturbed that participants in the decision to retract the study have remained nameless: "In a case like this, where many of those who denounced the study have long-standing, well-documented links to the GM industry and, therefore, a clear interest in having the results of the study discredited, such lack of transparency about how this potential decision was reached is inexcusable, unscientific and unacceptable. It raises the suspicion that the retraction is a favour to the interested industry, notably Monsanto."

In early 2013, *Food and Chemical Toxicology* acquired a new associate editor for biotechnology – Richard E. Goodman, a Monsanto employee from 1997 to 2004, and active member of the International Life Sciences Institute (ILSI). ILSI is backed by GM and agrochemical companies. "Goodman had no documented connection to the journal until February 2013," Claire Robinson and Jonathan Latham, PhD, wrote in an article for Independent Science News. "His fast-tracked appointment, directly onto the upper editorial board raises urgent questions. Does Monsanto now effectively decide which papers on biotechnology are published in *FCT*? And is this part of an attempt by Monsanto and the life science industry to seize control of science?"

Editor Hayes denied that Goodman or Monsanto had any role in retracting the study. He said in a December 10, 2013, press release that the decision was his alone. That decision satisfied GM proponents. It did nothing to further scientific understanding. By officially deleting the study from medical literature, other researchers are discouraged from replicating or further investigating long-term effects of this GM crop and Roundup herbicide.

As in Galileo's time, science succumbs – at least temporarily – to whoever yells loudest.

European Network of Scientists for Social and Environmental Responsibility. Journal's retraction of rat feeding paper is a travesty of science and looks like a bow to industry [press release]. November 29, 2013. Available at www.ensser.org. Accessed December 27, 2013.

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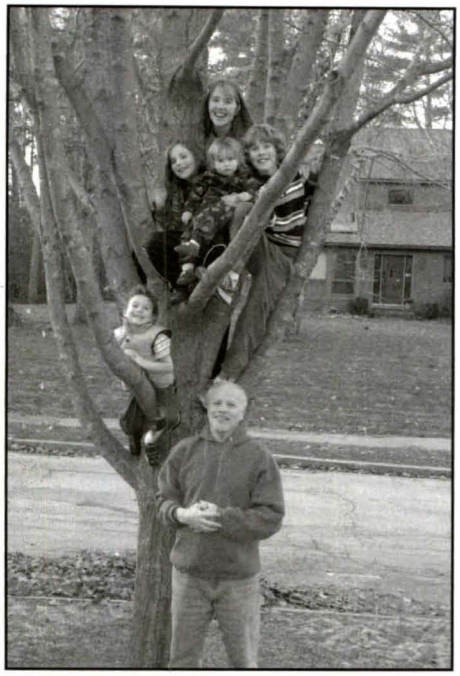

Literature Review & Commentary

by Alan R. Gaby, MD
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Probiotics for Nonalcoholic Fatty Liver Disease

A meta-analysis was conducted on 4 randomized controlled trials, including a total of 134 patients, that examined the effect of probiotic supplements on nonalcoholic fatty liver disease (NAFLD). In the pooled analysis, probiotics significantly decreased alanine aminotransferase (ALT) and aspartate transaminase (AST) levels and significantly improved insulin resistance, as measured by homeostasis model assessment. These results suggest that probiotics can decrease liver inflammation and improve glucose metabolism in patients with NAFLD.

Comment: NAFLD is a common condition in the US in both children and adults. It is characterized by hepatic steatosis (fat accumulation in the liver) that cannot be attributed to excessive alcohol consumption. Many patients with hepatic steatosis also have chronic hepatitis, in which case the condition is called nonalcoholic steatohepatitis (NASH). NAFLD is often asymptomatic, but it can progress to cirrhosis, particularly in patients with NASH. The cause of NAFLD is multifactorial, and risk factors include obesity and type 2 diabetes. Consumption of excessive amounts of fructose may also promote the development of NAFLD and NASH, as discussed below.

Animal studies suggest that NAFLD may be caused in part by microbial translocation (the movement of bacteria or bacterial products such as endotoxin across the intestines into the lymphatics or the visceral circulation). The beneficial effect of probiotics might be explained by their capacity to prevent the proliferation of pathogenic bacteria in the intestinal tract.

Ma YY et al. Effects of probiotics on nonalcoholic fatty liver disease: A meta-analysis. *World J Gastroenterol.* 2013;19:6911–6918.

Does Excessive Fructose Consumption Lead to Nonalcoholic Fatty Liver Disease?

Seventeen monkeys were fed ad libitum a low-fat, high-fructose (24% of calories) diet, while 10 other monkeys were fed ad libitum a low-fat, low-fructose (less than 0.5% of calories, with less than 3% of calories supplied as sucrose and glucose) diet. The duration of the feeding period was 0.3 to 7.0 years. In a second study, 10 monkeys were fed the high- or low-fructose diets described above for 6 weeks at caloric amounts required to maintain a stable weight. In the ad libitum study, monkeys fed the high-fructose diet developed hepatic steatosis in comparison with the control diet, and the extent of hepatic fat accumulation was related to the duration of feeding. Monkeys fed the calorically controlled high-fructose diet showed significant increases in biomarkers of liver damage, endotoxemia, and microbial translocation, although they did not develop hepatic steatosis.

Comment: Nonalcoholic fatty liver disease (NAFLD), described in the comment above, has become much more common in the past few decades. This increase in prevalence has coincided with higher fructose consumption, mainly in the form of high-fructose corn syrup. The results of the present study support previous animal research and both observational and experimental studies in humans indicating that high fructose consumption can lead to NAFLD. The adverse effect is related in part to the excessive energy intake that often accompanies high fructose consumption, but fructose also appears to have a deleterious effect independent of energy intake. Fortunately, the consumption of high-fructose corn syrup in the US appears to have decline over the past several years, presumably because of the well-deserved bad publicity that this sugar has received.

Kavanagh K et al. Dietary fructose induces endotoxemia and hepatic injury in calorically controlled primates. *Am J Clin Nutr.* 2013;98:349–357.

Vitamin D for Hepatitis C

Fifty patients with chronic hepatitis C virus (HCV) genotype 2-3 were treated with pegylated interferon-alpha-2a and ribavirin for 24 weeks and were randomly assigned to receive or not to receive 2000 IU per day of vitamin D. Vitamin D supplementation was begun 12 weeks before the start of drug therapy and was continued for the 24 weeks of drug therapy. Twenty-four weeks after treatment was completed, 95% of the

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patients receiving vitamin D and 77% of those not receiving vitamin D were HCV RNA negative ($p < 0.001$).

Comment: The results of this study indicate that vitamin D supplementation improved the viral response to pegylated interferon-alpha-2a and ribavirin in patients with chronic HCV genotype 2-3. An earlier study showed a similar beneficial effect of adjunctive vitamin D therapy in patients with HCV genotype 1. The mechanism of action of vitamin D is not clear, although it might be related to a nonspecific improvement of immune function.

Nimer A, Mouch A. Vitamin D improves viral response in hepatitis C genotype 2-3 naïve patients. *World J Gastroenterol.* 2012;18:800–805.

Green Tea Improves Blood Glucose Control and Insulin Sensitivity

A meta-analysis was conducted on 17 randomized controlled trials, including a total of 1133 subjects (mostly overweight or obese, and/or having type 2 diabetes or borderline diabetes), that examined the effect of green tea on glucose control and insulin sensitivity. Green tea consumption significantly reduced the mean fasting glucose concentrations by 1.6 mg/dl ($p < 0.01$) and significantly decreased the mean hemoglobin A1c (HbA1c) level by 0.30% ($p < 0.01$). When only the studies of high methodological quality were included, green tea also significantly reduced fasting insulin concentrations ($p = 0.03$).

Comment: This meta-analysis found that green tea consumption had a modest beneficial effect on blood glucose control and possibly on insulin sensitivity in overweight/obese individuals and in those with frank or borderline type 2 diabetes. Thus, green tea should be considered as part of a comprehensive program of diet, exercise, and supplementation with blood glucose-regulating nutrients and herbs.

Liu K et al. Effect of green tea on glucose control and insulin sensitivity: a meta-analysis of 17 randomized controlled trials. *Am J Clin Nutr.* 2013;98:340–348.

Magnesium Prevents Pregnancy-Induced Hypertension

Fifty-nine women (mean age, 29 years) in their first pregnancy were randomly assigned to receive, in double-blind fashion, 300 mg per day of magnesium (as magnesium citrate) or placebo, beginning in week 25 of pregnancy and continuing until delivery. At week 37, the mean diastolic blood pressure was significantly lower in the magnesium group than in the placebo group (72 vs. 77 mm Hg; $p = 0.03$). At week 37, the proportion of women who had an increase in diastolic blood pressure of at least 15 mm Hg was significantly lower in the magnesium group than in the placebo group (8% vs. 38%; $p = 0.01$).

Comment: Pregnancy-induced hypertension can have deleterious consequences for both mother and fetus. It is also frequently a harbinger of preeclampsia, which is characterized by hypertension, proteinuria, and edema and associated with increased maternal and fetal morbidity and mortality. Medical treatment options for pregnancy-induced hypertension are limited, since many antihypertensive drugs can harm the fetus. Intravenous administration of large doses of magnesium is a well-recognized treatment for preeclampsia. The results of the present study demonstrate that increasing magnesium intake earlier in pregnancy may help prevent preeclampsia from developing.

Other nutritional interventions that may help prevent pregnancy-induced hypertension and preeclampsia include increasing dietary protein intake and supplementing with vitamin B6 and calcium. Although sodium restriction often lowers blood pressure in people with hypertension, the adverse effects of sodium restriction during pregnancy appear to outweigh any potential benefit.

Bullarbo M et al. Magnesium supplementation to prevent high blood pressure in pregnancy: a randomised placebo control trial. *Arch Gynecol Obstet.* 2013;288:1269–1274.

'Raft Therapy' for Gastroesophageal Reflux Disease

One hundred ninety-five patients with nonerosive gastroesophageal reflux disease (GERD) were randomly assigned to receive, in double-blind fashion, 20 ml of sodium alginate suspension (20 mg/ml) 3 times per day or 20 mg of omeprazole once a day for 4 weeks. In intent-to-treat analysis, the proportion of patients who reported adequate relief from heartburn or regurgitation was 53.3% with sodium alginate and 50.5% with omeprazole (difference between groups not significant). The incidence of adverse events was around 5% in each group. These results suggest that sodium alginate was as effective as omeprazole for short-term symptomatic relief in patients with nonerosive reflux disease.

Comment: Proton pump inhibitors such as omeprazole are frequently used to treat GERD. By suppressing gastric acid production, these drugs can lead to impaired absorption of calcium, magnesium, iron, vitamin B12, and other nutrients and may also promote small-bowel bacterial overgrowth. Therefore, safer alternatives are needed for patients who require long-term treatment. Sodium alginate is a compound derived from seaweed. It interacts with gastric acid within a few minutes and forms a viscous gel that floats on top of the gastric contents like a raft and physically inhibits the reflux of gastric contents into the esophagus. In a previous study, sodium alginate was more effective than an antacid for providing symptomatic relief in GERD patients. The results of the present study suggest that sodium alginate is at least as effective as omeprazole.

Chiu CT et al. Randomised clinical trial: sodium alginate oral suspension is non-inferior to omeprazole in the treatment of patients with non-erosive gastroesophageal disease. *Aliment Pharmacol Ther.* 2013;38:1054–1064.

Vitamin D Requirements Differ Between Caucasians and African Americans

Serum levels of 25-hydroxyvitamin D (25[OH]D) and vitamin D-binding protein and bone mineral density (BMD) were measured in 2085 black and white individuals participating in the Healthy Aging in Neighborhoods of Diversity across the Life Span cohort. Participants were also genotyped for 2 common polymorphisms of the vitamin D-binding protein gene (rs7041 and rs4588), the prevalence of which differs between blacks and whites. Mean levels of 25(OH)D (15.6 vs. 25.8 ng/ml; $p < 0.001$) and vitamin D-binding protein (168 vs. 337 mcg/ml; $p < 0.001$) were lower in blacks than in whites. Genetic polymorphisms appeared to explain 79.4% and 9.9% of the variation in levels of vitamin D-binding protein and 25(OH)D, respectively. Mean BMD was significantly higher in blacks than in whites

(1.05 vs. 0.94 g/cm^2; $p < 0.001$), despite their lower levels of 25(OH)D. Among homozygous participants, blacks and whites had similar levels of bioavailable 25(OH)D.

Comment: Vitamin D-binding protein is the primary vitamin D carrier protein, binding 85% to 90% of circulating 25(OH)D. Vitamin D may be biologically inactive while it is bound to vitamin D-binding protein. In the present study, blacks, as compared with whites, had lower levels of 25(OH)D and vitamin D-binding protein, resulting in similar concentrations of estimated bioavailable 25(OH)D. The lower levels of vitamin D-binding protein in blacks appeared to be largely genetically determined.

These findings support the results of other research indicating that the reference range for 25(OH)D should be lower for blacks than for whites. Moreover, an observational study of black women found that those with a serum 25(OH) D level below 20 ng/ml (a level considered to indicate deficiency in whites) had a *lower* risk of suffering a fracture, when compared with women whose 25(OH)D levels were greater than 20 ng/ml. Thus, giving large doses of vitamin D to blacks for the sole purpose of raising 25(OH)D to a level considered desirable for whites may be inappropriate.

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.

25-Hydroxyvitamin D: Do We Really Know What the Levels Mean?

In 88 patients (median age, 60 years) who presented to the emergency department because of acute hyperglycemia, serum 25-hydroxyvitamin D (25[OH]D) levels were measured on admission and 6 hours after normalization of blood glucose (12–18 hours after admission). The mean serum 25(OH)D level increased from 12.3 ng/ml on admission to 28.2 ng/ml after normalization of blood glucose ($p < 0.001$). Serum 25(OH)D levels increased in all patients after correction of hyperglycemia.

Comment: These findings suggest that severe hyperglycemia leads to metabolic and endocrine compensations that result in a marked decrease in serum 25(OH)D levels. Correction of hyperglycemia increased 25(OH)D in a matter of hours from levels thought to indicate severe deficiency to levels consistent with normal or near-normal vitamin D status. Because 25(OH) levels increased so rapidly and so dramatically without vitamin D supplementation, it is likely that the low levels associated with hyperglycemia were not indicative of vitamin D deficiency. Other research has shown that 25(OH) is an acute-phase reactant, in that the level declines in response to inflammation. Consequently, in people with acute or chronic inflammatory conditions, a low 25(OH)D level may also not be indicative of vitamin D deficiency.

Gaby's Literature Review

Numerous observational studies have found that higher serum 25(OH)D levels are associated with better health outcomes. Because of those studies, it has become popular to use relatively large doses of supplemental vitamin D to push serum 25(OH)D to the levels associated with those better health outcomes. However, the association between higher serum 25(OH)D levels and better health might simply indicate that people with good blood glucose control and less inflammation are healthier than people with poor blood glucose control and more inflammation. When the results of ongoing randomized controlled trials are published over the next few years, we will have a better idea about the safety and efficacy of high-dose vitamin D. However, the randomized controlled trials that have been published so far suggest that high doses (such as 6500 IU per day or more) are less effective than moderate doses (such as 800–1200 IU per day) for situations such as osteoporosis prevention and treatment of multiple sclerosis.

To date, I have not found a compelling reason to recommend routine 25(OH)D testing in clinical practice, although I do frequently recommend empirical supplementation with 800 to 2000 IU per day of vitamin D.

Aksu NM et al. 25-OH-Vitamin D and procalcitonin levels after correction o f acute hyperglycemia. *Med Sci Monit.* 2013;19:264–268.

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Pathways to Healing

by Elaine Zablocki

Holistic MD Says, 'Change Starts at the Grassroots'

Heather Tick, MD, is a family physician who's developed special skills for dealing with chronic myofascial pain. Her recently published book, *Holistic Pain Relief*, offers a comprehensive review of ways to prevent and/or deal with chronic pain.

Tick's interest in natural healing started early. Even as a child, she was unusually aware of the importance of natural food. "I remember my friends would encourage me to bake with cake mixes. I would say, oh, no, there are too many chemicals in that mix."

Tick trained as an MD at the University of Toronto, but her medical training didn't include "natural" methods of healing. "I took my first acupuncture course while I was still a medical student, but it was not part of the curriculum," she says. "During that period I experienced shoulder pain that lingered for many months – but during the acupuncture course it disappeared with a few simple treatments. That impressed me so much. I had tried many conventional methods without any relief, but acupuncture stimulated something in my body that allowed it to heal itself."

When she started practicing as a family medicine doctor, Tick found that the most challenging cases involved chronic pain, often myofascial pain. "Myofascial pain refers to pain that affects both muscles and the fascia, the connective tissue that runs throughout our body," Tick said. "It is the commonest cause of pain. Even when we talk about other common causes of pain, like arthritis or postsurgical pain, they frequently include a component of myofascial pain. When you relieve the myofascial problem, often the other issues become more manageable."

Tick continued taking courses through the Acupuncture Foundation of Canada, and she learned about the pioneering work of C. Chan Gunn, MD, who developed a way to relieve myofascial pain called Gunn Intramuscular Stimulation (IMS). It uses the same thin, flexible needles used in acupuncture, but in a very different way. The treatment involves "dry needling" of affected areas of the body. The needle sites can be at the epicenter of taut, tender muscle bands, or they can be near areas where a nerve may have become irritated and supersensitive. This treatment helps the area to relax, helps the nerve to function normally again, and initiates the natural healing process.

Integrative Pain Clinics in Toronto, Arizona, and Seattle

Tick incorporated these methods into her practice, and eventually started an integrative pain clinic in Toronto. The staff included chiropractors, massage therapists, kinesiologists, naturopaths, physical therapists, a psychiatrist, and practitioners of healing touch and Reiki. Everyone learned from each other. "When you look at how change happens in medicine, it often manifests at the fringes, the grassroots, not at big institutions," Tick says. For example, initially she charged very low fees for the innovative Gunn IMS methods – something that would have been difficult at a less flexible organization. "As it became obvious that these methods were actually making a big difference for people, then I was able to charge more appropriately for my time. I wouldn't have had the freedom to go through that process at a big institution."

In 2007 Tick was invited to found the Family Medicine Integrative Pain Clinic at the University of Arizona, Tucson. The University of Arizona Health Plan wanted to explore, and pay for, new approaches for treating pain in Medicaid patients. "They were tired of paying for six surgeries on the same patient without seeing significant improvement. They had heard about my work, and they knew they needed a different approach," Tick says. "During my work in Arizona, I was able to demonstrate that my patients had fewer high-priced interventions, and good clinical results. There was a cost savings, even though the insurer was paying for unusual services that generally they would not have covered."

In 2012 the chief of pain medicine at the University of Washington Medical School invited Tick to move to university's Center for Pain Relief, an anesthesiology-based pain clinic. She sees about 10 new patients every week at the center, and the rest of her clinical calendar is made up of return visits, many of them for Gunn IMS.

However, a significant portion of her time at the Center for Pain Relief is reserved for teaching and research. Each year the clinic trains six "pain fellows," who are graduate anesthesiologists or physical medicine rehab doctors, training to be the pain specialists of the future. Tick is responsible for showing them the physical examination methods used to recognize myofascial pain and the special needling techniques of Gunn IMS. She also emphasizes

nutrition, appropriate use of nutraceuticals, and reducing inflammation. "The reception at the university has been excellent," she says. "My department is very open-minded and focused on results. People who may have been skeptical when I first arrived now recognize that I get good results, and they refer patients to me enthusiastically."

Heather Tick, MD

New Book on Holistic Pain Relief

In November 2013, Tick published *Holistic Pain Relief*, a 300-page book with chapters that include:

- Pain, Nature's Wake-Up Call
- The Changing Times
- A Visit with an Integrated Physician
- The Healing Diet: Lost Food Traditions
- Resolve Stress and Dissolve Pain: The Mind-Body Solution
- Healthy Habits
- Dietary Supplements
- Exercise
- Prescription Drugs
- Toxic Stew
- Your Team
- The Road to Recovery

Townsend Letter readers are already familiar with many of the methods that Tick discusses in this book. What makes it unusual, and very much worth reading, is the holistic attitude that examines interrelationships among diet, immune response, exercise, dietary supplements, and mind-body methods.

For example, think about sleep, something that affects so many aspects of our health. Ask Tick how we can develop better sleep habits, and she talks first about ways to corral your worries. "We see a lot of worriers. I ask them, is worrying helping you get what you want? OK, if worry is something you need to do, then pick one hour out of every day, one specific time, and schedule that as your worrying time. The rest of the day, if worries arise, you just tell them this is not their time."

Then Tick goes on to talk about the environment in which we sleep: it's important to have total darkness. It's important to have a minimum of electronics, preferably *none*, in the room where we're sleeping. "If you can, turn off your Wi-Fi before you go to sleep," she says. "We know there are effects, and some people are very sensitive. Just because you weren't sensitive last year, that may have changed, you may be sensitive now."

When you wake up early, use that time for relaxation, she suggests. Don't immediately turn on a light or open the computer. "Just lie there and say, 'Even though I may not fall asleep again, I'll use this time to rest my body and my brain.' When you do breathing meditation, you oxygenate your body, and you also activate the relaxation response and balance your sympathetic-parasympathetic system."

Practical Advice on Green Drinks

Towards the end of my conversation with Tick, she reemphasized the importance of a healthful diet. I confessed that as soon as we ended our phone call, I planned to eat a chocolate bar, to summon up energy for the second half of the day. "That's fine," she responded, "as long as it has 70% or more cocoa. That counts as health food. As soon as we're finished talking I'm going to make greens juice, and after that I also plan to indulge in a 70% chocolate bar that's sitting on the counter."

Personally, I haven't been preparing green drinks because they seemed so complicated, and I didn't know which juicer to buy, and there would be so much equipment to wash afterwards.

Tick was full of practical tips. "I use a masticating juicer, made by Omega, which doesn't heat the greens; it just slowly crushes everything." she said. "It doesn't take much space on my kitchen counter, and it's easy to clean. I have parsley, cilantro, celery, cucumber, ginger, kale, and collard greens waiting. I will add a carrot just for a bit of sweetness. It is the most refreshing thing; it is like instant energy."

She added that cilantro is an especially powerful chelating agent that can remove heavy metals from the body. "When we eat greens, we don't digest the cell walls," she added. "When we juice greens, then we can access enzymes and minerals stored within the cell."

Who could resist that? As soon as our phone call ended, I started shopping for a juicer.

Resources

Heather Tick's website: http://www.heathertickmd.com.

Tick H. *Holistic Pain Relief: Dr. Tick's Breakthrough Strategies to Manage and Eliminate Pain*. New World Library; 2013.

For more information about Chan Gunn and the Institute for the Study and Treatment of Pain:
www.istop.org
http://www.istop.org/drgunn.html
http://www.publicaffairs.ubc.ca/2011/12/01/pioneering-pain-management

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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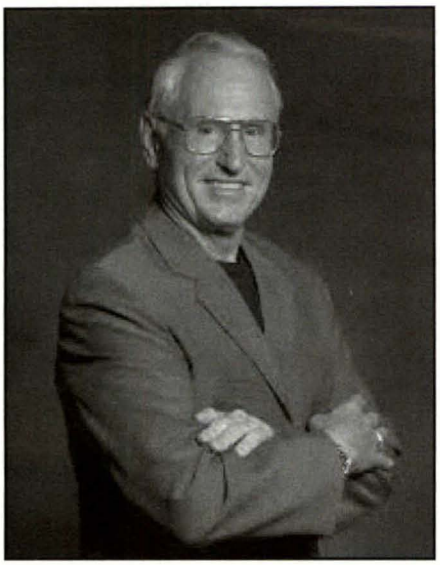
– NEW COLUMN –



F.A.C.T. – Just the Facts

by Dr. Garry F. Gordon, MD, DO, MD(H)
Gordon Research Institute

Metabolic Dysfunction and Diversity within the Human Microbiome

This is the first contribution to what I hope will be a regular feature, offered from the archives of the Gordon Research Institute's F.A.C.T. forum – a dynamic online community of health-care practitioners including physicians, dentists, chiropractors, nurses, dieticians, psychologists, physical therapists, and many others licensed within the health-care field.

The F.A.C.T. group, or "Forum for Anti-aging and Chelation Therapies," originated as a way to help doctors learn about and facilitate the use of the latest alternative therapies and nutritional supplement protocols in managing their patients. Over the years, F.A.C.T. has grown to a membership of over 3000 practitioners from 14 countries around the world. F.A.C.T. membership is free to qualified practitioners, and as members, they can discreetly consult on and discuss cases with one another; learn about new treatments and protocols; share their success stories; and gain access to an extensive catalog of information gathered from 55 years of ongoing research, conferences, and lectures on the latest developments in natural and alternative health.

As this issue of the *Townsend Letter* focuses on diabetes, liver toxicity, and metabolic disorders, I am excited to offer some samplings of F.A.C.T. forum dialogue concerning these conditions, along with today's epidemic proportions of obesity and the importance of nourishing the diversity of our internal "hidden" environment: the gut microbiome.

Many physicians and other health-care practitioners have long recognized that metabolic syndrome is a preventable "lifestyle" disease, acquired through both genetic and environmental factors. Obesity is a *risk* factor in developing metabolic syndrome, and we are learning that obesity can *result* from damages to our internal microbial composition – or microbiome – due to our modern diets.

One of the fastest-rising fields in medical research is the study of the human microbiome, which is used to describe the "collective population of all the non-human cells and genes that inhabit us," as Alice Park, veteran staff writer for *Time*, reports. "There are approximately 8 million different types of bacteria inhabiting our gastrointestinal system. Most of the cells in the human body aren't even human. Indeed, bacterial cells outnumber human cells 10 to 1." This new research has established direct links between our gut microbes and common human ailments such as irritable bowel syndrome, and reveals how microbial variations and differences in bacterial diversity may contribute to metabolic diseases and other chronic conditions, from obesity to asthma, cancer, and perhaps even autism.

For instance, the pan-European MetaHIT consortium conducted a study that examined bacterial genes present in the stools of nearly 300 Danish volunteers, both lean and obese, as well as markers of metabolic health. The researchers discovered that those participants with high inflammation, increased insulin resistance, obesity, and other metabolic markers also had a significantly lower genetic "diversity" of their gut microbiomes.

Another smaller-scale study conducted by the ANR MicroObes consortium in France placed 49 overweight or obese volunteers on a low-calorie diet. The participants who showed low genetic diversity in their gut microbiomes saw an increase in bacterial diversity and marked improvement in their metabolic condition while on the diet, suggesting that poor metabolic health and low-diversity microbiomes can be corrected through nutrition.

So we really are what we eat! I believe that genetically modified (GM) foods have played a significant role in the epidemic rise of chronic health conditions in our country. Our gut floras are being altered from ideal due to overuse of prescription antibiotics that we take and antibiotics injected into commercially farmed poultry and cattle, and killed off by the insecticides and pesticides that we ingest daily from plant sources. A report released June 2012,

GMO Myths and Truths, has brought into sharp focus what I have been writing about for years since meeting Mr. Jeffrey Smith, the executive director for the Institute of Responsible Technology and leading spokesperson on the health dangers of GM foods. He has single-handedly done more than any other person to try to stop Monsanto from killing all of us with its greedy approach to control the food supply of the planet. Autoimmune disorders, diabetes, metabolic syndrome, intestinal dysbiosis, "leaky gut" syndrome, GERD (reflux disease), and even cancer are all known to be linked to the GMOs and high-fructose content in commercial processed foods. Monsanto's GM corn contains a toxin called *Bacillus thuringiensis* (*Bt*), and it is turning our own intestines and cells into miniature pesticide factories, damaging the immune system and intestinal lining, and killing beneficial bowel flora. *Bt* toxin has been identified in the blood of both pregnant and nonpregnant women, as well as the umbilical blood of their babies.

Fortunately we can return to health by replenishing and rediversifying our gut microbiomes. Obviously we need to eat more healthfully, seeking out non-GMO and locally, organically grown foods whenever possible. We also need to augment our diets with quality vitamins and supplements, as well as protocols to assist with detoxification of the pollutants and toxins that we regularly ingest. I always suggest taking a probiotic supplement with acidophilus such as Kyo-Dophilus 9, so important when dealing with the constant exposure to GM foods that disturb normal bowel flora. I also recommend a quality fiber supplement, such as Beyond Fiber, to help detoxify the gastrointestinal tract and support the growth of beneficial probiotic flora.

For GI damage and healing of conditions such as ulcerative colitis and Crohn's disease, some may need additional therapeutic intervention, other than simple diet changes and daily detoxification. There are alternative therapies, including colonic ozone therapy and intestinal reflorastation, that are providing amazing benefit to many patients. Here are a few examples of questions, and suggested protocols, as discussed by our F.A.C.T. forum participants (names and responses redacted to protect member confidentiality).

Q: In the Spanish *Ozone* Magazine vol. 3, 2013, there is an article written by Dr. Velio Bocci (Italy), we all know he is an eminence in ozone therapy, and in this article he does not recommend ozone rectal insufflation. I have been using ozone since 2013, and many books that I have read (*Guia para el uso Medico del Ozono*, by Adriana Schwartz; *Principles and Application of Ozone Therapy*, by Frank Shallenberger; *The Use of Ozone in Medicine*, by Renate Viebahn-Hansel; *Ozono Aspectos Basicos y Aplicaciones*, by Silvia Menendez; *Ozone A New Medical Drug*, by Dr. Velio Bocci) do recommend rectal insufflations. What is the group's thoughts on this procedure? I will appreciate very much your comments! ~ J. O.

A1: Dear J. O.,
I have seen presentations on rectal ozone use and I have used it successfully; however, there are some cases that may not handle it well. With today's epidemic of GI-related illnesses, some are often only resolved with fecal transplants. Those are not the complete answer to everything and, of course, they may carry some risk of infection. Since the benefit to risk ratio has to guide your final decision, please know that many colon hydrotherapists have used ozone routinely for years with very few complaints. Nonetheless, we as licensed health professionals need to be sure to have an informed consent procedure, as there will always be someone who gets worse with any treatment. My best advice at this point would be low dose and not to do too much with any one treatment. Ozone will help lower the pathogens, and then reimplantation of beneficial bacteria should follow.
~G. G.

A2: Dear Dr. J. O.
First let me say that I am familiar with this paper and with my friend and respected colleague Dr. Velio Bocci. Dr. Bocci has indeed been at the forefront regarding the science of ozone therapy, especially as it pertains to cytokine production. The theory that Dr. Bocci presents that ozone reacts immediately with the cell wall of the rectum is entirely correct. In doing this it forms lipoperoxides. These lipoperoxides are then absorbed by the venous system and go directly to the liver. Then they are released into the blood stream. This makes it a very effective systemic therapy. How do I know that? Because on several occasions I have measured the serum lipoperoxide levels before and after rectal ozone and found them to be significantly increased. That said, rectal ozone therapy has been effectively used by myself and other clinicians all over the world for years. In short, it not only works, it works very well. ~ F. S.

Q: Has anyone heard of, or had favorable results, from fecal transplantation? ~ J. B.

A1: I attended a lecture on fecal implants in June 2012 at the International Association of Colon Therapists (I-ACT), where there was shown very impressive results in reversing irritable bowel and Crohn's disease. I have read elsewhere that skinny people have a certain beneficial bacterium in their gut that are missing from obese people. There seemed to be some indication in the report that this certain bacterium was a factor in keeping these people thin. Unfortunately, I can't remember where I read it, as I read so much health-related information. If this is so, fecal implantation from a healthy, skinny individual may benefit someone who is overweight. There is the concern of transplanting parasites, so the donor should do a parasite cleanse prior to the procedure. I've also read that fecal transplantation is having such great results that the FDA is trying to put a stop to it. This should in no way hinder progress, since anyone able to follow directions can do the procedure in the privacy of their home. They say that donation from a healthy relative is best. ~ I. B.

A2: Yes – when I started in medicine in the early 1960s, we did not have a lot of the drugs used today for gastrointestinal problems, and chronic diarrhea was a

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Just the Facts

pressing problem causing great electrolyte imbalance. We used sulfa drugs to completely sterilize the GI tract, went to immediate family members who were healthy, collected and mixed their stools, and after a few days gave rectal enemas to the afflicted person with great results. It can be life saving! ~ T. R.

Q: I was interested in asking the group their opinions about some of the current thought that probiotics are dangerous in Crohn's and, I presume, ulcerative colitis as well. I had placed one of my patients on high-potency probiotics and her GI told her to stop immediately. Apparently the fear is translocation of these bacteria into the bloodstream. Any thoughts? ~ D. G.

A1: Reflorastation (rectal introduction of bacteria): I pioneered this research in 1991–1994 and have developed the use of 20 strains. Numerous cases of Crohn's and UC have been helped, with no complaints of a down side. It can also resolve recurrent *C. diff*. There will always be bacteria in the GI tract; if it's sterile, where's our health? A healthy microbiota is essential for maintaining GI function and survival. Using healthy strains will proliferate rapidly and keep the pathogenic ones in check. Also, the tight junctions of the colonic epithelial cells (CEC) regain integrity with butyric acid, as this is a principle fuel for CECs: the only direct source is butter (3% butyrate), at least 2 tsp per day. Probiotics also support tight junctions in this barrier to decrease possibility of damage. ~ V. B.

A2: The question that I would ask is, does the specialist think the colon of this patient is totally sterile? If so, then there is some merit to his thinking. I would include, with your prescription of probiotics, immune modulators (not stimulators) and a product called Mucosa Compositum (a Heel product from Germany). Unless the colon is totally sterile, there is already translocation being attempted, and this is what is also behind the inflammatory process and the ongoing condition. Proceed with caution and monitor the progress. I believe that the probiotic would be absolutely warranted and in fact some *Lactobacilli* have shown very positive effects in moderating the severity of Crohn's.

~ A. P.

It is possible to stop GI stress and reverse metabolic syndrome naturally. I have seen such dramatic improvement in patients receiving "reflorastation," I really believe that everyone needs a healthier microbiome! I have seen patients begin taking good probiotics and fiber, while consuming the same diet, that doubled and even tripled their fecal volume following the use of colon reflorastation. I recommend visiting Dr. Vitoria Bowmann's site at www.myrealhealth.com and read some of the amazing success stories there to see how a reflorastation program can often avoid needless GI surgery and even bring pets back to life!

Fecal implants are now under FDA jurisdiction, and the expert behind the successful completion of the human genome project, Dr. Craig Ventner, explains that fecal implants would not be needed if we used the most advanced techniques to determine our particular flora imbalances and simply correct them. That approach will no doubt cost thousands of dollars, but from what I and other practitioners have experienced, for around $100, one properly administered "ozonated" colonic and one properly formulated implant will change most people's lives now.

For more information about the F.A.C.T. forum and how to apply for free membership, visit the Gordon Research Institute website at www.gordonresearch.com.

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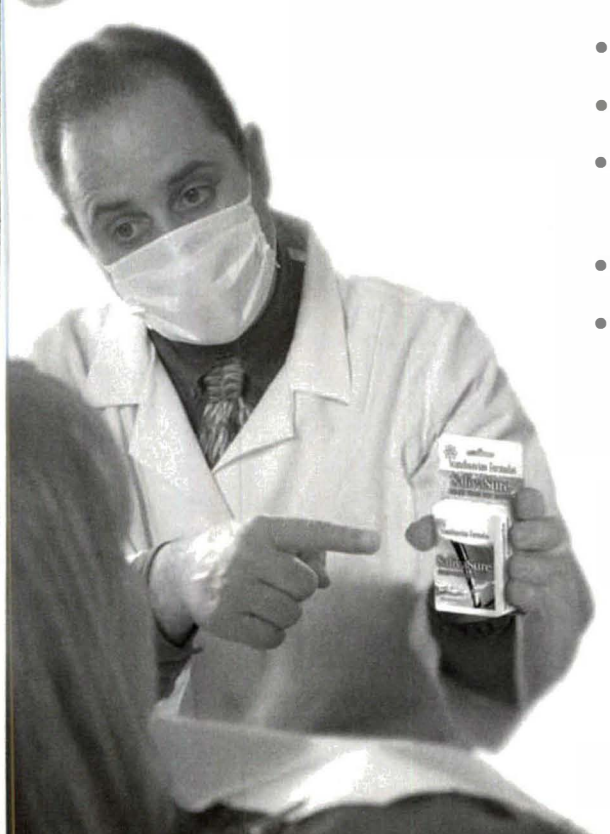

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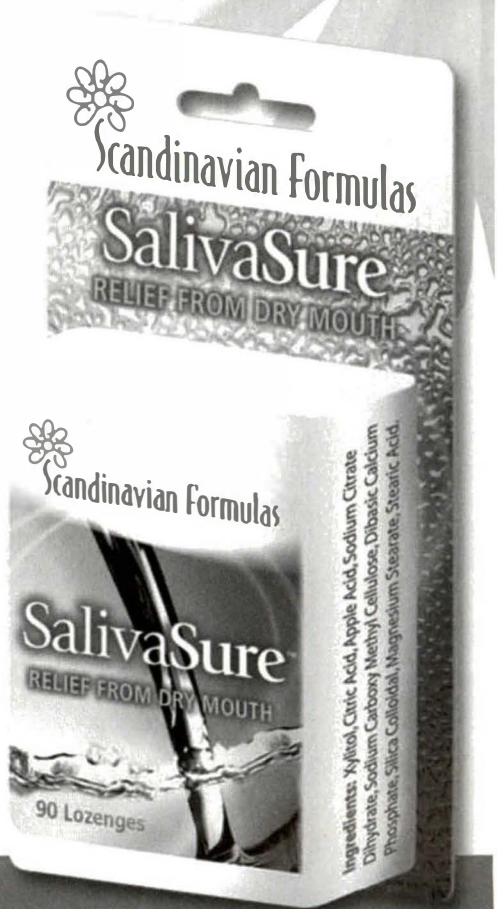

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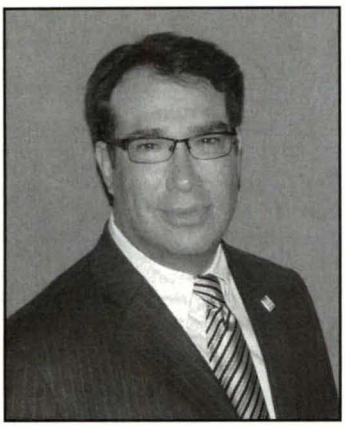

Anti-Aging Medicine

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

An Anti-Aging Approach to Diabetes Prevention

A group of diseases marked by high levels of blood glucose resulting from defects in insulin production, insulin action, or both, diabetes is the seventh leading cause of death in the US. The disease is also a major cause of heart disease, stroke, kidney failure, and adult-onset blindness.

Diabetes costs the US an estimated $116 billion (direct costs – medical care) and an additional $58 billion (indirect costs – disability, work loss, and premature deaths). Medical expenses for people with diabetes are over two times higher than for people without diabetes.

Further, we now know that blood sugar dysregulation may associate with other chronic, debilitating, serious medical conditions. Researchers from the University of Washington (Washington, USA) report that higher glucose levels correlate with an increased risk of dementia. Paul K. Crane and colleagues analyzed data collected on 2581 men and women, ages 65 and older between 1994 and 1996, enrolled in the Group Health Cooperative, who did not have dementia at the study's start; an additional 811 subjects enrolled between 2000 and 2002. Participants were asked to return at 2-year intervals for dementia evaluation, and 2067 of the participants, each of whom was a member for at least 5 years prior to the study's start and had at least five measurements of blood glucose or glycated hemoglobin (HbA1c) over 2 or more years prior to the study, had at least one follow-up visit. The final analysis encompassed 35,264 glucose measurements and 10,208 measurements of HbA1c obtained from 839 men and 1228 women who had a baseline mean age of 76. The participants included 232 patients with diabetes. During a median follow-up of 6.8 years, 524 participants developed dementia, consisting of 74 with diabetes and 450 without. Patients without diabetes and who developed dementia had significantly higher average glucose levels in the 5 years before diagnosis of dementia, equating to a hazard ratio of 1.18. Among the patients with diabetes, glucose levels averaged 190 mg/dL in those who developed dementia versus 160 mg/dL in those who did not, equating to a hazard ratio of 1.40. The study authors conclude: " Our results suggest that higher glucose levels may be a risk factor for dementia, even among persons without diabetes."

Type 2 diabetes, previously called non–insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes, accounts for 90% to 95% of all diagnosed cases of adult diabetes.

In this column, we review the latest study findings suggesting nutritional and lifestyle approaches that may help to minimize your risks of developing type 2 diabetes.

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Short Walks Protect Against Diabetes

High postmeal blood sugar is a strong determinant of excessive 24-hour glucose levels, and research suggests that people who eat a big afternoon or evening meal and often then are sedentary for the remainder of the day are at risk for rapid blood sugar spikes that could cause damage. Loretta DiPietro and colleagues from George Washington University School of Public Health & Health Services (Washington, DC, US) enrolled 10 men and women, ages 60 years and older, who were otherwise healthy but at risk of developing type 2 diabetes due to higher-than-normal levels of fasting blood sugar and to insufficient levels of physical activity. Subjects completed 3 randomly ordered exercise protocols spaced 4 weeks apart. Each protocol comprised a 48-hour stay in a whole-room calorimeter, with the first day serving as a control period. On the second day, participants engaged in either walking for 15 minutes after

each meal or 45 minutes of sustained walking performed at 10:30 in the morning or at 4:30 in the afternoon. All walking was performed on a treadmill at an easy-to-moderate pace. Participants ate standardized meals and their blood sugar levels were measured continuously over each 48-hour stay. The researchers observed that the most effective time to go for a walk was after the evening meal. The exaggerated rise in blood sugar after this meal – often the largest of the day – often lasts well into the night and early morning, and this was curbed significantly as soon as the participants started to walk on the treadmill. The study authors write: "Short, intermittent bouts of postmeal walking appear to be an effective way to control postprandial hyperglycemia in older people."

DiPietro L, Gribok A, Stevens MS, Hamm LF, Rumpler W. Three 15-min bouts of moderate postmeal walking significantly improves 24-h glycemic control in older people at risk for impaired glucose tolerance. *Diabetes Care*. June 11, 2013.

Lower Glycemic Load to Lower Diabetes Risk

Previously, a number of studies have shown that adherence to a Mediterranean diet – rich in olive oil and nuts as well as fruits, vegetables, and legumes, and limited amounts of dairy products, red meat, soda drinks, processed meats, and sweets – inversely associates with cardiovascular risks. Italian researchers report that following the traditional Mediterranean diet and limiting high-glycemic-load foods such as those high in refined sugars and grains may reduce a person's risk of type 2 diabetes. Carlo La Vecchia and colleagues from the Mario Negri Institute of Pharmacological Research (Italy) examined data collected on 22,295 study subjects who resided in Greece and participated in the European Prospective Investigation into Cancer and Nutrition (EPIC) trial. Over 11 years of follow-up, 2330 cases of type 2 diabetes were identified. The researchers observed that those subjects adhering closely to the Mediterranean diet were at lower risks of developing type 2 diabetes. Glycemic load was positively associated with a lower risk for diabetes for the highest versus the lowest glycemic-load quartile.

Rossi M et al. Mediterranean diet and glycaemic load in relation to incidence of type 2 diabetes: results from the Greek cohort of the population-based European prospective investigation into cancer and nutrition (EPIC). *Diabetologia*. 2013; doi:10.1007/s00125-013-3013-y.

Fiber Improves Metabolic and Cardiovascular Markers

Daily supplements of soluble fiber help to improve metabolic and cardiovascular measures among diabetics. Valesca Dall'Alba and colleagues from Universidade Federal do Rio Grande do Sul (Brazil) enrolled 44 type 2 diabetics, average age 62 years, and randomly assigned each to one of two groups: an intervention group, who consumed a usual diet supplemented with an additional 10 grams per day of guar gum, or a control group, who consumed a usual diet only. After 6 weeks, the fiber-supplemented group decreased glycated hemoglobin (HbA4c) by 0.31% and lowered trans fatty acid levels from 71 to 57 mg/L; their waist circumference dropped from 103.5 cm to 102.3 cm. The only change in the control group was a 0.9 cm reduction in waist circumference. The study authors conclude: "The addition of [soluble fiber] to the usual diet improved cardiovascular and metabolic profiles by reducing [waist circumference], [glycated hemoglobin], [urinary albumin excretion], and [serum trans-fatty acids]."

Dall'Alba V, Silva FM, Antonio JP, et al. Improvement of the metabolic syndrome profile by soluble fibre – guar gum – in patients with type 2 diabetes: a randomised clinical trial. *Br J Nutr*. April 2, 2013.

More Fruit Lessens Diabetes Risk

Whole fruits are an abundant source of fiber, antioxidants, and other phytochemicals that may help to promote overall health. Qi Sun and colleagues from Harvard School of Public Health (Massachusetts, US) analyzed data collected on 66,105 women enrolled in the Nurses' Health Study, 85,104 from the Nurses' Health Study II, and 36,173 men from the Health Professionals Follow-up Study. Every 4 years, participants were surveyed as to how often they ate various foods and on their diabetes status, among other measures. While all participants were free of major chronic diseases at baseline, 6.5% developed diabetes during follow-up. Adjusted hazard ratios pooled across the three studies for diabetes risk per 3 whole-fruit servings per week were: 0.74 for blueberries; 0.88 for grapes and raisins; 0.93 for apples and pears. Cantaloupe elevated the diabetes risk by 10%, whereas the risk was neutral for peaches, plums, apricots,

prunes, oranges, and strawberries. Interestingly, the researchers found that the same amount of fruit juice correlated with a significant 8% elevated risk of developing diabetes. The study authors conclude: "Greater consumption of specific whole fruits, particularly blueberries, grapes, and apples, is significantly associated with a lower risk of type 2 diabetes, whereas greater consumption of fruit juice is associated with a higher risk."

Muraki I, Imamura F, Manso JE, Sun Q, et al. Fruit consumption and risk of type 2 diabetes: results from three prospective longitudinal cohort studies. *BMJ*. 29 August 2013;347:f5001.

Dairy Decreases Diabetes

Dairy milk, cheeses, and yogurts are rich sources of calcium, a mineral that increases insulin secretion and may reduce insulin resistance. Dagfinn Aune and colleagues from the Norwegian University of Science and Technology (Norway) completed a meta-analysis of 17 cohort studies of dairy product intake and risk of type 2 diabetes. The team observed that high intake of dairy products was associated with a significant decrease in the risk of type 2 diabetes, with low-fat dairy products conferring the most pronounced effect. The study authors conclude: "This meta-analysis suggests that there is a significant inverse association between intakes of dairy products, low-fat dairy products, and cheese and risk of type 2 diabetes."

Aune D, Norat T, Romundstad P, Vatten LJ. Dairy products and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. *Am J Clin Nutr*. August 14, 2013.

Among Americans aged 65 years and older, 10.9 million – or 26.9% of this age group – have diabetes. Overall, the risk for death among people with diabetes is about twice that of people of similar age but without diabetes. Diabetes is likely to be underreported as a cause of death. Studies have found that about 35% to 40% of decedents with diabetes had it listed anywhere on the death certificate and about 10% to 15% had it listed as the underlying cause of death.

To stay updated on the latest breakthroughs in natural and accessible approaches that may help to reduce your risk of developing type 2 diabetes, visit the World Health Network (www.worldhealth.net), the official educational website of the A4M and your one-stop resource for authoritative anti-aging information. Be sure to sign up for the free Longevity Magazine e-journal, your weekly health newsletter featuring wellness, prevention, and biotech advancements in longevity. ◆

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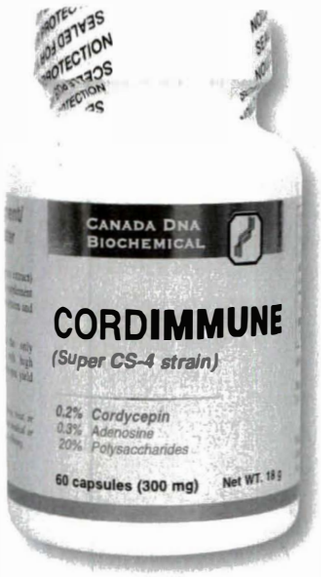

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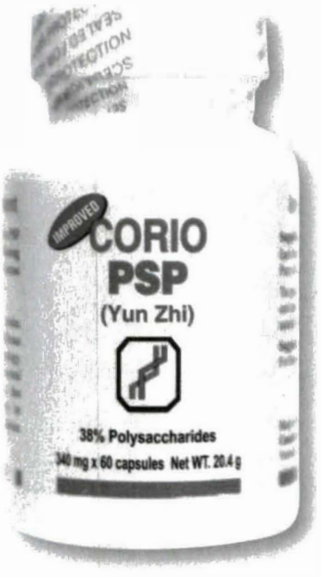

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The Role of Nutritional and Botanical Agents in the Management of Type 2 Diabetes Mellitus

by Mona Morstein, ND

Diabetes is reaching an epidemic level not only in the US, but also worldwide. There are 26 million patients diagnosed diabetic in the US, and 87 million who are prediabetic; essentially, 1 out of every 3 people in the US are – or are becoming – diabetic. If nothing changes, the Centers for Disease Control (CDC) predicts that by 2050, 50% of Americans will be diabetic. Worldwide, there are 350 million diabetic patients, with a concentration in areas of higher economic status and greater urbanization areas. 90% to 95% of diabetic patients are type 2, and the number diagnosed in the childhood or teenage years is also increasing. Worldwide occurrence of the autoimmune type 1 diabetes is also increasing.

The etiological factors for developing type 2 diabetes are multifactorial. They include: excess intake of refined sugar; excess intake of saturated fat; overeating; abdominal weight gain; lack of exercise; environmental toxins (mercury lead, arsenic, bisphenol A, persistent organic pollutants); nutrient deficiencies; genetics; gut dysbiosis; and hormone dysregulation. Insulin resistance is the key metabolic abnormality in type 2 diabetic patients, resulting in increased appetite, elevated glucose levels, higher BMIs, higher insulin secretion, and mixed hyperlipidemia.

There are many complications associated with being a prediabetic or diabetic patient, as a result of increased glucose and lack of antioxidants that lead to increased oxidation reactions. Diabetic damage occurs because of increased reactive oxygen species, such as superoxide anion radicals, hydroxyl radicals, peroxynitrite radicals, and lipid peroxidation. Diabetic patients have an increased risk of cardiovascular disease, eye problems (such as retinopathy and cataracts), nephropathy, and neuropathy. Physiologically this is because those body cells do not require insulin, and so cannot screen out excess glucose by becoming insulin resistant, as can fat and liver cells. Therefore, because eye, renal, nerve, and endothelial cells absorb glucose at the level that it is in the serum, a great deal of oxidative damage occurs to the cells and they can suffer devastating complications. Death from diabetes is usually caused by a heart attack or stroke. Diabetic patients have the highest occurrence of adult blindness, and are the highest population developing end-stage renal disease and nontraumatic limb amputations.

Standard conventional care of diabetic patients includes medications, beneficial lifestyle changes, and associated medications. There are the oral hypoglycemic medications: metformin, sulfonylureas, DPP-IV inhibitors, SGLT2 sodium-glucose transporter, and the thiazolidinediones. There are also diabetic injections: GLP-1 drugs and the various forms of basal and bolus insulin. Outside of the focus on medication, standard care encourages patients to stop smoking, lose weight, have good stress management, and eat healthfully, although many patients are not given specific directives or counseling in those regards.

There are three basic treatment goals for US diabetic patients: A1C $< 7\%$; blood pressure $\leq$ 130/80 mm/hg, and cholesterol < 200 and LDL < 100. These goals are in accord with the UKPDS (United Kingdom Prospective Diabetes Study) and DCCT (Diabetes Control and Complications Trial), which proved that the lower the A1Cs of a patient, the fewer complications developed. A *JAMA* study showed that an A1C over 5.5 indicates that the glucose level in the patient is damaging the body. Diabetic patients can often require 3 to 4 separate hypertensive agents to bring their BPs down to a safe level. On top of that, the CDC shows that 68% of Americans are either overweight or obese, and visceral weight is a key factor in insulin resistance. Even so, standard care is failing to control this disease worldwide. A World Health Organization (WHO) bulletin of 2011 stated that unfortunately 90% of American patients do not meet those three treatment goals.

Approaches using micronutrients and botanical agents have been shown in numerous clinical studies to afford the best chances of obtaining those treatment goals without risking the sometimes problematic side effects of hypoglycemia from overmedication of glucose-lowering agents.

A low-carbohydrate diet is recommended for type 2 patients. The Nutrition and Metabolism Society devotes its entire dietary research to showing that low-carb diets are not just appropriate to type 2 diabetes but also extremely safe and effective at lowering glucose levels, decreasing insulin resistance, enhancing appetite control, and promoting weight loss, as well as normalizing lipid panels. Exercise – including aerobic, resistance, and high-intensity interval training – needs to be offered in ways that motivate patients to perform it regularly. Sleep studies to rule out apnea are vital, and sleep needs to be from 6 to 9 hours to promote appropriate regulation of leptin and ghrelin. Diet diaries, nutrient status measurements, hormonal evaluation, gut dysbiosis, and environmental xenobiotic burdens can all serve as extremely meaningful tests to help discern all possible etiologies for type 2 diabetes development. Last, adding in dietary and botanical supplements has been shown in studies to be very effective in helping the body lower glucose levels, lower lipid levels, decrease blood pressure, and prevent and reverse diabetic complications.

Focusing on supplementation, some of the most studied, most efficacious, and most beneficial supplements include:

1. Zinc: Zinc is needed to produce, secrete and activate insulin receptors on the cell. Studies have shown that adding zinc to diabetic patients can be helpful. Hyperglycemia can cause pathological losses of zinc in the urine. Zinc also has an antioxidant effect on cells in diabetic patients.
2. Chromium polynicotinate: Chromium has a vital role in binding to the insulin receptor to activate it on body cells, reducing insulin resistance. In many studies, chromium as a supplement has been shown to lower glucose levels, lipids, A1C, and insulin in diabetic patients.
3. *Gymnema sylvestre*: Known as *gurmar*, or "sugar destroyer" in Ayurvedic medicine, *Gymnema* has been consistent in showing its benefits in patients with diabetes. Studies on the herb have shown that it may be helpful in lowering glucose levels. It was shown to regenerate pancreatic tissues, allowing more insulin to be produced, and help regulate insulin secretion. It also increases the utilization of glucose at the cell, via reducing insulin resistance, and can help decrease appetite and reduce sugar cravings.
4. Cinnamon: Studies continue on cinnamon and have shown that it lowers stomach-emptying times and postprandial glucose levels; it reduces glucose in type 2 diabetes patients who had poor diabetic control. It has also shown to be helpful in lowering insulin levels, blood pressure, and the hemoglobin A1C. This is a safe herb. *Cinnamonum cassia* (a.k.a. *Cinnamonum burmanii*) is the type of cinnamon with the best effect on patients.
5. Berberine HCL: A leading study on humans showed that berberine HCL equaled the effects of metformin on diabetic patients. In the pilot study, the A1C, fasting and postprandial glucose, plasma triglycerides, cholesterol and LDL, and fasting glucose and HOMAR were reduced, as well as body weight. Berberine is also a liver protectant and activates AMP protein kinase at the cell, which promotes GLUT 4 translocation, allowing more glucose to be absorbed from cells. This is very significant, and berberine is an important component in diabetic supplements due to its efficacy and its safety profile.
6. R-ALA: Alpha-lipoic acid has numerous benefits to the diabetic patient. It is both a water- and fat-soluble antioxidant and has been shown to protect patients with fatty liver from liver disease progression. It can help insulin resistance and has been shown to protect diabetics from developing complications in their nerves, eyes, and kidneys. It is very safe. The R isomer is the only active isomer in the body and, since it can now be stabilized, should be the form recommended to patients, instead of regular lipoic acid wherein half the isomers are the nonhelpful S isomer.
7. Taurine: Taurine is an inexpensive amino acid, underused as a diabetic treatment. It has been found to be a potent hypoglycemic agent, and it can also enhance the effect of insulin. One study showed that giving taurine to diabetic patients for a month required a reduction in their insulin dosing, to avoid taurine-induced hypoglycemia. It was also noted that patients had reductions in cholesterol and triglycerides as well. Taurine is found naturally in the eye tissue and heart tissue and is protective against oxidative damage in both.
8. Benfotiamine: Also known as allithiamine, this fat-soluble form of thiamine has been shown in studies to be very capable at reducing the formation of advanced glycation end products (AGEs), which are well known to lead to the development of diabetic complications. Benfotiamine increases the production of thiamine pyrophosphate, which increases transketolase activity; transketolase blocks glucose-induced damage by preventing AGE formation. Since AGE formation promotes oxidative damage throughout the body, benfotiamine has been shown to treat and improve retinopathy, nephropathy, and neuropathy
9. Bilberry extract: Bilberry extract is rich in bioflavonoids and anthocyanosides, and has a specific affinity for the eyes. In a rat study, it was shown that ingesting bilberry extract reduced hyperglycemia and insulin sensitivity via activation of AMP-activated protein kinase. In several studies, bilberry was analyzed in type 2 diabetes patients with retinopathy, and it was found to induce a clear improvement in their retinopathy, with marked reduction or disappearance of retinal hemorrhages. It may also be beneficial in improving microcirculation and lowering glucose levels. As retinopathy is a leading complication in diabetic patients, and diabetes is the main cause of adult blindness, this study is remarkably important.
10. Green tea leaf extract: Green tea contains the catechin EGCG, which has been shown in numerous studies to be a safe and effective antioxidant. It has been shown to improve glucose tolerance in patients. In a study in Japan, green tea was shown to reduce the risk for type 2 diabetes onset. Green tea was shown to decrease hepatic glucose production, and oversecretion of glucose from the liver is a continual problem, causing hyperglycemia in type 2 diabetes patients. Green tea has also been shown to be an effective antiangiogenesis factor, which may have a significant effect on preventing retinopathy. It has also shown to promote fat oxidation and thermogenesis.
11. Curcumin extract: Curcumin seems to have multiple benefits in diabetes. It has been shown to be a marked inhibitor of reactive oxygen species, which interferes with protein kinase C, thus providing a benefit in diabetes protection and the prevention of complications. It was shown to reduce progression in NAFLD (nonalcoholic fatty liver

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disease) patients, renal lesions, broad oxidative damage, and cytokine expression. Curcumin prevented retinopathy in streptozotocin-induced rats.

12. *Gingko biloba*: This plant has been associated with reducing the risk of dementia and cognitive decline, but it has also been shown in human studies to reduce fibrinogen levels and improve retinal capillary blood rate in type 2 diabetes patients with retinopathy. It was shown to protect diabetic kidneys in animal studies. Gingko has also been shown to inhibit or reduce functional and morphological retina impairments. It was shown to reduce platelet aggregation in type 2 diabetes patients, too.
13. Vanadium: This mineral has been shown to be an insulin mimetic, reducing insulin resistance. In numerous studies of the diabetic rat, vanadium has been shown to reduce elevated glucose and lipids. The best absorbed form of vanadium is bis(maltolato)oxovanadium(IV) – it is 2 to 3 times more potent than vanadyl sulfate and has shown less toxicity.
14. Resveratrol: This is a bioflavonoid that has been shown in diabetic studies to protect pancreatic cells, reduce inflammatory cytokines, and increase antioxidants. It may also help improve insulin's actions and lower levels of glucose, A1C, and insulin. It was also shown to help decrease body weight, systolic BP, cholesterol, and triglycerides.

Using a comprehensive alternative-medicine treatment protocol, many diabetic patients can avoid using medications and even reverse their diabetic condition so that they have well-controlled A1C levels, and also lower lipids, lose weight, and have better energy and well-regulated serum glucose readings. Diabetes is a condition that does not have to lead to progressive complications and early death from cardiovascular disease. It is preventable, treatable, and reversible when treated by astute physicians addressing all the obstacles to cures and setting up a winning treatment plan with their patients.

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Gluco-Beta Stimulator

by Gail C. Eiceman, RN, BS, CCN, and Elizabeth Hassel, BS

Assists in the control of diabetes and its associated physiological symptoms and conditions; potentially reduces blood sugar, regeneration/ repair of the pancreatic beta cells in the islets of Langerhans.

Introduction

Both traditional and natural health-care providers have a responsibility to assist in care of the epidemic of diabetes mellitus. The World Health Organization estimated that the number of diabetics has increased from 200 million worldwide in the year 2000 to 346 million in 2011.[1] Whether one is an allopathic or natural care practitioner, diabetes needs to be confronted. It is uncommon to review a patient history without coming across diabetes or its associated diseases/complications within the patient history, family unit, or family tree.

Diabetes is a chronic metabolic disorder that disrupts the biochemical pathways involving carbohydrate, fat, and protein metabolism. There are three types of diabetes. Type 1 is characterized as insulin-dependent diabetes. The hormone insulin regulates the glucose in the bloodstream. In type 1 diabetes, the beta cells of the pancreas, which are responsible for the secretion of insulin, are completely destroyed. Type 2 diabetes affects 90% of all diagnosed persons with diabetes and is also characterized as non-insulin-dependent diabetes.[2] This hyperglycemia involves an impairment of insulin effectiveness, or insulin resistance. The third type of diabetes occurs when the pancreas is overworking during a pregnancy; this occurs in 14% of all pregnant women.[3] Although the condition reverses upon delivery, women diagnosed with type 3 diabetes are 9.6 times as likely to develop type 2 diabetes after age 40.

Causations

The number of people affected by insulin-dependent diabetes is on the rise. Traditionally, insulin dependent diabetes only affected children; however, destruction of the pancreatic beta cells is occurring in adults now as well. Viral infections such as mumps, hepatitis, rubella, and other childhood diseases can destroy the beta cells.[2] This destruction may in turn ultimately lead to type 1 diabetes. Historically this type of diabetes was called juvenile diabetes because only early childhood diseases would lead to the complete destruction of these insulin-producing cells. However, in recent years it has been demonstrated that some prescription drugs, such as streptozotocin, statins, antidepressants, glucocorticoid steroids, and antipsychotics also destroy the beta cells.[2,4–7] Researchers concluded that patients taking selective serotonin reuptake inhibitors and tricyclic antidepressants for a year or more were at an increased risk for developing diabetes. Such pharmaceuticals cause significant weight gain and impairment of the glucose homeostasis.[5] In a recent study, it was concluded that "glucocorticoids cause insulin resistance by inhibiting glucose uptake and reducing glucose storage."[6] This study also confirmed that steroid use (e.g., prednisone) for over a year leads to the destruction of beta cells.[6] In addition, studies have shown that corticosteroid treatment also increases the urinary secretion of chromium.[8] An increased deficiency of chromium also contributes to the diabetic syndrome. Such steroids also include any dermal steroid creams used to treat skin infections or poison as well as steroids for eyes or nose.

Type 2 diabetes, or non-insulin-dependent diabetes, was most prevalent among the adult populations ranging from ages 50 to 70 years.[9] As the body ages, the beta cells of the pancreas become strained. The beta cells produce insulin; however, the body fails to respond to the hormone, causing insulin resistance. Typically, a diet rich in refined sugars is the cause. As a result of its attempt to rid the body of the excessive sugar in the blood, the pancreas overworks itself. An error in the target tissues for glucose, the liver, muscle, or adipose tissue is also possible.[10] The pancreas consequently will compensate by making more insulin; however, the cells resist the hormone, causing glucose to accumulate in the blood. It is common, as a result, to find such patients making over 300 times the amount of glucose necessary, suggesting an error in metabolism.

Unfortunately, there has been a dynamic shift in the age group of diagnosis. America is seeing a large

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number of children with type 2 diabetes due to the "Western diet" filled with excessive refined sugars.[10] Younger adults ranging from 30 to 60 years old are being diagnosed with type 1 diabetes. Such diagnoses are apparent because it has been shown that diabetics have 63% less beta cell mass.[11] This younger population seems to have a suppression of insulin levels, leading to the belief that the beta cell number is decreasing because of the destruction of the beta cells due to pharmaceuticals.

Table 1:
Chart of Associated Conditions

Heart disease
Stroke
Hypertension
Hyperlipidemia
Kidney disease
Blindness
Nervous system diseases
Neuropathies
Gastroparesis
Peripheral arterial disease
Ketoacidosis
Hyperosmolar hyperglycemic nonketotic syndrome
Skin conditions
Blood clots
Cellulitis
Xerostomia
Liver diseases
Impotence
High cholesterol
Steatosis
Optic neuritis
Overactive bladder
Restless leg syndrome
Fatigue
Foot problems
Dental diseases
Obesity

The associated conditions set out in Table 1 relate to the impact of hyperglycemia on the whole body systems. Increased blood glucose levels lead to an inflammation of the microcirculation of the kidneys, nerves, lens, pancreas, and blood vessels of the heart.[12] This inflammation is due the increase in the glycation end products because of the chronic elevated sugar levels in the blood. Diabetics statistically have a "two- to fourfold greater risk of cardiovascular disease, a fivefold increased risk of blindness and four times the rate of kidney disease," report Andus and colleagues.[13]

Diagnosis

The oral glucose tolerance test (OGTT) is typically used in the diagnosis of diabetes. This test is extremely stressful to the patient. The standard of fasting blood glucose is 70 to 105 mg/dL; above 140 mg/dL on two occasions is considered a diagnostic diabetes.[2] The GTT tests the blood glucose levels of the patient after administrating 75 g of glucose in 300 mL of water. There is a positive diagnosis of diabetes if the patient exhibits plasma glucose above 200 mg/dL at the 2-hour and 4-hour measurement.[2]

Another test, the hemoglobin A1C, measures the level of glycosylated hemoglobin. This diabetic marker is a one-time stick blood test that will predict a risk level or the severity of this disease. An A1C is a blood test that shows up to a 3-month pattern of the health of the pancreas, including an average blood glucose level. There is an increase in the percentage of hemoglobin bound to glucose when there is excessive sugar in the blood. The normal concentration is 5% to 7%.[2]

Clinically, we began to observe trends in blood sugars over 20 years ago. More recently, we have been evaluating our patients' hemoglobin A1C. The longer hyperglycemia occurs in blood, the more glucose binds to red blood cells and the higher the glycosylated hemoglobin. According to the American Diabetes Association (ADA), a diagnosis of diabetes is concurrent with an A1C at 7 or above.[14] However, most laboratories rate the A1C at below 5.6 as normal, 5.7 to 5.8 equates to prediabetic, and 6 or above equates to a diagnosis of diabetes. We are seeing a precedent of symptoms, including disruptions in the microcirculation of the tiny blood vessels of the feet, eyes, heart, and nephron units before the A1C diagnoses diabetes. The symptoms raise the question, if we regularly screen those patients with familial risk or onset of suspicious symptoms, is there a way to interrupt the progression of the disease and the associated diseases naturally?[15]

Allopathic Approach

Traditionally, diabetes has been treated with injectable insulin or oral agents. Insulin injections are most common among type 1. Side effects include swelling, itching, rashes,

Blood Test Levels for Diagnosis of Diabetes and Prediabetes

	A1C (percent)	Fasting Plasma Glucose (mg/dL)	Oral Glucose Tolerance Test (mg/dL)
Diabetes	6.5 or above	126 or above	200 or above
Prediabetes	5.7 to 6.4	100 to 125	140 to 199
Normal	About 5	99 or below	139 or below

Definitions: mg = milligram, dL = deciliter
For all three tests, within the prediabetes range, the higher the test result, the greater the risk of diabetes.

fast heartbeats, low blood pressure, and interactions with aspirin and foods.[16] A synthetic form of amylin, pramlintide, is used along with insulin and glucagon to also maintain blood glucose levels. Another injectable agent, exenatide, works to lower glucose levels by increasing insulin secretion. Pharmaceuticals include a class of oral medications used to stimulate the beta cells to release more insulin, such as sulfonylureas, meglitinides, and chlorpropamide. In addition, there are medications that block the breakdown of starches; these include alpha-glucosides inhibitors and DPP-4 inhibitors. Finally, the most widely used medication for diabetes is metformin. First synthesized in 1922 and observed in a clinical trial in 1957, metformin improves hyperglycemia by suppressing glucose production and conversion in the liver or gluconeogenesis.[17] Some of the side effects of metformin include bloating, diarrhea, nausea, upset stomach, lactic acidosis, and a metallic taste in the mouth.[16] Other complications that follow metformin are an overall increased risk of heart–disease related deaths.[18] It is clear that over the years, allopathic medicine has made headway in controlling diabetes and is vigorously trying to make an impact on the associated conditions. However, there is no repair mechanism for the error of metabolism that is causing this disease. Rather, these drugs can only balance blood sugar; therefore patients are on these prescription medications for the remainder of their lives.[16]

It is also worth noting that such antidiabetic pharmaceuticals are a burden to the health-care system. In 2002, it was reported that an estimated $132 billion was distributed to diabetes, and $92 billion of that was direct medical costs.[19]

Dietary Interventions

Dietary intervention is helpful in the care of a diabetic individual. It is known that Americans consume an average of 149.2 pounds of refined sugar in a year's time.[19] This equates to approximately 3 pounds per week and 41 teaspoons per day. This massive amount of refined sugar and refined flours causes an increased level of triglycerides, which increases the resistance to insulin. Type 2 diabetes can be controlled with a drastic diet intervention. Unfortunately, patient compliance is heavily weighed on such drastic intervention; thus physicians cannot rely on such treatment. The benefits of a high-complex-carbohydrate, high-fiber diet on the glycemic index versus a low-carbohydrate, high-protein diet are heavily disputed.[20] Some research supports a low-protein, low fat, high-carbohydrate diet due to the stress that protein places on the kidneys. It is also thought that increased carbohydrates lead to increased secretion of insulin.[10] Therefore, after much research the ADA now advocates an individualized diet with proportional amounts of protein, carbohydrates, and fat.

The glycemic index (GI) measures how much food affects a person's blood sugar and how fast the food is digested into glucose.[10] The higher the GI, the greater the rise in blood sugar after consumption. Many dietitians suggest that a low glycemic load and increased physical activity will stimulate glycogen synthesis and improve beta cell activity.[13]

Nutrition Interventions by a Complementary Care Medical Provider

Initially, natural health-care providers sought a product to treat diabetes that would intervene in the metabolic imbalance with the hope that such a product would decrease the need for pharmaceuticals, as well as combat the associated conditions that follow a lack of blood sugar control. To that end, we began to utilize chromium, biotin, cinnamon, and *Gymnema sylvestre* as individual products.

It is common to find a chromium deficiency among patients with type 1 and type 2 diabetes as well as gestational diabetes.[20] Chromium deficiency leads to impaired metabolism and nerve function.[8] Chromium also facilitates the cellular uptake of glucose by working with insulin; without this cofactor, the action of insulin is inhibited and glucose and insulin accumulate in the bodily systems.[2] In addition, chromium decreases blood lipid values such as cholesterol and triglycerides.[10]

Biotin is a water-soluble B vitamin that is involved in the metabolism of carbohydrates and lipids. This vitamin enhances the effects of chromium and increases the beta cell expression of the enzyme glucokinase, which is involved in the conversion of glucose to ATP.[22] This ATP fuels the mechanisms needed to regulate blood glucose. In a study that evaluated the effects of 600 ug of chromium with 2 mg of biotin on patients with an A1C greater than 7, at the end of the 90-day randomized, double blind trial, the mean A1C decreased by 0.54% in the study group. The mean fasting glucose also decreased by 9.8 mg/dL in the study group.[21]

Cinnamon as *Cinnamomum cassia* is thought to have insulin-stimulating properties due to its ability to enhance the insulin receptor autophosphorylation. This activation of the receptor increases insulin sensitivity.[19] By stimulating the receptor for insulin, C. *cassia* enhances regulation of sugar extracted from the carbohydrates.[16] In a study conducted by Khan et al. in 2003, the effects of cinnamon were evaluated in 60 type 2 diabetics on sulfonyurea medications. The trial measured the fasting serum glucose levels. At the end of this study, it was apparent that administration of 1 to 6 g of cinnamon per day decreased the fasting serum glucose levels ($p < 0.05$).[19] To the contrary, the placebo group's glucose

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levels rose from 0.6% to 2.7%. The test group demonstrated other improvements, including a decrease in cholesterol and triglyceride levels.[19]

The Indian herb *G. sylvestre* was traditionally used to suppress the sweet taste of sugar. For over 2000 years, in Ayurvedic medicine in India, *Gymnema* was traditionally used for glycosuria, urinary disorders, and diabetes mellitus.[23] The common name, *gurmar*, translates to "sugar destroyer."[24] *Gymnema* also contain gymnemosides and amino acids that are known to stimulate beta-cell function and glucose uptake and utilization.[21] In a research model, this herb was found to increase the activity of the glucose utilization enzymes.[12] Suggested mechanisms of *Gymnema* are thought to be its ability to inhibit intestinal absorption of glucose and increase the activity of the enzymes used in blood glucose regulation pathways.[23] The active "parts" of the Indian plant include a peptide gumarin, antisweet saponins, stigmasterol, quercitol, gymnemic acids, and amino acid derivatives betaine, choline, and trimethylamine. With these components, *G. sylvestre* has been shown to reduce blood glucose, glycosylated hemoglobin, and glycosylated plasma proteins.[24] The increase in insulin levels after supplementation support the claim that *Gymnema* repairs and rejuvenates the pancreatic beta cells.[23]

In a study evaluating the effectiveness of 400 mg/day of *G. sylvestre*, it was reported that there was a significant reduction in the fasting blood glucose levels and the insulin requirements in patients with insulin-dependent diabetes.[12] An extract of this herb doubled the number of islet and beta cells in the pancreas in one study conducted by Prakash.[20] Other studies reported an improvement of glycolysis, gluconeogenesis, and muscle glucose uptake and a decrease in protein glycosylation.[13] Though various studies, it is confirmed that *Gymnema* rejuvenated the pancreas and reversed damage to the beta cells.[16]

In a placebo-controlled, randomized study, researchers reported lower glucose/insulin ratio after supplementation, thus concluding a decrease in insulin resistance.[24] This decrease in insulin resistance was also assessed by an increase in beta-cell function. In this study, diabetic patients also had reduced symptoms such as suppressed hunger and decreased fatigue. Overall, there was a reduction in hyperglycemia, which reduces the metabolic risk of the development of secondary complications of diabetics.[24]

In a controlled, nonrandomized, nonblinded study of 47 patients with type 2 diabetes documented in 1990, 400 mg of *Gymnema sylvestre* was given to 22 patients for 18 to 20 months. Fasting glucose levels were 29% ($p < 0.001$) lower than baseline and the hemoglobin A1C deceased from baseline on average 11.91% to 8.48% ($p < 0.001$). Additionally, 5 patients were able to discontinue the hypoglycemic medications.[25] There were no significant changes in the oral hypoglycemic medications group. This plant has also demonstrated implications for weight loss, hyperlipidemia, and decrease in fatigue.[23,24,26]

The combination of chromium, biotin, cinnamon, and *G. sylvestre* is most effective in lowering glucose levels and AIC across the board. Independent nutrients were used synergistically for over 5 years in our practice. By continuously recording their blood sugar and routine A1C, we were able to see between 85% and 95% of our clients improve. They had regression of metabolic syndromes associated with diabetes such as less pain in their feet, kidney function improvement, and improvement of neuropathies associated with the eyes.

Unfortunately, about 5% to 10% did not respond due to noncompliance with the quantity of products in this regimen. At our request, Professional Health Products (PHP) became involved in the production of Gluco-Beta-Stimulator (GBS) in order to combine chromium, biotin, cinnamon, and *G. sylvestre* into one capsule. Within the last three years, we have noticed considerable improvement in the hemoglobin A1C by adding GBS to our client supplement regimen. This is very possible due to the availability a capsule with each of the four supplements instead of a combination of supplements; this lesser number of supplements also aids in client compliance.

Currently, we are undergoing a study in our practice to evaluate the change in hemoglobin A1C and the fasting blood sugars after administration of four GBS capsules a day for 1 year. Our study has approximately 40 clients, and we are monitoring their blood sugar every 2 to 3 months and their hemoglobin A1C every 4 to 6 months. However, we are continuously adding new clients to our study each week. Our preliminary data have shown great efficacy in the administration of GBS. In citing a few of our case studies, a 66-year-old female patient had a hemoglobin A1C of 6.5 in June 2012 and a random glucose of 140 mg/dL; within 6 months on GBS her A1C was reduced to 6.0 and her random glucose was 120 mg/dl (CS#16). Another patient was straddling the line of prediabetes and diabetic-associated symptoms for a number of years. In October 2012, his hemoglobin A1C was 12.7 and a random glucose of 305 mg/dL (CS#18). His doctor wanted to place him on insulin therapy right away, but he refused. When he turned to our care, we advised him to cut back his consumption of sweets and desserts and implement our GBS regimen of 4 capsules per day. Within 3 months his A1C went down to 7.3 and his random glucose was 128 mg/dL. Within the year, we expect that

his A1C will be below the diabetic threshold.

Improvements in some of the associated diseases of diabetes have been noticed with this product. In one case, a patient with a short-term diagnosis of kidney failure came into our practice. Her kidney function went up and down while being treated with the suggested kidney support nutrients. We suggested an evaluation of A1C to determine if her blood sugar was not regulated and was contributing to her fluctuations. Her A1C came back at a 6.6 (CS#28). Diabetes most acutely affects the microcirculation of the eyes, feet, heart, and kidneys. This patient's kidney failure was being complicated by an increased blood sugar. Her sugar was not being metabolized properly and therefore causing inflammation at the nephron units. After starting 4 GBS per day, her glomerular filtration rate tripled, the doctors halted her current dialysis regime, and it is hoped that a transplant is no longer needed. There are approximately five current clients in our study who are not improving. However, we believe that there is noncompliance and the clients are not taking 4 capsules of GBS per day. Our research indicates that administration of 4 GBS capsules per day for 6 to 30 months will regenerate the pancreatic beta cells and improve the metabolic disturbances caused by elevated sugar levels in the blood. Failure to comply with this regimen will not bring improvement.

As our study proceeds, we are questioning the appearance of patients' having an event whose root cause is a disruption in the microcirculation. Such events lead us to question many of the associated diseases of diabetes. Do we have the potential to look at people who have an associated disease of diabetes and repair the underlining sugar problem, thus halting the advancement of the associated diseases and diabetes?

Gluco-Beta Stimulator

Gluco-Beta-Stimulator is currently under a clinical trial at Nutrition Works, 543 West Franklin Street, Womelsdorf, Pennsylvania. Please contact the practitioners, Gail C. Eiceman RN, BS, CCN, and Elizabeth Hassel BS, Mastorial Candidate in Integrated Health and Nutrition, with any pertinent questions: 610-589-5182 or drv@nutritionworksedu.com.

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Gluco-Beta Stimulator

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Gail Eiceman, RN, BS, CCN, CLNC, has been a nurse for over 40 years. Gail received her nursing degree at Chester County Hospital, where she was given the outstanding award in pediatric nursing. Following nursing school, Gail's experience was broadened by serving as head nurse in an intensive care coronary unit, emergency room, and various other disciplines of nursing.

A personal illness led Gail to investigate the integration of her medical experience with the benefits of natural medicine. As her desire to bridge the gap between natural and traditional medicine grew, Gail sought further education, obtaining numerous certifications and degrees, including advanced nursing degrees, and as a certified clinic nutritionist (CCN).

In an effort to educate others, Gail opened her nutritional practice in 1983. It has evolved to include, among other areas, nutritional evaluations, metabolic typing, orthomolecular medicine, Chinese medicine, Ayurvedic therapy, amino acid therapies, homeopathy, and weight-loss programs and diets (including rotation diet for allergy). She has had the pleasure of hosting medical students from several medical schools for their natural medicine rotation education.

She is a founding member of the Community Care Group, a group of traveling health-care professionals who minister to the needs of the Amish communities. Gail's clinic now hosts satellite offices from many medical doctors and practitioners of various disciplines from around the world. She is a sought-after speaker and lecturer on radio, on television, and at conferences worldwide. Gail has developed numerous supplement formulas that are privately labeled and sold throughout the country.

Elizabeth M. Hassel, BS, is a 2011 graduate of Pennsylvania State University, where she received her degree in nutrition. Currently she is a candidate for her graduate degree in nutrition and integrative health from the Maryland University of Integrative Health in Laurel, Maryland. While a student at Penn State, she was active in the Student Nutrition Association, her major contribution being to THON, Penn State's student-run philanthropic organization that raises money for pediatric cancer. This is the largest student-run organization in the world, raising millions of dollars for children with cancer. Among other areas, Elizabeth understands the nutritional concerns of the cancer patient. Elizabeth was also awarded membership to Kappa Omicron Nu, an honor's society for the College of Health and Human Development. Upon completion of her master's degree, Elizabeth will be on track to sit for the Certified Clinical Nutrition Boards. Elizabeth feels fortunate to be mentored by Gail, with her years of professional expertise, research, and knowledge.

Elizabeth specializes in the treatment of patients with Lyme disease. After extensive research she has put together a natural Lyme protocol that works at combating the disease. She is also a candidate for membership of ILADS (International Lyme and Associated Disease Society). Elizabeth also specializes in natural bioidentical hormone replacement therapy.

Elizabeth is a fine example of demonstrating the importance of implementing proper nutrition and regular exercise into daily life in order to achieve optimal physical and emotional health.

Earthing: Is Hope for Diabetes Right Under Our Feet?

by Stephen T. Sinatra, MD, FACC, with Martin Zucker

What is Earthing?

Throughout virtually all of history, humans mostly walked barefoot or used semiconductive animal hides for footwear and bedding. We lived in contact with the Earth at all times. Today, we mostly live insulated, living and working above the ground (often very high above the ground), and wearing nonconductive shoes with synthetic soles. We rarely go barefoot outside. Consequently, our bodies have become chronically imbalanced with static electricity, free radicals, and inflammation.

Earthing refers to significant health benefits that result from making sustained direct physical contact with the Earth's natural, negative surface charge by walking barefoot outside or sitting, working, or sleeping indoors connected to conductive systems that transfer the charge from the ground into the body.

This subtle charge comes from the virtually limitless and continuously renewed reservoir of free electrons on the surface of the Earth. Maintaining contact with the ground allows your body to naturally receive and become charged with these electrons. When thus "grounded," you automatically absorb these free electrons which in turn instantly reduce electrical imbalances in the body and the oxidative free radicals involved in chronic inflammation and multiple diseases. The body's natural electrical state is restored.

As a result, people who are grounded feel better, sleep better, and have less pain.

For years we have received feedback from individuals with diabetes saying that their blood sugar and symptoms have improved after they start Earthing. Some have reported even being able to cut back on their medication dosage.

The growing popularity of Earthing indicates a wonderfully promising tool with which to both help prevent diabetes and also alleviate the symptoms. In my opinion, this is a big deal, given the alarming rise in diabetes, now estimated at 347 million people globally.

This article will focus on type 2 diabetes, the most common form of the disease (90% of cases), which involves not enough or inefficiently used insulin, the pancreatic hormone that regulates blood sugar. One main component in the diabetes scenario is inflammation. Excess fatty tissue in the abdomen produces inflammatory chemicals that suppress the actions of insulin. The body becomes more resistant to insulin. This in turn produces more inflammatory chemicals and interference. Blood sugar rises. Add obesity and stress to the mix, and you further increase the level of inflammatory chemicals.

Common causes are excess weight, poor diet, and physical inactivity. What's missing in the list of usual suspects, we strongly believe, and also in the consideration of the soaring rise of other chronic illnesses over the last half-century, is the increasing human disconnection from the Earth's natural, negative electric surface charge. This disconnection from the Earth parallels a proliferation in increasingly unnatural lifestyle practices, including sedentary work, less time spent in outdoor activities, and overeating nutrient-poor processed food full of refined carbohydrates. Loss of connection with the Earth's surface energy creates an electron deficiency that sheds light on an overlooked factor in the rise of diabetes.

Reconnection with the Earth helps in a number of significant ways:

Reduction of Inflammation

First of all, the influx of electrons into the body reduces chronic inflammation. That's a head-to-toe effect. Theoretically, it remedies a common electron deficiency by quenching/neutralizing positively charged free radicals involved in chronic inflammation.

Electrical Stability in the Body

Second, contact with the Earth restores the body's electrical stability, and this in turn has a major effect in restoring order to the normal functioning of all body systems. We are bioelectrical beings.

Calming the Nervous System

Earthing also counteracts stress by promoting a calming mode in the autonomic nervous system (ANS) that regulates functions such as heart and respiration rates and digestion. Earthing rapidly shifts the ANS

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away from a typically overactive sympathetic mode associated with stress. A study that I conducted with electrophysiologist Gaétan Chevalier demonstrated how Earthing improves heart rate variability (HRV), the very subtle variations in heartbeat intervals that are regarded as an important indicator of balanced ANS. ANS and HRV are commonly disturbed by stress and represents an increased risk for arrhythmias and sudden cardiac death. Moreover, abnormalities in HRV are regarded as early evidence of cardiovascular autonomic neuropathy, a serious but widely overlooked complication of diabetes that damages nerve fibers that supply the heart and blood vessels. Such abnormalities result in aberrant heart rate control and vascular dynamics.

Aiding Glucose Control

Earthing also appears to help control the blood glucose level. We have heard that from individuals with diabetes and seen objective evidence in an unpublished year-long laboratory study that showed a small but significant reduction in the glucose level of grounded rodents compared with nongrounded animals. Two other biochemical markers, triglycerides and alkaline phosphatase, were also lower, suggesting less risk of diseases linked to the metabolic syndrome, such as hypertension and diabetes.

Vastly Improved Blood Flow

Finally, there is Earthing's powerful effect on circulation, which may exert the biggest influence of all.

Earlier this year, another Earthing study in which I participated was published in the *Journal of Alternative and Complementary Medicine*. We grounded 10 healthy subjects for 2 hours, took blood samples before and after, and measured the negative charge on the red blood cells of each sample. This charge goes by the name of *zeta potential*; the higher the charge, the better ability of cells to repel each other and prevent unwanted clumping and clotting.

The results indicated a nearly 3-fold average increase of the zeta potential, with obvious significant improvements in the electrodynamics, blood cell movement, and aggregation of the red blood cells. Looking through a microscope, we clearly observed thinning and less clumping of the cells. This is extremely significant because so many diabetics suffer with poor circulation and neuropathy (nerve damage) in the legs and feet. The changes that we see help explain why diabetic patients describe signs of better circulation in their extremities.

Note: Earthing has significant effects on the physiology, including the potential to improve circulation, glucose, thyroid, and blood viscosity values. This may call for an adjustment in medication dosages. Any patient with diabetes who takes prescription medication should consult with his/her physician before starting Earthing.

In my ongoing research, I came across a fascinating 2008 study in the international journal *Biochimica et Biophysica Acta* that reported, for the first time, on the zeta potential of red blood cells in diabetics. The researchers, from the University of Calcutta, said that they discovered "a remarkable alteration" in the electrodynamics of red blood cells, and specifically a progressive deterioration of the zeta potential among diabetics and, at the worst, among diabetics with cardiovascular disease. Their research revealed a parallel between poorer zeta potential and hypercoagulability. In their words: "Blood becomes sludge so that it becomes increasingly difficult for the heart to pump, and the system becomes less efficient to perform the usual functions affecting macro and microcirculation."

I have personally witnessed improvements, some dramatic, in the circulation and symptoms of patients with diabetes, as well as in blood pressure and arrhythmias. We are now starting to see other doctors making the same observations. Here are two examples:

The Polish Experience

Polish cardiologist Karol Sokal and his neurosurgeon son Pawel have been actively researching grounding on the physiology for more than two decades.

In a conversation with them, they shared the following details:

> We have seen good things with diabetes. We were able to withdraw insulin for some people because they achieved a reduction in their blood sugar just from walking barefoot. We found that in some cases the combination of medication and grounding could even push the glucose level too low.
>
> Imagine telling someone that if you go barefoot you may be able to reduce or withdraw your insulin ... or some other medication. Yet that is what we found. It all depends on the level of glucose as to whether and when you can cut out the medication or reduce it. With oral medication, we observed that some people with diabetes could walk barefoot and not need antidiabetic drugs like Metformin.
>
> Here in Poland, you can't go barefoot outside around the year. You have to wait until late spring and summer before going barefoot. If people have stone or concrete floors in their houses, they can walk barefoot, or sit barefooted on the floor. Doing that for a few hours a day, people are often able to reduce their medication within a few weeks. Not everybody can spend that kind of time barefoot, of course.
>
> One of our experiments with blood sugar showed that continuous grounding for three days and two

nights was enough to decrease the level of glucose in patients who have diabetes. That result was on the basis of twelve volunteers, of which six were grounded. Further research with more people would be needed to see at what point sustained grounding could achieve a decrease in glucose enough to recommend that a doctor reduce the medication dosage. Perhaps a minimum of three nights may be enough for some people.

The Australian Experience

From David Richards, MBBS, an integrative family physician in New South Wales, we have received the following report on his experience with diabetes:

> I have been a general practitioner for over 30 years and I've never had anything that could help diabetic neuropathy. All we doctors can do is try to optimize blood sugar and control it. But that doesn't fix the problem of numb feet. Earthing has changed this dilemma altogether.
>
> In most cases, I have seen at least some improvement of foot numbness after an initial grounding session in my office of an hour or so where patients simply put their bare feet on an Earthing mat connected to the Earth.
>
> One diabetic woman sat in my office for an hour, both feet on an Earthing mat. Afterward she said that her numb feet had improved by 75%. She had never told me she had numb feet. After two sessions like that, her numb feet were totally resolved.
>
> I have had 21 out of 21 diabetic neuropathies with numb feet and now most are fully resolved. I now deliberately target diabetics, even those without complications. I believe Earthing offers some preventive help to even newly diagnosed diabetics by counteracting their inflammation and I imagine that the effect on red cells will help improve blood flow to all smaller vessels. In my practice, I personally draw blood, and I have repeatedly observed the change in blood viscosity. One patient whose neuropathy resolved used to have blood that would clot in a normal-sized venesection needle before even making it to the blood tube. Since starting Earthing that doesn't happen anymore!
>
> I have three kidney patients whose renal function has returned to normal. Several others are stable and haven't deteriorated further as was expected. If they remain stable they may never need dialysis.
>
> One patient likes to go fishing barefoot. He remarked how he had forgotten how sharp the rocks were and how hot the sand was! He could feel them now. Before, he couldn't. His diabetic kidney disease has stabilized.
>
> Another patient on the Earthing program now describes the condition as "slowly" progressive renal disease. I have never seen the term *slowly* attributed to renal disease.
>
> The brother-in-law of a good patient of mine reluctantly tried Earthing. He is on dialysis. His specialist told him, "I don't know what you are doing but keep doing it."
>
> I have seen diabetic eye disease stabilize in two patients. Another, with glaucoma, reported visual improvement, "like cling film being lifted from in front of the television screen."
>
> Another individual with a leaking heart valve has experienced resolution based on a recent echocardiogram. His specialist can't explain it.
>
> I find that medication needs generally are reduced after Earthing. One patient now only takes insulin if she is lax with her diet. Another has reduced daily insulin from 80 units down to 10 or 20. Prior to Earthing, one of them experienced considerable depression. The depression has improved with Earthing. These improvements occurred after several months of Earthing twice a week in my clinic.
>
> I actually warn all patients who start Earthing to be alert for improvements and be prepared to reduce doses of some medications, such as blood pressure, thyroid, and glucose meds, and, in particular, blood thinners. For those on blood thinners, such as Coumadin, I do standard blood clotting checks fortnightly for about two months, and if the blood is stable, then do it monthly. I haven't encountered any issues.
>
> Earthing brings into the treatment equation an entirely unusual prospect for people only expecting things to deteriorate. Most doctors expect only deterioration and to add more medication and/or to increase doses. As well as noticeable improvements and lowering medication, it seems to me that diabetics, over a long period of time, will have less heart disease, less stroke, and better health as a result of Earthing.
>
> Medicine doesn't have many "WOW" moments as such. It is mainly logical thinking with little scope for being somewhat creative. Medicine plus Earthing has provided me lately with some spectacular "WOW" moments.

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Integrative cardiologist Stephen Sinatra and health writer Martin Zucker are coauthors, along with Clint Ober, of *Earthing: The Most Important Health Discovery Ever?* (Basic Health Publications; 2010). The book has been published in 11 languages to date. For more information, visit earthinginstitute.net. ◆

Importance of Subtyping Diabetes Type 2

by Majid Ali, MD

In a previous column, I presented the oxygen model of diabetes and the crank-crankshaft model of insulin dysfunction.[1] In my book *Dr. Ali's Plan for Reversing Diabetes*, I presented several insulin profiles and illustrated two subtypes of diabetes type 2: 2A and 2B.[2] Simply stated, diabetes type 2A is a state of insulin toxicity created by insulin resistance and hyperinsulinism, whereas diabetes type 2B is an insulin-depletion state. In this article, I focus on the importance of subtyping diabetes type 2 and offer seven reasons for doing so, underscoring the profound clinical significance of the differences between the two subtypes.

In Tables 1 to 3, I present insulin and glucose profiles of three patients: (1) an individual in physiological insulin-glucose homeostasis; (2) a patient with diabetes type 2A; and (3) a patient with diabetes type 2B. Comparison of insulin profiles in Tables 2 and 3 illustrates the essential difference between the two subtypes. Later in this article, I present additional insulin and glucose profiles (Tables 4 and 5) to illustrate how diabetes type 2A and type 2B can be expected to respond to effective integrative dediabetization management plans (outlined in a previous column and described at length in my book cited above).

Table 1: Insulin and glucose profiles of a 77-yr-old metabolically fit 5' 5" man weighing 133 lb. He was seen for allergy treatment.

6.23.2010	Fasting	1 Hr	2 Hr	3 Hr
Insulin	<2	24	29	30
Glucose	78	96	75	71

Table 2: Diabetes type 2A. Insulin and glucose profiles of a 50-yr-old man with neuropathy and prehypertension.

11.26.2012	Fasting	1 Hr	2 Hr	3 Hr
Insulin	13.2	73.0	178.7	56.4
Glucose	137	246	275	191

Table 3: Diabetes type 2B. Insulin and glucose profiles of a 60-year-old 5' 10" man weighing 146 lbs with hypertension, GERD, recurrent sinusitis.

3.29.2010	Fasting	1 Hr	2 Hr	3 Hr	4 Hr
Insulin	<2	4	10	3	2
Glucose	104	300	166	62	69

Reasons for Subtyping Diabetes Type2

Diabetes type 2A with insulin excess and diabetes type 2B with insulin-depletion are quite different in their:

1. basic nature of the disorder
2. treatment goals of the disorder
3. explanations of the disorder for the patient
4. laboratory tests for assessing treatment effectiveness
5. expected duration of treatment for dediabetization
6. consequences of making exceptions in the dietary plans
7. rethinking insulin-dependent diabetes

1. Basic Nature of the Disorder

All clinical and pathological features in diabetes type 2A are caused by the two primary lesions of insulin resistance and hyperinsulinemia. By contrast, metabolic derangements in diabetes type 2B are caused by insulin deficit.

2. Treatment Goals for Diabetes Subtypes A and B

The primary treatment goal for diabetes subtypes A and B is fundamentally different. The goal in subtype A is to restore insulin's metabolic and energetic roles, and consequently lower its blood level. The primary treatment goal in diabetes subtype B is exactly opposite of that: create islet cell conditions so that insulin production can be resumed, as has been documented in experimental animal studies.

3. Explanations of the Disorder for the Patient

A core requirement for success in integrative medicine is to recruit the patient in her/his treatment plan for assuring strong compliance. This, of course, mandates that the patient be not only very well informed but also clear-eyed about the management plan. In my clinical work, I take time to explain that diabetes cannot be reversed nor its complications prevented by focusing on blood sugar levels. These goals are only possible by focusing on insulin dynamics and precise insulin measurements.

4. Laboratory Tests for Assessing Treatment Effectiveness

I assess the effectiveness of my integrative plan with the following "three-step-insulin-testing" approach:

A. a 3-hour insulin and glucose profile following a standard glucose load before beginning the program;
B. fasting and 1-hour post protein and fat food load insulin and glucose profile (a protein powder, lecithin, ground flaxseed, and organic vegetable juice are used for this purpose). Please look up online "Dr. Ali's Breakfast" for details;
C. a 3-hour insulin and glucose profile following a standard glucose load 1 year after beginning the program.

The profiles obtained in step B provides the patient the best indication of how her/his insulin response changes with an all protein and fat food load. The comparative study of the profiles in A and C categories provides a clear indication of the degree of "insulin optimizing" over a period of 1 year.

5. Expected Duration of Treatment for Dediabetization

Creating microecologic conditions for pancreatic regeneration in diabetes 2B requires a strong commitment both for the patient and the physician. A high level of patient compliance is needed over long periods of time (several months or longer) for the reasons given above. The required program for addressing toxicities of foods, environment, and thoughts is much more demanding in diabetes 2B than in diabetes 2A. Lowering blood insulin levels by improving insulin receptor function (by "degreasing the cell membrane") using dietary and detox measures can be achieved in most patients with diabetes 2A within some months.

6. Consequences of Making Exceptions in the Dietary Plans

Individuals on integrative dediabetizating plans cannot always avoid making exceptions in their dietary and detox program. It follows from points made in item 5 that such exceptions (wrong food choices, missed supplements, neglected detox measures, and others) will exact a larger toll from patients with diabetes 2B than those with diabetes 2A. So this crucial aspect of recovery must be clearly understood by them.

7. Rethinking Insulin-Dependent Diabetes

The prevailing opinion among diabetologists and endocrinologists worldwide is that individuals with so-called insulin-dependent diabetes require insulin treatment for rest of their lives. This is unfortunate. In many such cases the use of insulin can be safely discontinued. In Table 5, I present data that support my position.

Normalizing Insulin Homeostasis By Freeing Up the Insulin Receptor

In my book on reversing diabetes, I established that hyperinsulinemia is the result of insulin receptor dysfunction.[2] The insulin receptor is a protein that crisscrosses the cell membrane like a cord, with one end protruding to the exterior and the other to the interior of the cell. In previous publications, I offered the analogy of a crank and a crankshaft to explain insulin resistance and hyperinsulinemia.[1–3] In this analogy, insulin is visualized as a crank – a device that transmits rotary motion – and the insulin receptor protein as a crankshaft embedded in the cell membrane. The cell membranes become resistant to insulin action when they become greased and chemicalized – *plasticized*, so to speak – and hardened, immobilizing the insulin receptors embedded in the membranes. I introduced the term *cellular grease* for accumulation of oxidized lipids, misfolded proteins, altered sugars, molecular debris, and cellular waste caused by toxicities of foods, environment, and thought. One of the consequences of grease buildup on cell membranes is that the insulin receptor becomes turned and twisted, literally and figuratively. The crank-crankshaft model of insulin receptor dysfunction is based on my oxygen model of inflammation and is supported by a large number of studies linking inflammation with peripheral insulin resistance.[4–9]

The goal in my dediabetization plan is to degrease the cell membranes, free up the insulin receptors, restore insulin function, and so correct hyperinsulinemia.

Case Study 1

A 55-year-old 5'5" woman weighing 234 lbs. consulted me for fibromyalgia, hypothyroidism, allergy, and pruritus. Her previous doctors had performed tests for neither glucose intolerance nor hyperinsulinemia. Table 4 shows her insulin and glucose profiles at the time of initial evaluation.

I implemented my previously described integrative program for restoring insulin and glucose homeostasis (for more details, please consider my three-part video seminar *Reversing Diabetes,* downloadable from www.aliacademy.org).[1,3] The follow-up insulin and glucose profiles performed after 20 months of implementing the program showed a lowering of 1-hour blood insulin level from 107 to 44 uIU and a fall in the 1-hour glucose value from 198 mg/dL to 171 mg/dL. So, where a pretreatment insulin level of 107 uIU was needed to keep blood glucose level to 198, after the treatment only 44 uIU were required to drop the glucose level to 171 mg/dL, a clear evidence of much improved insulin efficiency.

Table 4: Normalizing insulin homeostasis by freeing up insulin receptor of 55-year-old 5'5" woman weighing 234 lbs. (Case Study 1)

3.11.2010	Fasting	1 Hr	2 Hr	3 Hr
Insulin	13	107	85	17
Glucose	110	198	137	56
12.21.2011				
Insulin	10	44	Not done	Not done
Glucose	109	171	Not done	Not done

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Beta Cell Regeneration and Increased Insulin Production in Diabetes Type 2B

Type 1 diabetes results from destruction of the pancreatic beta cells by beta cell–specific autoimmune responses.[5–10] In experimental models of diabetes type 1, in vivo expansion of the beta-cell mass and consequent restoration of normoglycemia has been reported. Betacellulin is one beta-specific growth factor that induces beta-cell growth and differentiation.[11–13] Application of this knowledge to human diabetes type 1 is problematic for three main reasons: (1) it is difficult to produce and sustain sufficient numbers of beta cells for sustained normoglycemia; (2) newly formed beta cells are vulnerable to autoimmune attack, which causes the disease in the first place; and (3) compliance with the pancreas regeneration program is not as big an issues in mice as it is for men (and women).

Case Study 2

A 51-year-old 5'9" man weighing 167 lbs. was treated with metformin for 1 year before consulting me. He discontinued metformin within 6 months of our program. His subsequent A1c values ranged between 5.5% and 5.8%, indicating healthful insulin and glucose homeostasis. Table 5 shows increased insulin production in his case. His subsequent A1c values ranged between 5.5% and 5.8%, indicating healthful insulin and glucose homeostasis.

Table 5: Increased insulin production due to beta cell regeneration in diabetes type 2B. The subject is a 51-yr-old man who received metformin for about two years before implementing the dediabetization plan. After discontinuing metformin within 6 months, his A1c values ranged between 5.5% and 5.8%.

9.17.2011	Fasting	1 Hr	2 Hr	3 Hr	A1c
Insulin uIU	3	13	23	8	7.9
Glucose	130	246	229	125	
4.7.2012					
Insulin	8.8	24.2	38.2	6.5%	
Glucose	137	241	182		
9.26.2012					
Insulin	10.9	29.6	42.6	19.4	6.6
Glucose	92	162	131	62	76

I anticipate the question, doesn't his April 7, 2012, glucose profile show that he is still diabetic? The issue of the differences in blood-sugar responses to the sudden and large glucose load (Glucola for testing) and "insulin-friendly" meals is important.[14,15] His low A1c values between 5.5% and 5.8% point to improved glucose tolerance. One can reasonably expect that response to Glucola-like load will also improve with time as insulin homeostasis improves further.

Notes

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The Continuum of Insulin Resistance

by Filomena Trindade, MD, MPH

Insulin resistance, or an increasing lack of sensitivity to the hormone insulin, is the common underpinning among many serious health concerns that we see today. To name a few: we see heart disease, premature death, cancer, and dementia all as a consequence of insulin resistance. What's more, insulin resistance is a major cause of premature aging and death in both the developed and developing worlds. It is arguably our biggest global health epidemic.

In my practice I see a new patient with insulin resistance every day. Insulin resistance has many faces. It does not always present the same way in every patient. For instance, one patient could present with cardiovascular disease, another with inflammation, and yet another with obesity – all with the common cause being insulin resistance. In short, the consequences of insulin resistance can prevent us from living a long, healthy life.

Never before in human history have we seen the numbers of new cases of type 2 diabetes that we are currently diagnosing today – particularly in children. The diagnosis of "adult onset," or type 2, diabetes in children has climbed astronomically. Over the last two decades, there has been over a 1000% increase in type 2 diabetes in children.[1] A mere 15 years ago, only 3% of all cases of diabetes in children were type 2 diabetes; now that number has climbed to 50%.[2] Furthermore, what is shocking is that 40% of children are now overweight and 2 million are morbidly obese (exceeding the 99th percentile for weight).[3] The good news, however, is that the causes of type 2 diabetes, metabolic syndrome, and insulin resistance are all completely curable and preventable. This is possible because these diseases are primarily caused by preventable environmental and lifestyle factors.

This article will focus on what I refer to as "the continuum of insulin resistance," with particular attention to early detection of insulin resistance and tools to reverse it in order to avoid the consequences as well as the progression to diabetes. My goal is to provide tools to help clinicians become better detectives with a high index of suspicion as we look for signs and symptoms of insulin resistance in our patients.

Insulin Resistance: The Bigger Picture

Insulin resistance is part of a bigger picture. That bigger picture is obesity, inflammation, and cardiovascular disease. The relationship between obesity and insulin resistance has been studied by countless researchers who maintain that one of the main reasons for the increase in diabetes and insulin resistance is obesity. I would actually say the opposite is true; that the reason we see such a big increase in obesity is because of insulin resistance. I am not disputing the fact that obesity can lead to insulin resistance; I am saying that a major cause of obesity is due to insulin resistance. Therefore, through my clinical experience and research, I believe that the major cause of weight gain is undiagnosed insulin resistance.

We know that people with diabetes suffer vascular disease at much higher rates. It is estimated that diabetics are 4 times more likely to die of heart disease than their nondiabetic counterparts. Furthermore, the rate of cerebrovascular accidents (CVAs) is 3 to 4 times higher in diabetics. These risks apply not only for the fully diabetic patient, however; they also encompass those who are "prediabetic." Patients with prediabetes are 4 times more likely to die of heart disease and have a 21% higher risk of stroke. Therefore, the prefix *pre-* in *prediabetes* is arguably not really "pre" any disease at all! People with prediabetes are already in a disease state because of such a high level of insulin resistance in their bodies. Therefore, it is not the diagnosis of diabetes alone that renders higher risk for major life-threatening diseases, but rather a patient's state of insulin resistance. This is the real problem and where our focus should be as clinicians.

As clinicians we need to ascertain why and how a patient became insulin resistant. How and where do we start? How do we identify insulin resistance, and how do we treat it? What is the root cause? Why is a person insulin resistant? Applying functional medicine principles to search for the answers to these questions is an objective of this article.

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Insulin Resistance

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Definitions: Insulin Resistance Continuum

Almost every day, I hear practitioners refer to metabolic syndrome and insulin resistance in the same sentence, almost as if they were synonymous. On the contrary, they are quite different, and this difference needs to be understood. Insulin resistance, impaired glucose tolerance, prediabetes, and diabetes mellitus type 2 are all part of a progressive continuum of dysfunction and it is important to know the definition of each in order to properly diagnose and treat patients. Thus, depending upon where the patient falls in this spectrum, clinicians can determine how aggressive the course and type of treatment must be. In any case, our main aim as clinicians should be to preserve pancreatic function as much as possible and reverse insulin resistance.

Insulin Resistance

Simply put, insulin resistance is a condition wherein insulin becomes less effective at lowering blood sugar. In other words, it is the inability of insulin to facilitate glucose uptake from the blood into the cell (because of poor insulin binding at the receptor cells). The body responds to this by stimulating the pancreas to produce more insulin so that some glucose can leave the bloodstream and enter the cells. Initially, the body's response is effective in that the excess insulin is able to keep blood sugar in the normal range. However, the first sign of imbalance lies in the above normal levels of insulin production.

Impaired Glucose Tolerance

Impaired glucose tolerance occurs when glucose rises above the normal range in spite of the pancreas's continuing to overproduce insulin. The rise can be seen after meals or in the fasting state. In many patients at this stage along the continuum, fasting glucose may be normal, but you will see an elevated glucose level after a meal or after a high glycemic load. Levels are elevated but not enough to qualify the patient as prediabetic. These are the patients in whom you see an elevated hemoglobin A1c (HgbA1c) despite a normal fasting glucose. Simply put, impaired glucose tolerance is when the pancreas is no longer able to keep blood sugar normal after a glucose challenge.

Prediabetes

As the pancreas continues to overproduce insulin it is not longer able to keep fasting blood sugar in the normal range. By definition it is a fasting blood sugar over 100 mg/dL to 125 mg/dL. As you can see, this is a severe and advanced state of disease. Close behind prediabetes is the end of the continuum. Therefore, prediabetes is clearly a state of major dysfunction and it is not "pre" any disease! It is a disease in and of itself.

Diabetes Mellitus Type 2

Fasting blood sugar of 126 mg/dL or higher, or a random blood sugar of over 200 mg/dL on more than one occasion.

Metabolic Syndrome vs. Insulin Resistance

The synergistic, aggregate effects of insulin resistance, obesity, hypertension (HTN), and dyslipidemia all form a construct called *metabolic syndrome*.[4] This name was established through the recognition by the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) 2004 update, of the importance of cardiovascular disease (CVD) risk factors. Metabolic syndrome was initially coined "syndrome X" by Gerald Reaven, as "a constellation of lipid and non-lipid risk factors of metabolic origin."[5] Risk factors for metabolic syndrome include visceral adiposity, high body mass index (BMI), insulin resistance, and high insulin. In order to have metabolic syndrome, a patient must have 3 out of 5 of the following characteristics present: increased waist circumference (greater than 40 inches for men and 35 inches for women), hypertension (blood pressure greater than 130/85 mmHg), elevated triglycerides (greater than 150 mg/dL), elevated fasting blood sugar (greater than 100 mg/dL), and decreased HDL (40 mg/dL in men and 50mg/dL in women).

Focus has recently shifted to insulin resistance as the dominant and independent predictor of age-related diseases. By definition, a normal blood sugar level is less than 100 mg/dL. However, we know that risks extend below that threshold. Studies have shown that a blood sugar greater than 87 mg/dL equals a progressive increase of diabetes type 2. Further, the lowest risk of progression from insulin resistance to diabetes type 2 is a fasting blood sugar less than 81 mg/dL.[6]

In the US we have seen rises in obesity in epidemic proportions in the last 20 years.[7] Among the American adults who are simply overweight, over 70% of them already have "prediabetes." Thus, as a consequence of undiagnosed and untreated insulin resistance, the American overweight have significant risks of cardiovascular disease and even death. The unfortunate piece is that most of these people don't even know that they have this problem and remain at risk. The issue is further aggravated by the fact that there are no current national screening guidelines and no reimbursement to health-care providers for diagnosing or treating anything but full-blown diabetes. Doctors are not trained or paid to properly diagnose or treat the biggest chronic disease in the US – insulin resistance. In sum, it is a well-known fact that obesity increases insulin resistance and thus diabetes risk. However, as I stated above, the reverse is also true. The most important *cause* of obesity is increasing insulin resistance. Once insulin resistance has been established, physicians next have to find out why a person developed insulin resistance in the first place.

Identifying Patients at Risk

It is not always as simple as looking at a patient's stature to tell whether s/he has insulin resistance. According to the National Health and Nutrition Evaluation Survey (NHANES) correlation study from 1999–2004, up to 25% of normal-weight patients (BMI less than 25) may be insulin resistant.[8] Further, some patients can be insulin resistant and still have normal fasting insulin levels, normal HgbA1c, and normal fasting glucose. So the question becomes, how do we identify the patients at risk? I believe that this is best addressed by looking at the various factors that influence genes and metabolism – both of which underlie the abnormal patterns of function seen in hyperinsulinemia.

My Protocol

I have developed my own treatment protocol for insulin resistance which incorporates functional medicine principles. This includes a thorough and detailed history as well as a complete physical examination. In taking a history from a patient, I look for basic imbalances in digestion/absorption/barrier integrity, in detoxification, hormone/neurotransmitter health, immune/inflammatory process, or mind/spirit equilibrium. The goal is to get to the underlying cause of illness. We want to connect the dots in the history and get to the root cause or the foundation of the dysfunction. So once I've investigated how each patient developed insulin resistance and I've established the underlying causes, I stage patients, based on their symptoms, along the continuum of insulin resistance. I then individualize a treatment protocol that incorporates certain basic standards (see Table 1).

Staging the Patient

Staging allows us to determine where along the continuum of insulin resistance each patient lies. It is the stage that will determine the treatment. It will also determine how likely patients are to progress to type 2 diabetes. In the continuum of insulin resistance, with illness on one end and wellness on the other, as we progress from insulin sensitive we become insulin resistant, then develop impaired glucose tolerance, then comes prediabetes, then finally diabetes.

There are three stages: stage 1 is when adiponectin (an adipose-derived protein) starts to decrease, in stage 2 insulin is already starting to increase, and in stage 3 the pro-insulin (the prohormone precursor to insulin) increases. Not everyone presents in precisely these stages. There may be variations. We also know that there may be some patients who fall between type 1 and type 2, and this is usually due to an underlying autoimmune disease.[9] This is valuable because manifestations of insulin resistance and metabolic syndrome all reside along the continuum of insulin resistance, and each stage will direct proper treatment. For instance, if someone starts out with insulin resistance and hyperlipidemia, it is the insulin resistance that is increasing the progression to glucose intolerance and prediabetes, so we would treat that first and foremost.

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Table 1: Insulin Resistance Assessment Protocol

Diet	• Processed foods • High in sugar and high-fructose corn syrup • Trans, hydrogenated, and saturated fats • Polyunsaturated omega-6 oils (except gamma linoleic acid [GLA]) • Low in vegetables, fruits and antioxidants • Low in fiber
Hydration	Assess hydration status, and source/content of water and liquids can be cause of insulin resistance (sugar and high-fructose corn syrup)
Food allergies/sensitivities	Modify and personalize elimination diet/ketogenic diet and/or functional testing for allergies and sensitivities
Oxidative stress and/or mitochondrial dysfunction	Assess clinically and with laboratory evaluation
Stress and adrenal fatigue	• Lack of exercise • Poor sleep
Hormone imbalance	Use history and physical as well as laboratory evaluation
Toxins	Heavy metals, persistent organic pollutants, endocrine-disruptors, volatile solvents, dirty electricity, electromagnetic radiation, suboptimal estrogen metabolism, etc.
Dysbiosis	Assess with comprehensive stool analysis
Infections	• Occult, esp. dental • Gastrointestinal (GI) • Viral, bacterial, and fungal
Nutrient deficiencies	Including vitamins, minerals, antioxidants, amino acids, methylating factors, and essential fatty acids. Assess clinically with history and physical and with functional and/or conventional testing
Prescription drugs	Prior statin (cholesterol lowering drug) use
Hyperinsulinemia causing insulin resistance; beta cell dysfunction	Review all above to look for root cause

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Laboratory Evaluation

Not all insulin-resistant patients develop diabetes. However, insulin resistance is the underlying reason for a variety of health concerns. For example, it constitutes increases in cardiovascular risk. Consequently, we see again that it is very important to identify the people with insulin resistance and promptly treat them in order to halt and reverse disease progression. Laboratory evaluations are another tool to help guide us in our assessment of patients' status along the continuum of insulin resistance.

Most conventional ranges for laboratory results are very broad because we are looking at disease ranges and not functional ranges. A general guideline is that normal functional medicine ranges are in the middle to upper three-quarters of conventional ranges. This helps when analyzing results for patients who can only do conventional labs.

Hemoglobin A1C

Hemoglobin A1C (HgbA1C) was developed to see if diabetic patients were being compliant with their medication. Put simply, it measures the amount of glucose that is bound to our hemoglobin. It was not developed as a screening tool, although it is being used as one nowadays. So what does it mean if a HgbA1C is elevated? Where does that place the patient on the continuum? The answer is that if a HgbA1C is 5.4 or higher, the patient has impaired glucose tolerance. If the HgbA1C has changed, the patient already has hyperglycemia. However, it might be only postprandial and not in the fasting state, so we need to have patients check the postprandial blood sugars at home.

At this point along the continuum, we want to preserve beta cell function and aggressively address the underlying cause. HgbA1c is an independent risk factor for cardiovascular mortality: "The predictive value of HgbA1c for total mortality was stronger than that documented for cholesterol concentration, body mass index and blood pressure."[10]

HOMA-IR

HOMA-IR is a homeostatic model assessment for insulin resistance. It is a calculation based on plasma levels of fasting glucose and insulin. It is used to assess insulin sensitivity. I think that there are better ways of assessing this and have thus provided more means below.

Adiponectin, Insulin, and Pro-Insulin: Staging the Progression of Insulin Resistance to Prediabetes and Diabetes Type 2

Adiponectin protects against atherosclerosis, moderates fat tissue, promotes insulin sensitivity, and decreases hepatic glucose and lipid production. Adiponectin decreases before insulin increases. It is a marker of insulin sensitivity. We can also look at insulin, pro-insulin, HgbA1C, fasting glucose, and 2-hour postprandial and 30-minute insulin levels after a 75g glucose load. This can be done through any conventional laboratory as well as through functional labs. With a functional lab we get the results plotted on a colorful graph. With conventional labs we would have to plot the results on a graph to ascertain where the patient is. In optimal control, adiponectin will be normal, fasting insulin will be 5 to 7 (conventional laboratory value), HgbA1C would be 5.3 or less, and fasting sugar should be less than 81 mg/dL. The risk of diabetes significantly increases when the fasting blood glucose is greater than 87 mg/dL.[6]

In stage 1, adiponectin is declining and fasting insulin is still normal. Postprandial insulin might be elevated, but our primary determining factor of stage 1 is a normal fasting insulin. Pro-insulin is normal. Glucose is normal too. Adiponectin is a key link that needs to be restored as much as possible because low adiponectin is a marker for insulin resistance, which means that the patient is more at risk for dyslipidemia. With that, there is increased risk for vascular injury and progression along the continuum toward type 2 diabetes. Plus decreasing adiponectin also tends to be associated with increasing inflammatory markers. At stage 1, we would see low adiponectin, normal HOMA-IR (although it could be slightly elevated), normal glucose, normal HgbA1C, normal insulin, and normal pro-insulin.

Treatment includes diet and lifestyle changes. Focus is on body composition and making sure that patients are eating the most healthful diet possible. Many experts recommend a Mediterranean-type, low-glycemic-load diet, but I think that the diet needs to personalized to each individual.

Stage 2 progresses from stage 1. Adiponectin is decreasing, insulin is starting to increase, and pro-insulin is still normal. There could be early beta cell impairment. There will be a higher normal HOMA-IR, higher than normal insulin, even a high postprandial glucose, and fasting glucose can be borderline as well as average glucose's possibly being mildly elevated (or not at all). Usually stage 2 treatment consists of lifestyle changes and supplementation. We do not start pharmacotherapy until early into stage 3, and even then we may be able to reverse it with diet, nutrition, lifestyle modification, and nutraceutical support. Again it is case dependent.

In stage 3, pro-insulin is increasing. Elevated pro-insulin means that the pancreas is struggling to keep glucose normal. The pancreas is trying to send out insulin as fast as it can before the final cleavage has happened. In stage 3, there is low adiponectin, high HOMA-IR, high insulin, elevated pro-insulin, possibly high glucose, and high HgbA1C. Some patients can maintain normal or close to normal fasting glucose even with these numbers. However, the moment you challenge them with a glucose load, their postprandial level will be high. Elevated pro-insulin means

that the final cleavage to produce insulin has not happened. They may not be diabetic. They might not even fulfill the full criteria for prediabetes (remember the ADA definition for prediabetes is a fasting glucose level of 100–125 mg/dl). The number one treatment aim in a patient in stage 3 is to preserve beta cell function as much as possible. There may be a totally normal fasting glucose, but in most cases the postprandial glucose will increase the moment you challenge them with a high-glycemic-load meal. Having patients check postprandial glucose levels also helps them learn what particular foods increase their glucose level.

Treatment: My Approach

Table 2 presents my approach for the treatment of insulin resistance. You will need to address these factors both at baseline and throughout the course of treatment.

Table 2: Insulin Resistance Treatment Protocol

- Foundation is nutritional support with wholesome food (fresh, whole, unprocessed, organic, colorful) with 9–11 servings vegetables per day.
- Identify the underlying functional imbalances, prioritize, and address.
- Personalize the elimination diet or modified ketogenic diet according to individual patient needs.
- Lifestyle modification: individualized stress reduction, alcohol consumption, smoking cessation.
- Exercise: tailor to individual patient needs.
- Nutritional supplementation: personalized based on clinical exam and laboratory testing.
- Mind-body-spirit connection: find and foster purpose and meaning in life.
- Assess need for pharmacological treatment based on functional testing, patient needs, and response to above approach.

Insulin Resistance

Dietary Management

Dietary management for the patient with insulin resistance includes decreasing insulin stimulation. Dietary modifications that decrease insulin release include exploring fiber, good and bad fats, and simple and complex carbohydrates, and taking the time to educate patients about the difference. It is important to make sure that they have protein at every meal and with every snack. Eliminate most inflammatory foods, including wheat, dairy, soy, corn, and nightshades. Give agents that increase cellular responsiveness to insulin, including chromium, alpha lipoic acid, magnesium, CoQ10, and protein kinase modulators, to name a few.

To summarize, their diet should be a low-carbohydrate, low-glycemic-load diet that incorporates

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healthful fats. This will help decrease inflammation. Include organic, fresh, whole, unprocessed, colorful food. Eliminate sugar, trans fats, some saturated fats, and food allergens. Address the areas of dysfunction or imbalance, and prioritize. The elimination diet is helpful to identify and remove any dietary source of inflammation.

Phytochemicals

Many phytochemicals work as tissue specific kinase response modulators (SKRMs). Kinases are enzymes that facilitate insulin function. These are going to affect cellular communication and cellular signaling. Some dietary phytochemicals that modulate these pathways include berberine, cinnamon, ginseng, quercetin, resveratrol, green tea extract, and hops extract.

Nutrients known to modify insulin responsiveness at the cellular level include chromium, alpha-lipoic-acid, CoQ10, vitamin D, magnesium, vitamin C, vitamin E, omega-3 fatty acids, and chromium. A recent study on chromium and insulin resistance in children showed good results using 400 mcg chromium chloride.[11]

Micronutrient Recommendations

- Chromium: Generally give 1000 mcg/daily if insulin resistant. Likely most effective if deficient, but difficult to test.
- Vitamin D: Test 25(OH)D and supplement as appropriate (or supplement 2000–5000) IU/daily. Vitamin D levels should be 50–80 ng/ml, depending on whether other medical conditions are present. A study showed a positive correlation of 25(OH)D concentration with insulin sensitivity and a negative effect of hypovitaminosis D on beta cell function. Subjects with hypovitaminosis D are at higher risk of insulin resistance and the metabolic syndrome. Increasing 25(OH)D from 10–30 ng/mL can improve insulin sensitivity by 60%.[16]
- CoQ10: Generally supplement in patients with metabolic syndrome, insulin resistance, hypertension, or mitochondrial dysfunction. COQ10 dose depends on functional levels: optimize to >2 mcg/mL (plasma). In a patient with high oxidative stress or mitochondrial dysfunction, you may need to supplement at a much higher dose. We know that 120 mg/day of coenzyme Q10 improves glycemic control and blood pressure in NIDDM (non-insulin-dependent diabetes mellitus). 200 mg of CoQ10 daily improved HgA1C and blood pressure in NIDDM patients.[12,13]
- Alpha-lipoic acid: Doses of 600 to 1800 mg/day of alpha-lipoic acid (ALA) can improve insulin

sensitivity in patients with type 2 diabetes. And 600–1200 mg/day of ALA may improve microcirculation and diabetic polyneuropathy.[14,15]

- Magnesium: Epidemiological studies show that high daily Mg intake is predictive of a lower incidence of NIDDM. Poor intracellular Mg concentration is found in NIDDM and in hypertensive patients. Daily Mg administration in NIDDM and insulin-resistant patients restores intracellular Mg concentration and contributes to improve insulin sensitivity and glucose uptake.[17] Magnesium supplementation has been shown to improve insulin sensitivity.[18] Many patients have a hard time absorbing magnesium intracellularly. A buccal swab is the best way to assess intracellular magnesium. Patients with low magnesium are at a slightly higher risk for atrial fibrillation and arrhythmias. Many of these patients may also need potassium. I use magnesium glycinate because it is going to have less effect on the gut in terms of causing loose bowels and it is generally well absorbed. I generally start at 200–400 mg of a chelated magnesium and increase to bowel tolerance if normal kidney function is established.

Exploring Detoxification

Toxins can be another underlying problem causing insulin resistance. Toxic endocrine disruptors affect estrogen and estrogen metabolism (endocrine disruptors in the etiology of type 2 diabetes mellitus).[19] The literature shows that even a GGTP in the high normal range is associated with insulin resistance. Start to monitor GGTP. Consider it high if it is 30 IU/L or higher. If it is over 40 IU/L then glutathione production needs to be improved. Low-dose organochlorine pesticides and polychlorinated biphenyls predict obesity, dyslipidemia, and insulin resistance among people free of diabetes.[20] Metals may also be a problem and can contribute to insulin resistance.

Exercise

Exercise is extremely important. According to the WHO, adults aged 18 to 64 should do at least 150 minutes of moderate-intensity aerobic physical activity or 75 minutes of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate and vigorous-intensity activity. Aerobic activity should be performed in bouts of at least 10 minutes' duration. For additional health benefits, adults should increase their moderate-intensity aerobic physical activity to 300 minutes per week, or engage in 150 minutes of vigorous-intensity aerobic physical activity per week, or an equivalent combination of moderate and vigorous-intensity activity. Muscle-strengthening activities should be done involving major muscle groups on 2 or more days a week. Exercise alters skeletal muscle metabolism and improves glucose uptake, reduces low-density lipoprotein, raises HDL, lowers blood pressure, and reduces inflammation and oxidative stress.[21] In a Diabetes Prevention Program Research Group 2002 study, 3234 prediabetics were randomized to placebo, metformin, or lifestyle modification (≥7% weight loss and ≥150 min/week of physical activity) for 2.8 years. Compared with the placebo group, lifestyle intervention decreased incidence of type 2 diabetes by 58%. Metformin (850 mg b.i.d.) decreased type 2 diabetes mellitus by only 31%.[22]

Assess how much a patient is moving his/her body and design a program that fits the patient. It is extremely important to devise an appropriate exercise regimen for each patient that incorporates aerobic and weight training and reevaluate at regular intervals and change as appropriate. Interval training has worked well for many of my patients. Generally, I review some of the published studies with patients and give them the choice between diet/lifestyle and physical activity versus medication, including the potential side effects. Typically patients always choose diet and lifestyle. I inform them if they do not change their diet, lifestyle, and stress reduction, I can pretty accurately predict what their outcome will be. Are they willing to take those risks? I have found that when I explain how diet, nutrition, exercise, and lifestyle modification has been proved superior to prescription medications, patients are not only amazed but choose and succeed with the former.

Stress and Autonomic Dysfunction

The effect of stress on insulin resistance is very important to explore: Autonomic dysfunction contributes to heart disease and vascular disease. Autonomic dysfunction can be measured by heart rate variability. Lower heart rate variability is correlated with impaired pancreatic function in patients with coronary artery disease.[23] As your heart rate variability decreases, you progress from insulin resistance to impaired glucose tolerance to diabetes. With this connection, the dysregulation of the autonomic nervous system can now be linked to visceral adiposity and insulin resistance. In a study of subjects with either a family history of DM or no family history, subjects genetically predisposed to NIDDM had more visceral fat and lower insulin sensitivity compared with controls. Visceral fat (not subcutaneous fat) was associated with lower heart rate variability.

Sleep

Sleep is extremely important. The average amount patients should be sleeping is 7 to 7½ hours per night. I encourage my patients to sleep at least 8 hours per night. What is the quality of their sleep? Are they waking up multiple times? Are they feeling rested when they wake up? Sleep deprivation may lead to insulin resistance and subsequently, to diabetes mellitus.[24] Lack of sleep can affect insulin resistance in several different ways. It can cause insulin

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resistance due to inflammation, changes in glucose metabolism, altered appetite, and HPA changes. Also, obstructive sleep apnea can affect insulin resistance, metabolic syndrome, and disordered breathing, so we need to have a high index of suspicion for this in our patients.

Conclusion

We have established that insulin resistance is a disease within and of itself, contributing to numerous chronic and life-threatening conditions and affecting countless undiagnosed patients. However, once again, the good news is that insulin resistance as well as the progression to diabetes can not only be prevented but treated and reversed as well. Therefore, it is our responsibility as clinicians to track down early cases of insulin resistance before they advance into later stages along the continuum and to reverse the damage that has occurred. Likewise, it is our duty to offer an effective protocol to those who already suffer from a clinical diagnosis of diabetes or prediabetes.

Functional medicine tools help us identify the underlying dysfunctions and the root causes in a personalized manner. Using our clinical evaluation as well as laboratory measurements including adiponectin, fasting insulin, pro-insulin, HgbA1c, postprandial insulin, and glucose, we can assess where the patient lies along the continuum of insulin resistance. Then, once the stage of insulin resistance has been identified, we can tailor a treatment plan in order to prevent further progression to diabetes and reverse beta cell dysfunction. As needed, treatment options may address any of the following areas of a patient's life: diet, sleep, stress, exposure to toxins and ability to detoxify, exercise, and/or micronutrient consumption. In conclusion, by way of acknowledging the role of insulin resistance in the bigger picture of obesity, diabetes, and cardiovascular disease, we are able to recognize how vitally important it is to incorporate the effective diagnosis and treatment of insulin resistance into clinical practice.

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Nonalcoholic Fatty Liver Disease in Chronic Hepatitis C

by Lyn Patrick, ND

Nonalcoholic fatty liver disease (NAFLD) is epidemic among overweight and obese individuals in developing nations and affects approximately 30% to 46% of all adults in the US.[1] Insulin resistance is the main risk factor for this condition, and NAFLD is considered the hepatic manifestation of cardiometabolic syndrome.

Another risk factor for NAFLD is chronic hepatitis C virus infection (HCV). It is considered an epidemic for a reason: 200 million people in the world have chronic hepatitis C, including up to 5 million in the US.[2,3] Fatty liver in chronic hepatitis C is an epidemic within an epidemic: up to 70% of those with chronic hepatitis C will have steatosis.[4]

Fatty liver is important in HCV for a number of reasons: steatosis increases risk for failing standard antiviral therapy, and the more severe form of nonalcoholic steatotic hepatitis (NASH) increases risk for progression to cirrhosis and hepatocellular carcinoma.[5–7]

Insulin resistance is also the main mechanism in the genesis of NAFLD in HCV, and the virus itself increases risk for insulin resistance and type 2 diabetes; up to 70% of HCV-infected individuals over age 40 in a recent NHANES study had type 2 diabetes.[8]

So, the logical question arises for clinicians, should all patients with diagnosed NAFLD be screened for chronic hepatitis C? And should all chronic hepatitis C patients be screened for NASH, the progressed form of NAFLD? And, as importantly, what are the treatment approaches for this epidemic within an epidemic?

To address the first question: should a patient with fatty liver disease not caused by drugs; alcohol; metabolic disease; environmental exposure to solvents, PCBs, and so on; or bariatric surgery be tested for hepatitis C? The answer is *yes*, unless you can pinpoint another cause. And even then, if the patient is between ages 47 and 67, the answer is doubly *yes*. The American Association for the Study of Liver Disease Practice Guidelines for NAFLD, published June 2012, agrees that HCV testing is appropriate and so does the Centers for Disease Control, whose guidelines for testing were recently published in August 2012.[9,10]

And the second question, do all HCV-infected individuals need to be screened for NAFLD? There are no guidelines for screening or treatment specifically for HCV-infected persons, only the suggestion that measures to improve insulin sensitivity and reach a body mass index under 25 would increase chances of sustained viral responses (the definition of successful standard treatment).[11] This recommendation may stem from the fact that steatosis is common in HCV; but, aside from successful antiviral therapy, there is no clear strategy for how to intercept the fibrosis process.[12]

Steatosis in HCV infection follows the same ethnic risks as it does in the general population. It is more common in Latinos than in Caucasians, and more common in Caucasians than in African Americans. Interestingly, African Americans are for the most part spared from HCV-related steatosis. And, as in the general population, alcohol, obesity, diabetes, and hyperlipidemia are major risk factors for steatosis in those who are HCV infected.[13] Weight loss and exercise, the only approved treatment strategies for NAFLD, are specifically relevant in the above risk groups, particularly if standard treatment is suggested.

HCV-infected individuals, though, are different than their HCV-negative counterparts, as they could be considered "doubly blessed": the virus itself affects insulin signaling pathways even in the absence of obesity, leading to insulin resistance. Lifestyle modification in not always enough to reverse the inflammatory effects of the viral infection, because the infection itself leads to the production of free radicals that drive steatosis. This is particularly important in genotype 1 (the majority of HCV in the US) patients, in whom even successful antiviral treatment does not improve fatty liver, since the signaling turned on by the virus cannot be turned off in its absence.[14,15] With genotype 3 patients, who are at the highest risk of fatty liver, this does not appear to be the case. In these patients, the virus itself appears to affect lipid synthesis in the liver, and viral clearance improves steatosis posttreatment.[12]

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The mechanisms involved in virally induced steatosis and fibrosis include interactions between oxidative stress, inflammation, and altered cell signaling – resulting in increased liver cell apoptosis and likelihood of both fat accumulation and lipid peroxidation in hepatocytes.[16]

Diagnosis

The actual diagnostic criteria for NAFLD in HCV are essentially the same as in individuals who are HCV negative. But because serum ALT/AST levels and imaging tests (abdominal ultrasound, CT, and MR) cannot reliably assess steatohepatitis and fibrosis in NAFLD, there is increasing interest in using fibrosis scoring to evaluate the need for liver biopsy, the gold standard in diagnosis of NAFLD and NASH.[9] The American Association for the Study of Liver Disease (AASLD) guidelines include the formula-based NAFLD Fibrosis Score, which is based on six readily available variables (age, BMI, hyperglycemia, platelet count, albumin, AST/ALT ratio). It is calculated using the published formula (http://nafldscore.com).[9] In a meta-analysis of 3064 patients in 13 studies, NAFLD Fibrosis Score could effectively predict and exclude advanced fibrosis and may be helpful along with other blood work (FibroSure or FIBROSpect) in determining the need for liver biopsy when ultrasound is not definitive.[17] Elevated ferritin, as in the general population, is also a risk factor for steatosis in those with HCV infection.

Screening for NAFLD simply using the symptoms of metabolic syndrome used for the general population may not be effective for HCV-infected individuals, at least those with genotypes 1 and 2. While metabolic syndrome occurs in 28% of the HCV-negative population with NAFLD, Italian researchers found that metabolic syndrome was only present in 6% of those with both NAFLD and genotype 1 or 2 HCV infection.[18] Those with HCV/NAFLD were more likely to be insulin resistant (elevated fasting glucose and elevated fasting insulin), be male, and have fibrosis on liver biopsy than their NAFLD counterparts without HCV. For those with genotype 3, central obesity and metabolic syndrome are more prevalent. Because up to 80% of individuals with genotype 3 virus have moderate to severe steatosis, it should be presumed, especially in patients with fibrosis.[12]

Treatment Options

In most HCV patients with nonalcoholic fatty liver, overnutrition and excessive carbohydrate intake, particularly fructose, can lead to elevated glucose and/or free fatty acids in the liver. These free fatty acids are subject to oxidation, resulting in stellate cell activation, mitochondrial dysfunction, and subsequent fibrosis.[19]

There is a consensus that the inclusion of omega-3 fatty acids, high monounsaturated fatty–acid containing food, fresh fruit and vegetables, and low–glycemic index, high-fiber foods and reduction of saturated fats, simple carbohydrates, and sweetened drinks are universally recommended.[20] Because dietary conditions contributing to insulin resistance may play an active part in HCV fatty liver, caloric restriction, weight loss, and exercise have been studied as therapeutic interventions. One study looking at 19 HCV overweight or obese patients with before-and-after liver biopsies showed that exercise-induced weight loss with as little as 2.6% body weight resulted in a reduction in steatosis. In two lean patients with genotype 3 in this trial, weight loss was also accompanied by a significant reduction in steatosis.[21] In a trial of obese HCV patients with steatosis, physical activity and dietary–intervention induced weight loss (as little as 5%) resulted in a reduction of both ALT and fasting insulin that was sustained after the weight loss plateaued.[22] The significant effect of such modest amounts of weight may be the influence of exercise and calorie restriction on adipocytokines, particularly adiponectin, which is reduced in insulin resistance and obesity.

Testosterone

Adiponectin has strong anti-inflammatory and insulin-sensitizing properties, and has been shown to reduce hepatic steatosis, prevent liver fibrosis, and reduce insulin resistance. Along with exercise-induced weight loss, omega-3 fatty acids, thiazolidinediones, and testosterone replacement have all been shown to normalize adiponectin synthesis and secretion.[23] Men with low testosterone are 5 times more likely to have NAFLD than men with high normal testosterone, even after adjusting for BMI and blood lipids.[24] And men with HCV who are undergoing standard treatment with interferon, or who already have advanced disease, are at risk for low testosterone levels.[25,26]

Antioxidants

Depressed levels of antioxidants have been found in HCV; blood levels of glutathione, vitamins A,C, and E and selenium were found to be significantly lower than in matched HCV-negative controls.[27] These levels were accompanied by elevated levels of oxidant stress markers that correlated with steatosis and fibrosis in these patients. Evidence of oxidant stress is also seen in HCV patients with minimal fibrosis. Impaired oxidation of free fatty acids causing oxidant stress in the liver is one of the mechanisms for steatosis in HCV, and hyperactivity of nitric oxide synthase, impaired mitochondrial function, and net depletion of antioxidants such as glutathione are all thought to contribute as triggers for steatosis.[28]

Vitamin E specifically quenches free radicals found in hepatic tissue. A small study in HCV patients with 1200 IU alpha-tocopherol for 8 weeks resulted in blockage of the pathway

for stellate cell activation, preventing steatosis and fibrosis progression and an improvement in liver biopsy.[29] Other antioxidants, including zinc, N-acetylcysteine, and betaine, are under study for their ability to inhibit steatosis and subsequent fibrosis in HCV.[30,31] Low serum zinc levels are observed in hepatic fibrosis and hepatic encephalopathy and recently have been shown to correlate with insulin resistance in HCV.[32] Serum zinc is also inversely correlated with serum ferritin, and high ferritin levels are a common finding in both HCV NAFLD and NAFLD in the general population. Historically, dosing studies with zinc have been limited to extremely high doses of 400 to 600 mg zinc oxide in alcoholic cirrhosis-related hepatic encephalopathy. Recent studies, however, using 35 mg elemental zinc (as zinc L-carnosine) have shown dramatic improvements in necroinflammation, particularly in HCV patients with iron overload.[33]

Vitamin D

Vitamin D deficiency has been commonly reported in HCV patients, and low vitamin D in HCV infection is correlated with liver fibrosis.[34,35] Vitamin D has also been shown to reduce the extent of hepatic lipid peroxidation in animal models, which suggests that it modulates oxidative stress in viral hepatitis.[36] Because low blood vitamin D has been shown to impair ability to respond to standard treatment and supplementation during treatment to improve chances of response to standard treatment, assessing D levels and supplementation D in HCV is becoming more accepted.[37]

Notes

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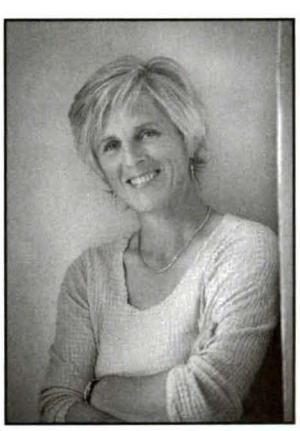

The Importance of Your Intestinal Tract for Health and Longevity

by Dr. Leonard Smith

One paradox of aging is the simple fact that inflammation (some now call it *inflammaging*) can be slowly claiming your health without your even feeling it. This silent inflammation is root cause of most, if not all, chronic disease, and must be addressed in order to achieve health well into old age. In some cases, silent inflammation is not so silent, as manifested in such debilitating conditions as fibromyalgia, chronic fatigue, and arthritis, to name a few. Important to understand is that inflammation anywhere in the body usually starts with the gut, and especially the aging gut.[1]

Studies indicate that with aging there are marked reductions of several important probiotic species, especially *Bifidobacterium* and *Bacteroides*, along with a reduction in short-chain fatty acids (SCFAs).[2] These bacterial imbalances can set the stage for improper immune sensing by the gut-associated lymphoid tissue (GALT), leading to increased inflammation and intestinal permeability (commonly known as leaky gut syndrome). The result is an increased production of many inflammatory proteins (IL-6, TNF-alpha, hsCRP, IL-1beta, IL-17, and fibrinogen, to name a few) both in the GALT and in peripheral blood mononuclear cells (PBMCs), which keeps your local gut and your entire systemic immune system dysregulated and out of balance, creating widespread, systemic inflammation.[1]

When immune-driven inflammation reaches a high enough level, many disease conditions may result, including cardiovascular disease (beginning as vascular endothelial dysfunction, or leaky artery syndrome), liver and renal dysfunction, dozens of autoimmune diseases, neurological diseases (often, leaky blood–brain barrier), obesity, insulin resistance, and the unheralded epidemic that is type 2 diabetes, as well as numerous infectious diseases. It is interesting to note that HIV and aging share cellular immunologic similarities. Both include expanded populations of memory T cells with reduced function and shortened telomeres as a result of constant antigen burden and persistent immune activation.[3]

Furthermore, chronic "leaky gut" along with immune dysregulation can lead to a hypoimmune state and set the stage for many diseases of viral origin, including viral hepatitis, HIV/AIDS, and even Alzheimer's with intraneuronal amyloid-beta plaque. It has been discovered that amyloid-beta is not simply cellular junk, but has a real purpose. Amyloid-beta is now thought to be an antimicrobial peptide made by the brain to fight viruses such as herpes simplex 1 virus and others.[4,5] When amyloid-beta cannot be eliminated quickly enough, neuronal death results. Other serious conditions following the same pattern include Hodgkin's disease years after Epstein-Barr virus and chronic (or reactivated) cytomegalovirus (CMV), which may be the agent causing the highly lethal brain tumor, glioblastoma multiforme (GBM).[6] Recent studies have shown that valganciclovir, an expensive and potent antiviral drug, more than doubles survival with GBM, and many deceased patients have shown viable CMV viruses in the brain on autopsy.[7]

There are at least five areas of health that can be problematic with age: poor diet, inadequate sleep, irregular elimination, inactivity, and stress – all of which can be associated with gut bacterial imbalances that lead to immune dysfunction and systemic inflammation. With correction in these areas, it is likely that more people will add life and quality to their years, as well as help avoid such downstream consequences as the conditions mentioned above.

Diet and Supplements

Some combination of the Mediterranean and Paleolithic diets will be ideal for most people. These diets are low in simple carbohydrates, refined sugars, trans fats, highly processed food, and saturated fats, while being high in vegetables; legumes; gluten-free grains such as quinoa, millet, amaranth, and buckwheat; seeds and nuts; and lower-glycemic fruits in moderation. Choosing organic and non-GMO foods is important, especially with all animal-derived foods. Supplementation with digestive enzymes, probiotics, omega-3 oils, vitamin D, and a multivitamin is recommended with meals.

Digestive enzymes would include a combination of betaine HCl, proteases, amylase, and lipase. For

probiotics, select a multistrain formula with about 50 to 100 billion colon-forming units (CFUs) per capsule of *Bifidobacteria* and *Lactobacilli*. In addition, consider taking the fungal probiotic *Saccharomyces boulardii* in a dose of 10 to 20 billion CFUs daily with meals. Take omega-3 oils high in DHA (500–2000 mg) and EPA (1000–3000 mg) in divided doses with meals daily. Adding a vitamin D3 supplement of at least 5000–7000 IU daily, taken with your largest plant-based, fat-containing meal to enhance absorption, is advised. Be sure to check your vitamin D and calcium levels with a physician at least 2 to 4 times per year. A good multivitamin-mineral-antioxidant with the active forms of B vitamins most days is also a beneficial way to stay healthy and avoid cancer.[8]

In addition, there are many natural antiviral treatments, including foremost vitamin C, vitamin A, selenium, zinc, mushroom extracts, oil of oregano, neem leaf extract, colloidal silver, garlic, St John's wort, elderberry, green tea, echinacea, and licorice.

Hydration

Drink at least 2 quarts per day of quality filtered or spring water (about half your body weight in ounces of water). It is crucial for your entire body – including your gut lining and bacteria – to drink plenty of clean water. Your gut epithelial lining and underlying lamina propria (together known as the mucosa or mucosal lining) are the major source of your immune system. It is estimated that 60% to 70% of the immune system is located in the intestinal tract and comes in contact with 20 tons or more of food, and an enormous number of microbes, in a lifetime. Our immune system functions best with large amounts and multiple species of beneficial and commensal (neutral, nonpathogenic) bacteria.

Fiber, Prebiotics, and Fermented Foods

Our beneficial bacteria, by fermenting soluble fiber, produce SCFAs – mainly butyrate, propionate, and acetate. Butyrate not only is a major energy source for the colon, it also helps prevent dysfunctional colonocytes from becoming polyps or cancer by increasing apoptosis in precancerous cells. Furthermore, butyrate and propionate have also been shown to have a beneficial effect on the immune system by dampening dendritic cell function and slowing down adaptive immunity.[9] This can be very important to prevent an upregulated, dysfunctional immune system from overresponding with inflammation to normal flora. This often happens with age and is also seen with inflammatory bowel conditions.[1] So a high-fiber, plant-based diet (at least 80% of diet) helps attract the optimum numbers of species and beneficial bacteria into our intestinal tract. This is the diet most attractive to beneficial and most commensal gut bacteria. These bacteria transform the food that we eat in many beneficial ways before the intestinal lining absorbs it.

Prebiotics, which act as foods for our beneficial bacteria, come from plant polysaccharides such as inulin, which selectively increases *Bifidobacterium* and tends to decrease pathogenic bacteria.

Eating cultured or fermented foods, such as yogurt, kefir, kimchi, miso, sauerkraut, and fermented vegetables, all of which contain beneficial bacteria, is a natural way to support gut flora. These foods have been consumed for thousands of years. Instructions on how to make these foods at home are readily available on the Internet.

Sleep

Sleep can be a big problem with aging. Generally, most people need at least 6 to 8 hours each night. Less than 5 hours of sleep per night is associated with increased calcification of the coronary arteries.[10] With insufficient sleep, the autonomic nervous system is unbalanced and has adverse effects on immune function and increases inflammation. Gut bacterial imbalance can also interfere with sleep, causing bloating, gas, and abdominal discomfort. Sleep studies are important and will often detect sleep apnea, a correctable condition. For many people, taking melatonin (which decreases with age), 5-HTP, and vitamin B6 could be all that is needed to attain restful sleep.

Elimination

Bowel elimination usually becomes more difficult with aging. First consider hydration, fiber, and exercise. It may be necessary to supplement with herbs for the intestinal tract and magnesium oxide or magnesium citrate to achieve daily, large-volume bowel movements. Colon hydrotherapy can also be helpful periodically to help maintain regularity and detoxification.

Exercise

Exercise is essential to good health. Some combination of aerobics (which can be as simple as walking daily), resistance training, and stretching can do wonders for balancing your immune system as well as improve your mental state. Exercise is also a way to clear the body of various toxins. A recent research article showed that with mice, regular exercise was associated with increased abundance, biodiversity, and composition of the gut microbiota, and these microbiotas were more resistant to changes when exposed to polychlorinated biphenols (PCBs) than in the nonexercised mice.[11]

Stress Management

Stress may be the biggest problem with aging, often due to decreased hormones; increased cortisol and sarcopenia; decrease in vision, hearing, taste, smell, strength, and balance; sleep difficulties; and pain from inflammation in joints and muscles. Intestinal dysbiosis can also cause stress or may be the result of stress.[12] In either case, there are often increased pathogens, including overgrowth of *Candida* (which lowers innate immunity by decreasing natural killer cell function) and not enough

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strains or numbers of beneficial bacteria. Without taking probiotics and eating the right diet, it can be difficult to maintain healthy gut flora while dealing with chronic stress.

Exercise, meditation, spiritual practices, cognitive behavior therapy, yoga, or tai chi can all be helpful when dealing with stress, as well as rebalancing the gut bacteria with right diet, prebiotics, and probiotics.

Diagnostic Testing

There are several diagnostic specialty tests that can be helpful in checking for inflammation and active, asymptomatic viral and/or bacterial infections such as *Helicobacter pylori*. Most infections can be monitored by measuring the body's production of IgG antibodies for chronic infection and IgM antibodies for more acute or active infections. Measuring a viral load with a PCR test gives more quantitative information, but these tests are more expensive.

Other tests to determine your inflammation and immunity profile would include:

- Nutra Eval by Genova/Metametrix: measures 120 different analytes covering antioxidants, vitamins, neurotransmitters, dysbiosis, toxin levels, and RBC minerals, toxins, and essential fatty acids;
- Genova/Metametrix or Doctor's Data: comprehensive digestive stool analysis with parasites;
- Doctor's Data or Genova/Metametrix: heavy metal testing;
- 25-OH vitamin D blood level (generally keep between 50–80 ng/mL); work closely with a doctor with knowledge of all aspects of vitamin D. The Vitamin D Council is an excellent resource. You can get home kits for 25-OH vitamin D from ZRT Labs.

These tests and many others can be ordered via your health-care practitioner. In addition, tests can be ordered online through www.labtestingdirect.com.

The Mind Component

If we think that what we feed the body is important, please realize that what we feed the mind and soul is even more important. Perhaps the condition that we actually want to "catch as it goes viral" is inner peace. Be on the lookout for symptoms of inner peace. The hearts of a great many have already been exposed to inner peace, and it is possible that people everywhere could come down with it in epidemic proportions. This could pose a serious threat to what has, up to now, been a fairly stable condition of conflict in the world.

Some signs and symptoms of inner peace (by Saskia Davis, RN):

- a tendency to think and act spontaneously rather than on fears based on past experiences.
- an unmistakable ability to enjoy each moment.
- a loss of interest in judging other people.
- a loss of interest in judging self.
- a loss of interest in interpreting the actions of others.
- a loss of interest in conflict.
- a loss of the ability to worry.
- frequent, overwhelming episodes of appreciation.
- contented feelings of connectedness with others and nature.
- frequent attacks of smiling.
- an increasing tendency to let things happen rather than make them happen.
- an increased susceptibility to the love extended by others as well as the uncontrollable urge to extend it.[13]

If we can cultivate even some of these symptoms, it will likely help restore our autonomic and hormonal balance, as well as heal our immune and endocrine systems and help rebalance our gut flora.

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Leonard Smith is a retired general, vascular, and cancer surgeon as well as an expert on nutrition and natural supplementation. For the past 30 years, Dr. Smith has studied countless holistic medical programs, including those focusing on nutrition, supplementation based on lab testing, exercise, sleep, detoxification, stress management and the relevance of mental and spiritual attitude with regard to healing. He is currently on the volunteer faculty of the Department of Surgery and is a medical advisor and lecturer for the Division of Integrative Medicine at the University of Miami, Florida. Acknowledging the effectiveness of whole organic foods and nutritional supplementation, Dr. Smith strives to stay on the cutting edge of research and keep pace with the latest advances in the field of functional nutrition. In his role as medical director for Advanced Naturals, he is involved extensively in the research and formulation of new products.

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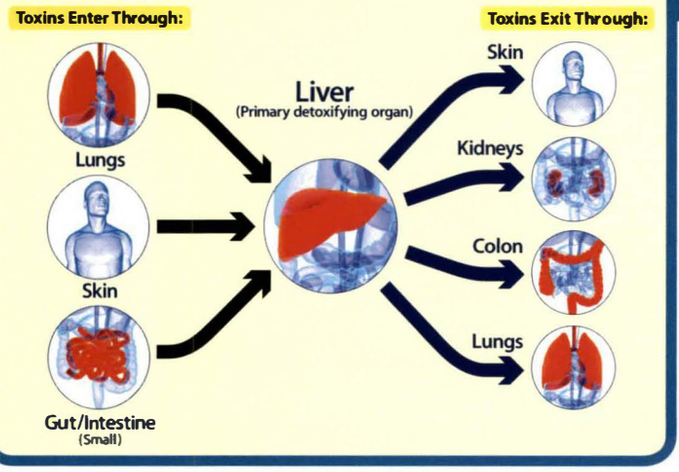

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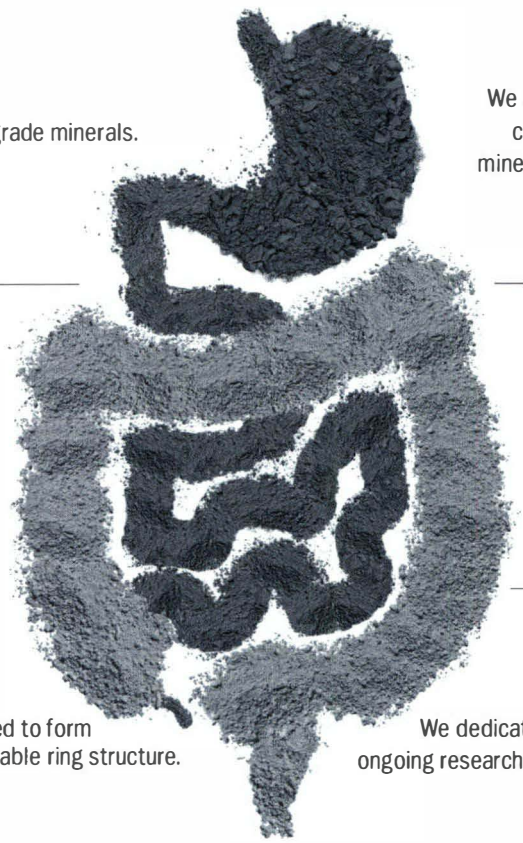

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Introducing Baby to Solid Foods

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

The scientific consensus on when solid food should be introduced into a baby's diet has shifted dramatically. Those of us who were trained in years past left school with complex schedules that stringently delayed introductions of potentially allergenic foods. The common practice in pediatrics was to delay solid-food introduction, especially of highly allergenic foods such as egg and cow's milk, in the belief that this would prevent the development of atopic conditions such as allergic rhinitis, eczema, and food allergies. The goal was to delay introducing allergenic foods until 12 months (cow's milk and dairy), 24 months (eggs), or even 36 months of age (fish, tree nuts, peanuts).

We need to forget this idea. Such schedules are no longer appropriate, as recent studies suggest that these delays may actually increase risk of allergies.

A recent paper by Palmer et al. reminds us of this change. Palmer conducted a double-blind, randomized, controlled trial in which 86 4-month-old infants with moderate to severe eczema were divided into two groups and about half (n = 49) were fed 1 teaspoon of raw whole egg powder mixed into their daily rice cereal until they were 8 months old. If what we were taught were true, this early introduction of egg, in particular raw egg, should have wreaked havoc, dramatically increasing their allergies. The "control group" ate rice cereal without the raw egg powder.

By 12 months, 33% of the infants in the egg group vs. 51% of infants in the control group were diagnosed with IgE egg allergy. Although this difference was not statistically significant, the egg-fed children were trending toward a lower risk of allergy; early introduction of a highly allergenic food, raw eggs, did not increase risk.[1]

The Palmer study is not alone in questioning the validity of delaying food introductions.

Filipiak and Zutavern reported in 2007 on the association between solid food exposure and eczema. Among 4753 infants, there was an increased risk of eczema for those who avoided egg in their first year of life. Based on these data, the authors found no evidence to support "... a delayed introduction of solids beyond the fourth month nor a delayed introduction of the most potentially allergenic solids beyond the sixth month of life for the prevention of eczema."[2]

In 2008, Zutavern et al. reported that in a group of 2073 children, delaying introduction of solid foods past 4 or 6 months did not reduce the incidence of developing atopic conditions. In fact, food allergies were actually more frequent in children who had been exposed to solid foods later in life.[3]

In the Palmer study, no protective effect against development of atopy was seen as a result of early exposure to raw egg. This lack of protective effect could certainly be due to the population included in the study. At baseline, 36% of the infants already had elevated egg-specific IgE levels, and 31% of these patients in the egg group had an allergic reaction to the egg powder. This information indicates that children with moderate-to-severe eczema are already sensitized to egg before they are ever fed it. Further studies are

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Caution with High-Nitrate Foods

Babies less than 6 months old should not be fed home-cooked beets, carrots, collard greens, spinach, or turnips, as this may cause methemoglobinemia, a blood disorder in which an abnormal amount of methemoglobin, a type of hemoglobin, is produced. Methemoglobin cannot release oxygen. While most cases of methemoglobinemia are genetic, some drugs can cause the condition, including benzocaine, certain antibiotics, nitrites (used as food additives), and nitrates (from foods). These vegetables, particularly beets, are high in nitrates.

The nitrates in foods may be converted to nitrites in young babies. It is difficult not to notice methemoglobinemia, as the baby's skin turns blue. In the US, nitrates are removed during commercial manufacturing, so these vegetables when store-bought should be safe. Breast-feeding protects infants from developing this condition, even if they are exposed to high levels of nitrate.[10,11]

Introducing Baby to Solid Foods

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needed to investigate the cause of this presensitization. The authors of this study suspect transfer of maternal antibodies in utero or through breast milk. Ultimately, the implications of this study are twofold. First, caution is advised when introducing allergenic foods to infants with eczema due to the presence of existing IgE antibodies to foods that they have never eaten before. Secondly, as already mentioned, the early introduction of egg does not appear to increase the risk of developing an IgE egg allergy in this high-risk group.

Late introduction of solid foods may actually make allergies worse. A study published in 2010 analyzed data from a 994 children who were part of a prospective, birth cohort study and found that "... late introduction of potatoes (>4 months), oats (>5 months), rye (>7 months), wheat (>6 months), meat (>5.5 months), fish (>8.2 months), and eggs (>10.5 months) was significantly directly associated with sensitization to food allergens. Late introduction of potatoes, rye, meat, and fish was significantly associated with sensitization to any inhalant allergen. In models that included all solid foods that were significantly related to the end points, eggs, oats, and wheat remained the most important foods related to sensitization to food allergens, whereas potatoes and fish were the most important foods associated with inhalant allergic sensitization. ... Late introduction of solid foods was associated with increased risk of allergic sensitization to food and inhalant allergens."[4]

Another current study also needs to be mentioned. Published in November 2013 in the *Journal Pediatrics*, a paper by Kate Grimshaw et al. brings another element into the food introduction story: breast-feeding. Exclusive breast-feeding for the first 4 to 6 months, and continuing to breast-feed as solid foods are introduced into an infant's diet, reduces risk of food allergies as the children grow up.

Grimshaw's team followed a group of 1140 infants from birth to 2 years. The mothers completed diaries detailing the babies' diets and noting any foods that they suspected of triggering allergic reactions. The researchers later tested to confirm these suspected allergies. They identified 41 babies with confirmed food allergies, and compared them with 82 age-matched babies without allergies. They report that 17 weeks is a crucial line. Introducing solid foods before 17 weeks increased risk of developing allergies. Continuing to breast-feed as cow's milk was introduced protected against allergies.[5]

While the current study shows that early egg introduction does not increase the risk of IgE egg allergy, it did reveal that early egg exposure leads to significant elevations of egg IgG4 antibody levels. The mechanism may be similar to that of immunotherapy, which includes suppression of mast cells, basophils, and IgE-positive B cells through exposure of allergens in small doses over long periods of time. Through this process of immunotherapy, the B cells start to favor the production of IgG4, a Th1 dominant process, rather than the production of the Th2 IgE antibody. This shift from IgE to IgG4 production seems to indicate a shift of the immune response from Th2 dominance to Th1 dominance.[6] While this immune shift may explain the aforementioned benefits of early exposure for the prevention of atopy and food allergies, it may pose other unknown health risks. For example, there is a correlation between early cow's milk exposure and Th1 dominant type 1 diabetes mellitus (T1DM). A 2013 epidemiologic profile in *Scientific World Journal* elaborates on the connection, explaining that T1DM has an earlier age of onset,

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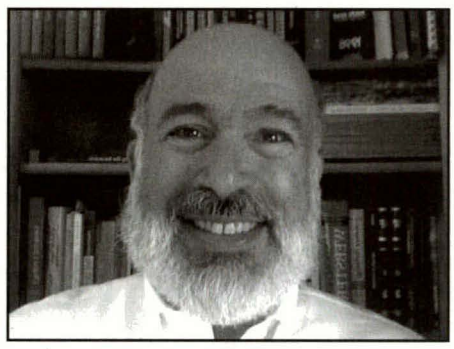

Jacob Schor, ND, graduated from National College of Naturopathic Medicine in 1991. He is currently president of the Oncology Association of Naturopathic Physicians and is a member of the AANP's board of directors. He is a regular contributor to the *Townsend Letter* and an associate editor of the Natural Medicine Journal. He was the first recipient of the AANP's Vis Award in 2009.

around 4 years old for those infants exposed to cow's milk under 3 months old, and the overall risk for T1DM is highest when milk is given before 4 months old.[7] Further research ought to be done regarding the effect of early solid food introduction on Th1 dominance and the incidence of Th1-dominant autoimmune diseases. While early exposure might reduce atopy by shifting from IgE-mediated Th2 dominance to IgG4-mediated Th1 dominance, there may be other health implications.

Timing of solid food introduction does indeed change risk of developing T1DM. A September 2013 paper tracking the DAISY cohort (Diabetes Autoimmunity Study in the Young) suggests that solid foods are best introduced in a window between 4 and 6 months to lower risk. This is a longitudinal, observational study that is tracking 1835 children at increased genetic risk for T1DM who have been followed from birth with complete assessment of their diet as infants.

Either early introduction or late introduction of solid foods increased the risk of T1DM. Early introduction nearly doubled risk (hazard ratio [HR], 1.91; 95% CI, 1.04–3.51) while late introduction appeared to triple risk (HR, 3.02; 95% CI, 1.26–7.24). Early exposure to fruit and late exposure to rice and oats specifically worsened the hazard ratio, (HR, 2.23; 95% CI, 1.14–4.39, and HR, 2.88; 95% CI, 1.36–6.11, respectively). Breast-feeding at the time of introduction to wheat/barley conferred protection (HR, 0.47; 95% CI, 0.26–0.86). [8]

It seems that early introduction overemphasizes Th1 antibody production while delayed introduction overemphasizes Th2 antibody production. It would be nice if we could consider "biochemical individuality" when it comes to timing food introductions instead of these one-size-fits-all instructions. Perhaps if one has a family history of autoimmunity, waiting longer to feed solids might be better. If one has family history of atopy, was not breast-fed, or was not vaginally delivered, it might be best to feed solids early. But these thoughts are just conjecture; we have no evidence to support these ideas.

Current instructions for food introduction are very different from what we once believed. Parents should still delay introducing solid foods until the infant is about 4 months old but then they should introduce all foods by 6 months. Later introduction provides no benefit, and it may even increase risk of allergies and possibly diabetes. Breast-feeding during the food introduction period may reduce these risks.

Current Official Guidelines

A comprehensive set of new guidelines for introducing solid foods was published in January 2013 in the *Journal of Allergy and Clinical Immunology* and is available for free online.[9] They suggest that once an infant over 4 months old has been given and has tolerated a few nonallergenic solid foods, more allergenic foods can be introduced rather quickly, though still one at a time.

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A Positive Alternative for Learning Disabilities

review by Hyla Cass, MD

Reversing Dyslexia: Improving Learning and Behavior without Drugs, by Dr. Phyllis Books, DC, CNN
Square One Publishers; 115 Herricks Road, Garden City Park, New York 11040
© 2013; softcover; $16.95; 146 pp.

Most of us, doctors and laypersons alike, see dyslexia as a heartbreaking and often hopeless learning disorder. Unfortunately, modern medicine labels learning issues too narrowly, ignoring new and positive ways that people can work through the problem. With *Reversing Dyslexia*, however, Texas-based chiropractor and dyslexia specialist Phyllis Books, DC, CNN, is poised to change how doctors can see and treat this disability.

In her brave new book, Dr. Books challenges the existing medical and educational models of dyslexia. From the first page, she establishes her text as a positive and uncomplicated manual for those who refuse to accept traditional methods as the only solution in the face of this condition. She further educates her readers by explaining the various theories of dyslexia and explores specific symptoms, revealing how strongly those same symptoms, once diagnosed, can affect a person's self-image and emotional health.

Overcoming learning disabilities is *not* impossible, according to Dr. Books; it just requires a combination of patient-centered tactics that encompass elements of biology, neuroscience, and psychology, along with a more healthful diet, exercise, and a compassionate mindset among all involved. Dr. Books also draws on her excellent skills to evaluate a host of therapies that she believes can facilitate rewiring the brain, which helps eliminate dyslexia early in the game.

If I have any criticism, it is that this book does not equip caregivers or educators with the means to tackle and hopefully undo the resulting trauma so often associated with dyslexia. However, it does something even greater for those whose lives have been touched by dyslexia. *Reversing Dyslexia* presents a solid and valuable outline of the problem, and acts as a guiding light to help both doctor and patient find a shared way toward overall wellness and recovery. ◆

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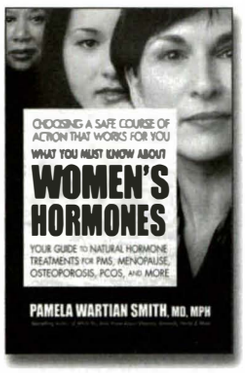

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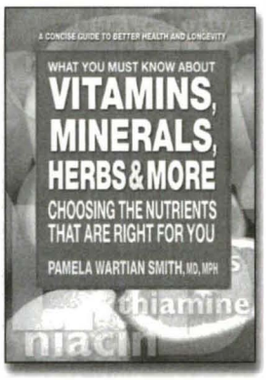

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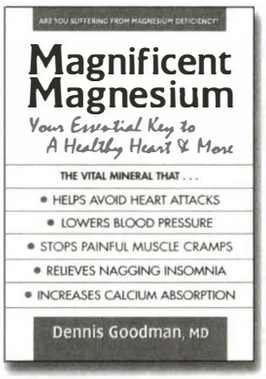

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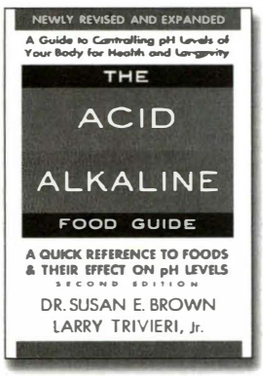

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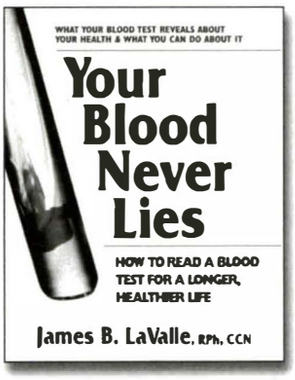

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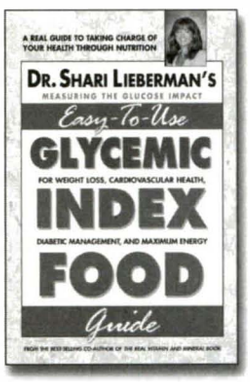

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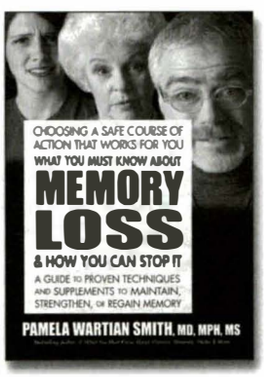

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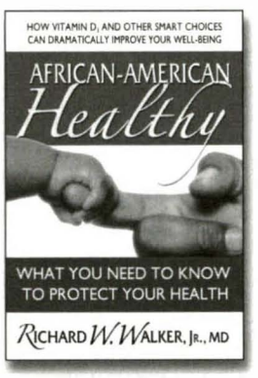

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A Primer for Our Overweight and Diabetic Patients

review by Jonathan Collin, MD

No More Diabetes, by Gary Null, PhD
Skyhorse Publishing
© 2013; 439 pp.; $24.95

Readers of the *Townsend Letter* are familiar with author and radio host Gary Null, PhD. Null has written numerous series in this publication detailing the risks of fluoridation and vaccination; most recently he raised concerns about Gardasil, the vaccine for HPV. He has written of and supported the AIDS dissidents who dispute the causal relationship of HIV and AIDS. Null is also well known for his advocacy of nutritional medicine and supplementation; he has previously reviewed the evidence in support of vitamin C and vegetarianism. He strongly advocates that the basis for approaching disease is through major lifestyle changes – change in diet, exercise, supplementation, stress management, and reduction in medication. Null's championing of nutrition is disdained by convention physicians who prefer minimal dietary intervention and intensive pharmaceutical prescribing. In *No More Diabetes,* Null examines nutritional and lifestyle changes to reverse diabetes and prevent metabolic syndrome.

Null thinks that the standard American diet, chock-full of sugary pastries, sodas, and candies, is the key culprit in creating insulin resistance. Hamburgers and french fries, high-fat pastas and casseroles, pizza, and other fast food substantially raise blood fat and glucose levels and offer little metabolic support for controlling insulin levels and increasing insulin sensitivity. The dearth of vegetables, whole fruits, whole grains, legumes, and nuts in the typical diet deprives the body of the nutrients needed to reverse insulin resistance. Reduction in adiponectin and lectin resistance lead to increasing glucose, insulin resistance, and reduction in appetite satiety. Invariably there is resultant weight gain, increasing abdominal girth, blood pressure, and LDL. Metabolic syndrome and prediabetes are now increasingly developing in adolescents who eat a fast-food diet and engage in minimal exercise.

In addition to a radical change in diet, Null argues, nutritional supplementation must be aggressive. His program may be excessive, but each of the nutrients has glucose- and insulin-controlling activities. Null would supplement people with chromium, vitamin C, biotin, vitamin B6, vitamin B12, calcium, magnesium, potassium, manganese, zinc, selenium, quercetin, EFAs, GLA, l-carnitine, inositol, glutamine, vanadyl sulfate, B complex, garlic, *Gymnema sylvestre*, ginseng, alpha-lipoic acid, grapeseed extract, NAC, CoQ10, turmeric, maitake, proteolytic enzymes, DHEA, silymarin, cinnamon, and more herbals.

Null recommends that, in addition to the dietary and supplement changes, individuals exercise actively. He would like people to do stress reduction either through counseling or by meditation and breathing exercises. Null thinks that teaching individuals in group sessions about diet, supplementation, exercise, and stress reduction offers the strongest means to bringing about lifestyle change. His book reports the gratifying results in many people who engage nutritionally in reversing their metabolic dysfunctioning.

Null's book offers ample referencing; however, to make the book more readable for the public, he does not footnote his references. Still the book is an excellent read if for no other reason than the abundant vegan, gluten-free recipes provided for breakfast, lunch, dinner, and dessert.

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Optimizing Metabolism

by Ingrid Kohlstadt MD, MPH
www.INGRIDients.com

Change for Diabetes

Introduction

With diabetes, small changes go far when repeated daily. As health-care providers, we can help our patients the most when we empower them to bring the message home. With nutrition, the "take-home" is especially important because change in one family member's diet is most successful when the entire family changes. Bringing dietary change home to the whole family is a job for a well-equipped change agent. This column therefore equips doctors and their patients for change – health behavior change along with change of the nickel and dime kind. Each "My doctor said ..." is backed with US currency.

Communicate That There Is No Substitute to Natural Sweetness

In the 1950s, organizations representing people with diabetes advocated for saccharin, based on the interpretation of the science available at that time. Now, more than half of a century later, the metabolic process underlying type 2 diabetes is understood with more detail, and high-intensity sweeteners are shown to accelerate the process.

Honey, maple syrup, and orange juice concentrate are naturally sweet substances that are very complex metabolically. Each has been proved to have ingredients that help process the sweetness in the human body. Glucose levels don't rise to the same extent that they do with refined sugar.

Natural sweeteners other than refined sugar represent only 1% of the sweeteners consumed in the US. To that, I suggest we rise to our ideals: We are the nation that named Utah the "Beehive State" and minted maple syrup on the Vermont quarter.

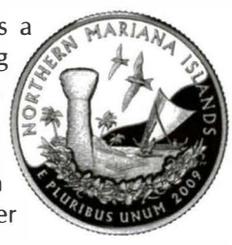
Advise Patients to Diversify

What if we asked patients to count the different plants that they used to nourish themselves each day? Instructions would note that the larger the list, the better. From a behavior change perspective, this could be more instructive and motivational to healthful behavior than some of the other counting, measuring, and monitoring characteristic of diabetes management.

For one, the exercise would draw awareness to plant power, which we usually mistakenly confine to food. Plants improve our health and nutrient status in many other ways: noncaloric beverages, poultices, topical oils, spices, gum, medications including the diabetes drug metformin, supplements, and inhaled essential oils. Each confers health benefits through phytonutrients.

When people consider plant power, the usual response is to diversify. Chances are that your patients' financial advisers have told them the same thing. Diversifying is smart advice that can be applied to nutrient portfolios as well as financial portfolios.

Diversifying your plant portfolio is a message on the quarter commemorating the Northern Mariana Islands. Here three edible plants form a lei (mwar), representing a wish for someone's health and happiness. While this coin is from the US *Mint,* it depicts another herb, basil.



Ask About Protein Intake

The medical community is polarized on the health effects of animal protein. As I have come to understand it, the protein is not unnecessary but is accompanied by unwanted side effects. The health goal therefore, as I see it,

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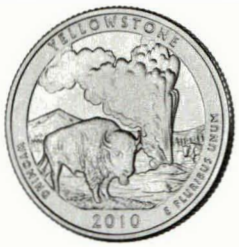
is not to remove animal protein as a food source in patients who currently eat it, but to minimize the metabolic side effects of protein. Choose lean protein sources, use little, eat only with alkalinizing foods, and do not prepare with high heat or charring.



In the 1990s I served as a primary care medical doctor for an American Indian nation. At the time there was an ongoing study of bison ranching in which I was not involved. However, I became very interested in this study with favorable results because I could see measured benefits in my patients. In short, I noticed that bison *behooved* them. I began better understanding how patients with diabetes especially need protein because the disease process misspends protein on energy rather than on its intended use to repair vital structures.

Bison-ranching is viewed in a broader context that holds much greater sway over our food selection than any health research. These majestic methane-makers, although no longer prevalent on the plains, are a favorite theme on US coinage. Recent bison coinage writes a wise prescription.

1. Take no more than you need. It's a rule that most cultures consider a sacred trust, and is essential to physical well-being.
2. Free ranging is better for our health.
3. Our health is entwined with the land.

Guide Patients to a Spa-Hah Moment

Today public health and commerce are pitted against each other in countless ways. Yet there is one work of literature renowned for its sentinel depiction of this dilemma. *An Enemy of the People*, a 19th-century play by Heinrich Ibsen of Norway, presents a highly regarded doctor who discovers that the thermal baths on which his town's wealth is built are sickening tourists due to contaminated water. Dr. Thomas Stockmann proposes a remediation plan to no avail. Citing costs and the risk of negative publicity, the town rejects the plan and brands Stockmann a public enemy.

130 years following the influential Ibsen play, doctors still weigh the pros and cons of medicinal spas. Patients with diabetes are indeed more susceptible to infections and have more difficulty processing the chlorine and other sanitizing chemicals that vaporize in spas. Even where there is clear health benefit, spas require significant out-of-pocket costs, which appropriately make doctors hesitate to recommend them.

Arkansas's 2010 commemorative quarter points to a solution for today's doctors and their patients. To be affordable to most patients, an out-of-pocket medical treatment should cost quarters – not dollars. US research helped make the benefits of spas accessible to more people. The greatest medicinal value of thermal hot springs such as the one depicted on the coin is minerals. Two minerals of measured medicinal value are magnesium and sulfur. And magnesium and sulfur comprise the Epsom salts that I recommend to my patients. The portable quarter-cost spa is named after a town in England that didn't turn on its doctor.

In Summary

Change always meets resistance. Sometimes changes at home are the hardest for our patients to make. Now we can advise our patients to be the messenger of *change*. It's no *coin*cidence.

Images are provided from the US Mint (usmint.gov).

Ingrid Kohlstadt, MD, MPH, FACN, FACPM, is the founder of INGRIDients Inc., where she has edited *Advancing Medicine with Food and Nutrients*, 2nd edition (CRC Press; 2012). On the faculty of Johns Hopkins Bloomberg School of Public Health, Dr. Kohlstadt is researching an approach to leverage nutrition more fully in disease prevention.

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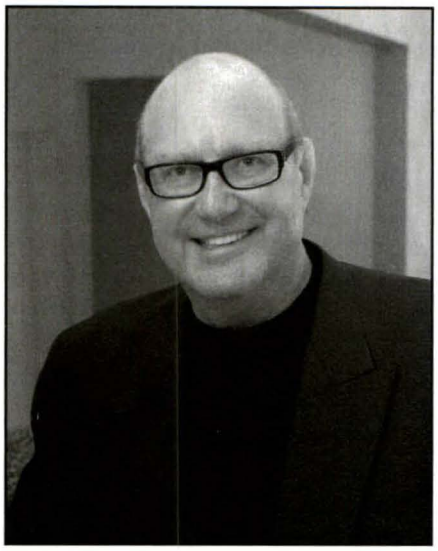

Monthly Miracles

by Michael Gerber, MD, HMD
contact@gerbermedical.com

Nevada Homeopathic and Integrative Medical Association 2013 Annual Fall Seminar: Part 2

Paul Ling Tai, DPM, FACFS, AABPS, ABAARM, DACBN: Serotonin Biochemistry in Stress, Anxiety and Depression; Vitamin D Deficiency–Diagnosis and Treatment; Melatonin and Your Health

Tai, author of 12 books, is the chairman of the Department of Postgraduate Medical Education at University of Health Science Antigua School of Medicine. He is a professor of aging and regenerative medicine, professor of clinical nutrition, and president of the Brazil American Academy of Aging and Regenerative Medicine. He is a captivating speaker who concentrates a great deal of scientific information and focuses on treatment protocols.

In his serotonin presentation, he reminds us of this neurotransmitter's regulation of mood, appetite, sleep, memory, and learning. Optimal utilization of serotonin also requires adequate levels of thiamine, folic acid, and B12. It stimulates cellular growth and repairs liver damage. Since serotonin is degraded in the digestive tract and does not cross the blood–brain barrier, supplementation with tryptophan and more efficiently 5-HTP (5 hydroxytryptophan) is recommended. He also reviews the negative effects of antidepressant drugs such as MAOIs, SSRIs, and tricyclics and serotonin metabolism. One new source of serotonin augmentation comes from an Argentinean plant, pampas prairie bush.

Vitamin D deficiency causes a host of human illnesses, reports Tai, such as cancers, osteoporosis, heart attacks, diabetes, hypertension, multiple sclerosis, rheumatoid arthritis, and developmental defects in children. It also suppresses pro-inflammatory cytokines and improves mood. He gives many references to support widespread deficiency in the world's population and supports oral and transdermal supplementation to promote health at up to 10,000 IU of D3 per day with good evidence of safety.

Lack of melatonin in humans can be caused by lifestyle and lack of darkness in our lives. Melatonin, manufactured in the pineal gland at night, regulates all the anterior pituitary hormone production and regulates their diurnal secretion. Melatonin inhibits growth of breast cancer and amyloid-beta deposits in the brain; helps regulate T4 to T3 conversion; is lower in cases of depression and suicide, autism, epilepsy, diabetes, alcoholism, and prostate cancer; and is an antioxidant and free-radical scavenger. It has been used successfully for sleep disorders and children with neurodevelopment disabilities.

Louisa Williams, MS, DC, ND: Leaping to the Source! Dr. Divya Chhabra's Constitutional Homeopathy Method

Williams, author of *Radical Medicine*, a 1100-page book of profound intervention in a profoundly toxic age, resides in Marin County, California.[1] She is also a cofounder ART (autonomic response testing) with Dietrich Klinghardt. "Leaping to the Source!" is a review of Chhabra's method of diagnosis and treatment with homeopathic remedies. The wife of famous Indian homeopath Rajan Sankaran (both are from Mumbai) uses a strong emphasis on the five senses and doesn't work with miasms, kingdoms, or levels, and doesn't mix homeopathic systems. She listens for denial, repetitive and peculiar speech, verbal slips, and inappropriate hand gestures. Childhood issues around food, fear, dreams, and acute illness are important clues. "The Leap" to the remedy involves spontaneous movement from the rational to the irrational disease state and lands on the source: "Patient leaps over the wall." Williams suggests free association: first image that comes to mind. Begin with "black," a universal abstract word, to get into the unconscious mind. A Lyme patient stated that her symptoms felt like a huge force pushing down on her like a pressure cooker and then flowed back up, creating an unpleasant, bubbling spring, like air bubbles in her head, that wasn't gas. Every cell was vibrating, shaky like a witch's cauldron – slimy, smelly, dark steamy stuff. "The core of me is unstable like a toxic well producing massive toxins [both hands go straight up] exuding all these gaseous fumes. I feel explosive."

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The remedy that Williams selected was geyser water, heated mineral water that erupts periodically, triggering a violent chain reaction of boiling steam explosions with smelly, hydrogen sulfide water – in particular, water from Yellowstone Park's Old Faithful geyser, Aqua Fida vetusta 200C, a new remedy obtained in 2005. The patient recovered remarkably and her positive Lyme test became negative. Great stuff! (Get our videos for the full presentations.)

Michael Margolis, DDS: The Connection between Your Oral Health, Total Body Health and Degenerative Diseases

Margolis received his doctor of dental surgery degree from the University of Texas in 1983 and is a past president of the International Academy of Biological Dentistry and Medicine. He speaks nationally and internationally on topics of holistic dentistry. You can review many of his manuscripts and charts relating pathology in the various teeth to distant physical and psychological symptoms at mydentistaz.com.

Holistic dentistry stresses the use of nontoxic restorative materials for dental work and focuses on the impact that dental toxins and hidden dental infections can have on the patient's overall health. Holistic dentists treat the teeth, jaws, the throat (autonomic nervous system), and related structures, with specific regard to the effect of treatment on the entire body.

Margolis reviewed many of the most commonly overlooked dental problems that can cause systemic disease, including leaving the periodontal ligament intact after dental extractions. Its continued presence can signal the bone that the tooth is still present and bone doesn't heal properly, leaving chronic infections that can affect the whole body. Root canal therapy leaves up to 3.5 miles of living tubules (protein) that are subject to chronic bacterial infections and promotion of jaw infections, which can have terrible systemic consequences. German biological doctors call root canals "a corpse in the attic." The resulting cavitations, infected bone tissue, frequently appear normal on dental X-ray but can be found with a Cavitat ultrasound device, which demonstrates reduced density of bone in maxilla and mandible adjacent to root-canal and wisdom-tooth areas. The reduced-density areas are frequently areas of infection. (See Cavitat.com.) In my experience, these infections can also be documented by EAV devices such as the Biomeridian. I recently had a hypertensive man on high doses of three antihypertensive drugs drop his systolic by 50 points in a month (from 186 to136 mmHg) by treating root-canalled teeth and wisdom-tooth areas. The patient treated the areas with ozonated coconut oil on small cotton ball rolls for 20 minutes per day for a month in the buccal membrane next to the diseased tooth. I also inject the buccal membranes with these dental issues with neural therapy using procaine, Arthrokelan A, Pleo Not, Pleo Nig, and ozone weekly when possible or until improved. Could hypertension be caused by infected teeth? In this case and many others, I think so.

Oral pathology and infected teeth and bones can also be detected by thermography. Cancer, neurological diseases, and increased coagulation risks have been linked to dental infections. Margolis notes that many organisms have been cultured from diseased teeth and bones by DNA dental testing. These microbes cause pathology in the heart, nerves, lungs, red blood cells, oral cancer, liver, spleen, and gallbladder.

Frank Shallenberger, MD, HMD: Highlights of the Second Annual Congress of the American Academy of Ozonotherapy

Shallenberger has published several books, including his most recent, *The Principles and Application of Ozone Therapy: A Practical Guideline for Physicians*. He has formed and incorporated the first medical ozone society in the US, the American Academy of Ozonotherapy, and is the developer of Prolozone, an injection technique that has been shown to regenerate damaged joints, herniated discs, degenerated joints, tendons, and soft tissues. Videos of his entire seminar or individual lectures are available at www.aaot.us. In his lecture he reviewed several speakers from his seminar.

Of the many great presentations at his spring conference, that by Damon Whitfield, DO, on treating dental cavitations with ultraviolet-treated whole blood stands out. His preparation used a 3 ml syringe with 0.2 ml heparin 5000:1, 1 to 2.5 ml of blood with 10 to 20 minutes' irradiation in Tom Lowe's light box for 10 to 20 minutes of UV-B, UV-C. He injected 4 quadrants – wisdom teeth relate to the heart, extraction sites, cavitations, and root canals with 1 to ½ ml each. He treated for an average of 4 to 6 times every 2 to 4 weeks with a very good treatment response.

Intravenous ozone therapy by the direct method was presented by Howard Robins, DPM, from New York. He injected directly ozone from 14 to 45 or 50 gamma in a volume of 5 to 240 cc at a rate of 1 cc every 5 seconds or slower from 1/week to 2×/day. The dose is increased gradually if well tolerated and allows for use of smaller veins with more eligible patients, only takes 1 to 12 minutes to complete, and can be administered 2 treatments per day, 6 days per week with lower cost to the patient and faster results.

Cheryl Burdette, ND, reported on cellular biomarkers for mitochondrial function after ozone therapy. Nuclear factor-like 2 (Nrf2) is a transcription factor that when activated increases the expression of antioxidant enzyme systems. Nrf2 is a master regulator of cytoprotection and increases detoxification, regulates production of phase 2 enzymes, enhances stability and turnover of proteins, reduce inflammation, protects against neurodegeneration,

is antitumorigenic, and promotes apoptosis and longevity. Nrf2 is activated in a dose-dependent manner after endothelial cells are treated with increasing doses of ozonated serum at 20, 40, and 80 gamma of ozone.

Adam Weglein, DO, gave his experiences with platelet-rich plasma injections in osteoarthritis. He noted that platelets release many bioactive proteins responsible for attracting macrophages, mesenchymal stem cells, and osteoblasts, which not only promotes removal of necrotic tissue, but also enhances tissue regeneration and healing. Platelet-derived growth factor stimulates cell replication and promotes angiogenesis and epithelialization. PRP works much better when combined with Prolozone therapy.

Jorge Flechas, MD, MPH, presented on the effects of oxytocin and pain. Oxytocin significantly increases thresholds for visceral pain and induces analgesia in acute and chronic low-back pain. Oxytocin has been found low in the following conditions: depression, autism, AIDS, multiple sclerosis, low thyroid, chronic stress, chronic opioid use, Parkinson's disease, and fibromyalgia.

Ozone Insufflation Protocol

Shallenberger reviews intestinal insufflation of ozone. Ozone works through the action of peroxide induction and antioxidant enzyme stimulation. Studies show that intestinal insufflation produces the same level of peroxides and antioxidant systems as major autohemotherapy (infrared intravenous blood irradiation and ozonation) and is much easier, cheaper, and faster. His protocol involves a #14 or #16 male catheter and a 200 cc glass syringe. Insert the catheter 4 inches into the rectum. Start with 100 cc at 20 gamma and work up as tolerated to 200 cc at 40 gamma (ppm). Attach the syringe to the catheter and inject over 30 to 60 seconds. It is best, although not necessary, to do this after a bowel movement or a coffee enema. Treatments are performed 7 days per week for 3 weeks. Then take a 2-month break and repeat. Continue this 3 weeks on and 2 months off indefinitely.

Coffee Enema Instructions

Coffee enemas are used to detoxify the liver, not to relieve constipation. The coffee is absorbed by the rectal veins and goes immediately to the liver. It acts to stimulate the liver to release bile, and in the process toxins are released as well. To prepare the enema, boil 3 rounded tablespoons of drip-ground organic coffee in a quart of water, then simmer for 15 minutes. Let cool down to body temperature. (Or use ice to cool the coffee, and some would add 1 tbsp Epsom salts to relax the colon). Lie down on a towel on the right side (some prefer left side) with the legs curled. Adjust the bag height so that it runs in slowly enough not to be uncomfortable. Retain for about 10 minutes, and then release in toilet. It takes some practice!

Monthly Miracles

Kimchi Moyer, LAc: Using Regulatory Blocks as a Guide for Pleo Sanum Application, with Case Studies to Highlight the Approach

Kimchi Moyer, from Santa Rosa, California, has a long and distinguished career in bioenergetics in clinical practice, beginning with Oriental medicine and evolving into Sanum products and terrain modulation. She is a master of electrodermal screening (EDS), focused mainly on the Vega Bio-Expert system from Germany. She also uses several other methods of health assessment, including the Computer SEG (Segmental Electrograph), darkfield microscopy, BTA (biological terrain assessment), genetic traits in the iris, Chinese tongue and pulse diagnosis, and heart rate variability measurement.

Biological Energy Primer

Moyer begins her lecture by defining all living system as controlled by a bioelectronic field of energy/information to which all material processes are subordinate. In our organism, chemical processes are actually biophysical processes. Molecules are formed from atoms by means of electron exchange; that is, energetic processes. And we are already a product of quantum physics. No metabolic

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reaction in the body can take place without the transfer of the relevant information. Matter obeys energy. Blood follows Qi (Traditional Chinese Medicine principle). Reality consists of fields. "Below the level of elementary parts, matter exists only as a wave or it does not exist" (Prof. Dr. H. P. Duerr, German atomic physicist, student of Heisenberg). "If you want to find the secrets of the universe, think in terms of energy, frequency and vibration" (Nikola Tesla).

Reality consists of fields. Matter consists of three parts: mass, 1 billionth part of reality, energy, and information (fractal). Moyer reminded us that today's physical sciences continue to concern themselves with just a 1 billionth fraction of realty; the "remainder" is unfortunately ignored. Our fields are electric and magnetic, electric fields induce magnetic fields, and vice versa. A strong electric field is called a potential field and it is the force of the fields that holds the structure together.

Diseases equal a loss of coherence and regulation. Disturbances arise from emotional chaos (loss of order), toxic substances from outside (interference), outside information (radiation), and changed water structure (geopathic stress). From this paradigm, disease is a disorder of a dynamic process of regulation that involves the entire organism. Permanently disrupted regulation is viewed as the root cause of many systemic illnesses, and is often connected to environmental pollutions, whether external or internal.

Reaction is regulation. Regulation is adaptation, and the ability to regulate is the key to health. Regulation can be positive, negative, rigid, hyper-, or hyporegulation. Moyer gave examples of positive regulation measured on the SEG and negative regulation, rigid regulation, and hyper- and hyporegulation after presenting different areas of the body with a frequency challenge and measuring the body's electromagnetic response.

Basic Vega Workup Parameters

Moyer's basic Vega workup uses a binary feedback system (yes/no) using resonance and galvanic skin response (GSR) as a way to measure a shift when a substance is introduced into the circuit with the body. This feedback mechanism allows her to obtain the information that the organism requires to return to coherency. Moyer establishes a biological index (energy level), health assessment phase system, establishing the originating organs, checking for intoxication (nosodes), organ involvement percentage, deficiencies percentage, metabolism percentage, emotion percentage, immune state, allergy organs percentage, food and cystic and degenerative process: organs percentage.

Case # 1

A 1-year-old child with no teeth erupting. After examination, Moyer found 100% left kidney deficiency secondary to mercury intoxication. After a body detox patch, one patch per week to the left foot only, 2 weeks later the baby began to grow normal teeth.

Case #2

A 45-year-old male former sumo wrestler from Japan with diagnoses of diabetes, frequent diarrhea, difficulty standing for long periods. He consumed prodigious amounts of sushi, tempura, pudding, cake, ice cream, 500 cc of diet cola per day, and no water. His daily diet contained oily tuna and beef, foie gras, oily Chinese food, truffles, oysters, blowfish, 2 glasses of Kirin beer, 2 glasses of whisky, ice cream, and cake, ending with pudding again. After Moyer's examination she found that he had parasites and salmonella and needed *Acidum nitricum* comp. angina comp. chloreamphenicol, cholesterin, prostate, nephritis. He was also full of molds, yeasts, and other fungi. Moyer treated with Pleo Not D5, 2 sips; Pleo San Strep, Pleo San Salm, and Thymoject.

The patient was 100% allergic to alcohol, eggs, red meats, fish, fats and oils, potatoes, rice, corn, wheat, cheese, coffee, dairy, nuts, sea salt, green and black tea, sugars, honey, chocolate, and sweet fruits. Moyer recommended that he eat poultry, vegetables, peas, seeds, brown rice, and nonsweet fruits. She also gave Pleo Not caps 3 per day on weekdays, Pleo Quent caps 3/d, Pleo Not sups 1 daily on weekdays, Pleo Muc caps 2/day on weekends. Tropocor 12 tabs for 2 doses. L-tyrosine 2× per day. Same 2× 1 per day, Bach flower remedies, Okoubaka 30 drops 2× per day for parasites, chromium GTF 5 tabs 2 times per day, vanadyl sulfate 5 caps 2 times per day, R-lipoic acid 4 caps 2 times per day, ethyl EPA 2 caps 2 times per day, and a host of other herbs and nutrients. She also recommended Pleo Not sips 2 at once, Pleo San Strep, Pleo San Salm, Pleo Quent D5 2 per day, coenzyme comp 2 per day, B Komplex, and B-12 Forte 2 per day plus Demarco vitamins 3 cc injected daily.

Two months later the patient reported from Japan that his blood pressure was normal and he was no longer

diabetic. He had more energy and could work a long day without feeling sleepy ... just feeling great.

She presented 3 more cases that were even more impressive. Please order the DVD.

HA (Health Assessment) Phase System

In a brilliant extrapolation of the Hans Reckeweg table of homotoxicology, Moyer has added two more phases to the original 6 phases from Reckeweg. As diseases progress into the higher phases, patients lose their ability to regulate. Food and remedy choices become more limited. Herxheimer reactions increase due to increase in regulation rigidity. Herxheimer reactions also increase as patients shift into lower phases. As patients increase ability to regulate, they gain energy even though they may have some energy loss at the beginning. In contrast, when patients lose the ability to regulate, they lose energy. The HA phase system includes Moyer's new ideal phase 0 and a transition phase 7. The usual Reckeweg table includes phase 1, excretion; phase 2, inflammation; phase 3, deposition; phase 4, impregnation; phase 5, degeneration; phase 6, dedifferentiation. In lay terms, we go from colds to cancer as our system unravels.

Our regulation ability wanes as we move into higher phases. As we advance into higher HA phases, we have fewer food choices, remedy choices, and cooking methods. As the HA phase increases, we need to prescribe fewer fungal remedies and more bacterial remedies, in Moyer's experience. She has constructed a series of diets based on the HA phase from 1 to 6 and a chart of the effective use of Pleo Sanum remedies in each phase. She is planning to have test kits available in the near future to help the practitioner determine which phase the patient is in to promote more accurate prescribing and dietary suggestions.

Moyer's phase treatment principle is important because it explains why some diets work for some people but not for others, also why a diet may work today but not tomorrow. There is no one perfect diet. There is only the "Phase Appropriate Diet."

Contact Kimchi Ho Moyer, LAc, at 707-539-0888; Santa Rosa, CA; www.livinginresonance.com.

Alexander Popp: Photon Measurement and Treatment

The very eloquent son of the famous Fritz Popp from Germany presented an extensive review of photon measurement in humans and animal models. Their new diagnostic and treatment machines offer an elegant treatment of our photon energetics to promote health and treat disease.

James Forsythe, MD, HMD: Update-Outcome Based Investigation on 500 Cancer Patients – 40 Months Using CST + IPT

Forsythe is a graduate of University of California San Francisco medical school and one of the first oncologists in Nevada. He has an extensive resume that includes 14 books and many teaching positions and journal articles.

Monthly Miracles

The goal of Forsythe's 40-month study on 500 cancer patients was to prove that integrative cancer treatments not only work but were superior to current 5-year survival statistics (*Clinical Journal of Oncology*) of 2.1% in adult stage IV cancers after 6 years of chemotherapy. His three goals of the study were to prove that using genetic chemosensitivity testing on circulating tumor blood cells (CST) provides a blueprint for patients by pinpointing the most effective chemotherapy drugs, targeted agents, hormonal therapies, and natural supplements in order to produce lasting, durable remissions and possible "cures."

He uses fractionate IPT (insulin potentiated therapy) after learning the most effective treatments from the CST testing. Utilizing intravenous and oral Poly-VMA, alpha-lipoic acid and palladium, IV and orally, IV nutrients and antioxidants, with careful monitoring of blood parameters, his clinic has achieved remarkable results.

The Forsythe Immune and IPT Lite Protocol of 500 patients over 40 months of study gave the following results: Survivors: 295/500 (59%).

Notes

1. Williams L. *Radical Medicine*. San Francisco/Vienna; International Medical Arts Publishing; 2007.

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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.

MARCH 22: THE ROLE OF NUTRITION AND NUTRACEUTICAL SUPPLEMENTS IN INTEGRATIVE CARDIOVASCULAR MEDICINE with Mark Houston, MD in Stamford, Connecticut. CONTACT: Biotics Research, 800-231-5777; http://www.bioticsresearch.com

MARCH 22: RUBIMED THERAPIST TRAINING (Level 1) in San Francisco, California. Natural remedies for emotional issues. CONTACT: 1-888-415-0535; http://www.Terra-Medica.com

MARCH 26-29: THE AMERICAN ACADEMY OF OZONOTHERAPY ANNUAL MEETING 2014 in Dallas, Texas. CONTACT: 775-450-3766; admin@aaot.us; http://www.regonline.com/aaot2014

MARCH 28-30: CARDIOMETABOLIC ADVANCED PRACTICE MODULE-Transforming the Assessment, Prevention, and Management of Chronic Metabolic and Cardiovascular Disorders in Boston, Massachusetts. CONTACT: https://www.functionalmedicine.org/Cardiometabolic

MARCH 29: PATHOGENIC PRECURSORS AND CHRONIC PAIN in Seattle, Washington. Identifying and eliminating pathogenic causes of pain and limited ROM. Also, an introduction to Verfied Priority Analysis, a specialized muscle testing technique. CONTACT: Grant Clarke, 415-613-3341; gclarke@goenergetix.com

APRIL 4-6: 9TH ANNUAL JOINT AMERICAN HOMEOPATHIC CONFERENCE in Long Beach, California. Presented by the National Center for Homeopathy. CONTACT: http://www.homeopathycenter.org

APRIL 4-6: DESERET BIOLOGICALS SYMPOSIUM in Lake Buena Vista, Florida. CME credits available. CONTACT: 800-827-9529; bill@desbio.com; http://www.desbio.com/symposium

APRIL 4-6: AMERICAN ACADEMY OF ANTI-AGING MEDICINE FELLOWSHIP MODULES & IV SYMPOSIUM in Denver, Colorado. Also, **OCTOBER 16-18** in New Orleans, Louisiana. CONTACT: 888-997-0112; http://www.A4M.com

APRIL 5-6: KLINGHARDT ACADEMY presents AUTONOMIC RESPONSE TESTING (Level 1) in Jenkintown, Pennsylvania. Also, **APRIL 12-13** in Kenmore, Washington. CONTACT: phone 908-899-1650; fax 908-542-0961; info@klinghardtacademy.com; http://www.klinghardtacademy.com

APRIL 5-12: WALSH RESEARCH INSTITUTE 11th MEDICAL PRACTITIONER TRAINING PROGRAM in Gold Coast, Australia. Organized and managed by Bio-Balance Health Association with William J. Walsh, Ph.D., Judith Bowman, M.D., and Albert Mensah, M.D. CONTACT: http://www.biobalance.org.au/events

APRIL 6: HOMEOPATHIC MEDICAL ASSOCIATION (UK) AGM & ANNUAL CONFERENCE in London, England, United Kingdom. CONTACT: 01474 560336

APRIL 10-12: 37th ANNUAL HOLISTIC DENTAL ASSOCIATION SYMPOSIUM – Healing Through Dentistry in Dallas, Texas. CE credits. CONTACT: 305-356-7338; director@holisticdental.org

APRIL 11-12: BASTYR UNIVERSITY presents TREATING EATING DISORDERS-CONCEPTS & APPLICATIONS in Kenmore, Washington (near Seattle). CONTACT: 425-602-3152; http://www.bastyr.edu/continuing-education

APRIL 11-13: SOUTHWEST CONFERENCE ON BOTANICAL MEDICINE in Tempe, Arizona. TCM approaches to inflammation; herbal gastroenterology; acute glaucoma; new studies on *Urtica* (nettle) and more. Herb walks / medicine making. CE credits. Early bird registration March 5. CONTACT: (541) 482-3016; http://www.botanicalmedicine.org

APRIL 11-13: GREAT PLAINS LABORATORY PHYSICIAN EDUCATIONAL WORKSHOP in Kansas City, Missouri. Expand your knowledge of biomedical testing, interpretations, and treatment protocols from organic acids, IgG food allergy, adrenal exhaustion, and other core laboratory evaluations. 24 CME/CEU credits. CONTACT: http://www.greatplainslaboratory.com/home/eng/kc_training.asp

APRIL 22-23: 13th ANNUAL INTERNATIONAL CONFERENCE ON DOSE-RESPONSE – Preconditioning Adaptive Responses in Biology and Medicine @ University of Massachusetts in Amherst, Massachusetts. CONTACT: 413-577-8102; http://www.Dose-Response.org

APRIL 25-26: THE ADVANCED PK PROTOCOL COURSE – Neurometabolic Phospholipid Therapy in Millville, New Jersey. CONTACT: http://www.PKProtocol.com

continued on page 90 ➤

Best of Naturopathic Medicine Competition 2015

The *Townsend Letter* is pleased to announce the Best of Naturopathic Medicine Competition for 2015. Naturopathic students, faculty, researchers, and practitioners are invited to submit papers. Winners will receive an award and publication in the Feb/March 2015 *Townsend Letter*. Papers should be submitted by October 31, 2014. Details for submitting papers can be found on page 13.

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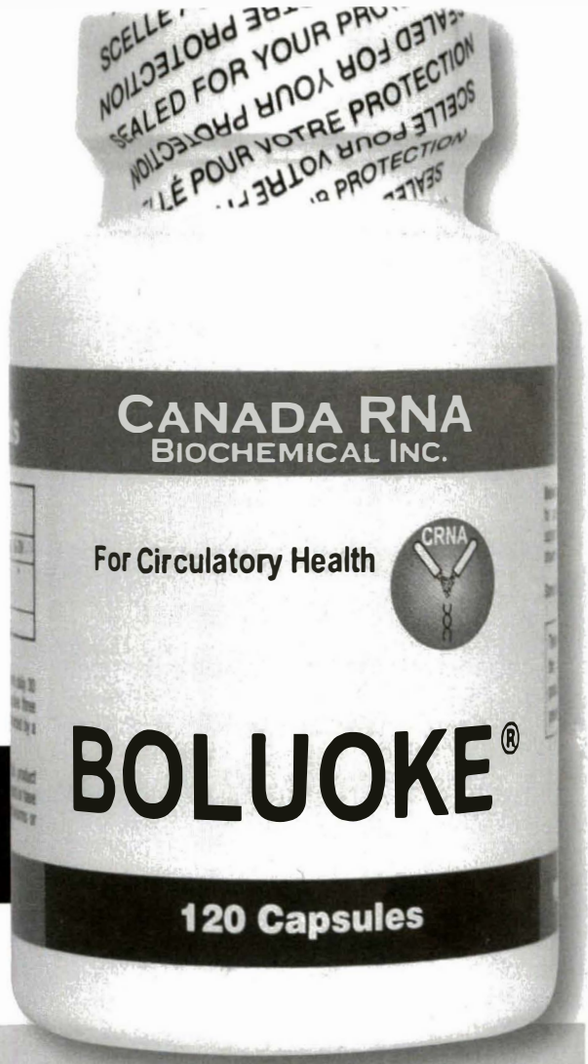
- ✔ Modifies CA-cell adhesion: ↓P-Selectin, ↓E-Selectin
- ✔ Decreases microbial resistance: breaks down biofilm
- ✔ No significant effect on INR or PTT



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The statements herein have not been evaluated by the FDA. This product is not intended to diagnose, treat, or prevent any disease.

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Calendar

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APRIL 25-27: 58th ANNUAL NORTHWEST NATUROPATHIC PHYSICIANS CONVENTION – Why We Do What We Do: The Principles of Naturopathic Medicine in Vancouver, British Columbia, Canada. CONTACT: http://www.nwnpc.com

APRIL 25-27: 43rd ANNUAL INTERNATIONAL ORTHOMOLECULAR MEDICINE TODAY CONFERENCE in Vancouver, British Columbia, Canada. Internationally-known physicians and researchers will present sessions on current advances in orthomolecular psychiatry, endocrinology, oncology and general medicine. CONTACT: 416-733-2117; http://www.csom.ca/omt-2014-registration/

APRIL 25-28: 6th ANNUAL INTERNATIONAL CONGRESS OF ANTIBODIES 2014 in Dalian, China. CONTACT: www.bitlifesciences.com/ica2014/

APRIL 26-27: BASTYR UNIVERSITY presents TREATING TRAUMA WITH CHINESE MEDICINE: UNTYING THE KNOT in Kenmore, Washington (near Seattle). CONTACT: 425-602-3152; http://www.bastyr.edu/continuing-education

APRIL 28-29: INTERNATIONAL VITAMIN D CONFERENCE – Vitamin D, Sun and Human Health in Oslo, Norway. CONTACT: http://oslo2014.d-vit.eu/

MAY 2-4: BIOLOGICAL MEDICINE 2014 LYME CONFERENCE in Bellevue, Washington. CONTACT: phone 908-899-1650; fax 908-542-0961; info@klinghardtacademy.com; http://www.klinghardtacademy.com

MAY 2-4: WORLDLINK MEDICAL presents MASTERING THE PROTOCOLS FOR OPTIMIZATION OF HORMONE REPLACEMENT THERAPY featuring Neal Rouzier, M.D. in Salt Lake City, Utah. Also, **AUGUST 29-31**. 18.5 CME Credits. CONTACT: 888-222-2966; http://www.worldlinkmedical.com/courses/bhrt-series/part-i/may-2014

MAY 10-11: BASTYR UNIVERSITY presents AURICULOTHERAPY ADVANCES IN PAIN & ADDICTION TREATMENTS in Kenmore, Washington (near Seattle). Also, **JUNE 6-7**. CONTACT: 425-602-3152; http://www.bastyr.edu/continuing-education

MAY 14-17: AMERICAN ACADEMY OF ANTI-AGING MEDICINE ANNUAL WORLD CONGRESS, FELLOWSHIP MODULES & BOARD CERTIFICATION EXAMS in Orlando, Florida. Also, **DECEMBER 10-13** in Las Vegas, Nevada. CONTACT: 888-997-0112; http://www.A4M.com

MAY 28-30: METABOLISM, DIET AND DISEASE 2014: Cancer and Metabolism in Washington, D.C. CONTACT: http://www.metabolism-diet-and-disease.com

MAY 29-31: THE INSTITUTE FOR FUNCTIONAL MEDICINE ANNUAL INTERNATIONAL CONFERENCE-Applying Clinical Nutrition Through the Functional Medicine Lens in San Francisco, California. CONTACT: https://www.functionalmedicine.org/AFMCP

MAY 30-JUNE 1: WORLDLINK MEDICAL presents ART OF CARING IN MEDICINE featuring Gregory Petersburg, DO in Tucson, Arizona. AMA PRA Category 1 credits. CONTACT: 888-222-2966;http://www.worldlinkmedical.com/courses/art-of-caring/

MAY 30-JUNE 1: KLINGHARDT ACADEMY presents AUTONOMIC RESPONSE TESTING (Level 2) in Horsham, Pennsylvania. Also, **AUGUST 23-24** in Kenmore, Washington. CONTACT: phone 908-899-1650; fax 908-542-0961; info@klinghardtacademy.com; http://www.klinghardtacademy.com

MAY 30-JUNE 2: MEDICINES FROM THE EARTH HERB SYMPOSIUM in Black Mountain, North Carolina. Topics: Dietary medicine and cancer; herbs for trauma and loss; environmental influences on autoimmunity; ADHD updates and options; targeting hypercoagulation for cancer. Early bird savings April 17. CONTACT: 541-482-3016; http://www.botanicalmedicine.org

MAY 31: RESTORING GROUND REGULATION @ Westin San Francisco Airport in Millbrae, California. Combined use of homeopathy, botanicals, and nutritionals for acute and chronic issues. CONTACT: Grant Clarke, 415-613-3341; gclarke@goenergetix.com; http://www.bioenergeticresources.com

JUNE 7-8: ARIZONA NATUROPATHIC MEDICAL ASSOCIATION SPRING CONFERENCE in Tempe, Arizona. CONTACT: 480-921-3088; http://www.AzNMA.org

JUNE 7-8: BASTYR UNIVERSITY presents ESOTERIC ACUPUNCTURE in Kenmore, Washington (near Seattle). CONTACT: 425-602-3152; http://www.bastyr.edu/continuing-education

JUNE 27-29: KLINGHARDT ACADEMY presents INJECTION TECHNIQUES & SKILLS 2014 – Neural Therapy in Bellevue, Washington. CONTACT: phone 908-899-1650; fax 908-542-0961; info@klinghardtacademy.com; http://www.klinghardtacademy.com

JULY 11-13: HORMONE ADVANCED PRACTICE MODULE - Re-establishing Hormonal Balance in the Hypothalamic, Pituitary, Adrenal, Thyroid, and Gonadal Axis in Denver, Colorado. CONTACT: https://www.functionalmedicine.org/Hormone

JULY 11-13: DETOX ADVANCED PRACTICE MODULE-Understanding Biotransformation and Recognizing Toxicity: Evaluation and Treatment in the Functional Medicine Model in Denver, Colorado. CONTACT: https://www.functionalmedicine.org/Detox

JULY 17-21: ONDAMED 20 YEAR ANNIVERSARY in the Black Forest of Southern Germany. CONTACT: +1 845-534-0456/0, support@ondamed.net; http://www.ondamed.net

SEPTEMBER 8-12: APPLYING FUNCTIONAL MEDICINE IN CLINICAL PRACTICE-A Five-Day Foundational Course in Functional Medicine in Scottsdale, Arizona. CONTACT: https://www.functionalmedicine.org/AFMCP

SEPTEMBER 10-13: AMERICAN ACADEMY OF ANTI-AGING MEDICINE FELLOWSHIP MODULES, BHRT SYMPOSIUM & BOARD CERTIFICATION EXAMS in Phoenix, Arizona. CONTACT: 888-997-0112; http://www.A4M.com

SEPTEMBER 15-17: PREVENTING OVERDIAGNOSIS @ Oxford University in Oxford, United Kingdom. CONTACT: http://www.preventingoverdiagnosis.net

SEPTEMBER 19-21: INTEGRATIVE MEDICINE FOR MENTAL HEALTH 5th ANNUAL CONFERENCE in San Antonio, Texas. Presented by Great Plains Laboratory. CONTACT: http://www.greatplainslaboratory.com/home/eng/kc_training.asp

SEPTEMBER 21-26: KLINGHARDT ACADEMY WHIDBEY ISLAND RETREAT in Clinton, Washington. CONTACT: phone 908-899-1650; fax 908-542-0961; info@klinghardtacademy.com; http://www.klinghardtacademy.com

OCTOBER 11-12: NEW KLINGHARDT PROTOCOLS in Kenmore, Washington. Open to non-ART practitioners. CONTACT: phone 908-899-1650; fax 908-542-0961; info@klinghardtacademy.com; http://www.klinghardtacademy.com

OCTOBER 18-19: KLINGHARDT ACADEMY presents AUTONOMIC RESPONSE TESTING (Level 1) in Jenkintown, Pennsylvania. CONTACT: phone 908-899-1650; fax 908-542-0961; info@klinghardtacademy.com; http://www.klinghardtacademy.com

OCTOBER 28 - NOVEMBER 3: 41st BIOLOGICAL MEDICINE TOUR TO GERMANY & BADEN-BADEN MEDICINE WEEK. Join us for our 41st group tour with the theme "Clinical Applications in Biological Medicine". Program includes participation in the famous "Medicine Week" Congress, exclusive OIRF English language lectures from renowned German clinicians and researchers (including Dr. Juliane Sacher and Dr. Olaf Kuhnke) as well as instrumentation, clinic and pharmacy presentations. CONTACT: Occidental Institute at 800-663-8342; phone 250-490-3318; fax 250-490-3348; support@oirf.com; www.oirf.com

OCTOBER 31-NOVEMBER 2: WORLDLINK MEDICAL presents MASTERING THE PROTOCOLS FOR OPTIMIZATION OF HORMONE REPLACEMENT THERAPY featuring Neal Rouzier, M.D. in Nashville, Tennessee. 18.5 CME Credits. CONTACT: 888-222-2966; http://www.worldlinkmedical.com/courses/bhrt-series/part-i/october-2014/

NOVEMBER 6-9: ENERGY REGULATION ADVANCED PRACTICE MODULE in Miami, Florida. CONTACT: https://www.functionalmedicine.org/Energy

NOVEMBER 6-9: GI ADVANCED PRACTICE MODULE-Restoring Gastrointestinal Equilibrium: Practical Applications for Understanding, Assessing, and Treating Gut Dysfunction in Miami, Florida. CONTACT: https://www.functionalmedicine.org/GI

NOVEMBER 7-10: HEALTHY MEDICINE ACADEMY'S FOURTH ANNUAL INTEGRATIVE CANCER MEDICINE SYMPOSIUM in Phoenix, Arizona. Focus on clinical applications. Keynote Speaker: Keith Block, MD, the father of integrative oncology. 32.25 AMA; 36 ND CMEs; & more. CONTACT: 303-499-1223 www.healthymedicineacademy.com, info@healthymedicineacademy.com

NOVEMBER 8-9: ARIZONA NATUROPATHIC MEDICAL ASSOCIATION FALL CONFERENCE in Tempe, Arizona. CONTACT: 480-921-3088; http://www.AzNMA.org

NOVEMBER 15-16: KLINGHARDT ACADEMY presents AUTONOMIC RESPONSE TESTING (Level 2) in Horsham, Pennsylvania. CONTACT: phone 908-899-1650; fax 908-542-0961; info@klinghardtacademy.com; http://www.klinghardtacademy.com

DECEMBER 5-7: KLINGHARDT ACADEMY presents APPLIED PSYCHONEUROBIOLOGY in Redmond, Washington. CONTACT: phone 908-899-1650; fax 908-542-0961; info@klinghardtacademy.com; http://www.klinghardtacademy.com

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Kyowa Hakko USA Announces GRAS Self-Affirmation for the Amino Acid L-Ornithine

Kyowa Hakko USA Inc., the wholly-owned subsidiary of Kyowa Hakko Bio Co. Ltd. (Kyowa), has announced it has completed GRAS (generally recognized as safe) self-affirmation for the valuable amino acid L-ornithine.

L-ornithine is an amino acid that is used to build muscle by stimulating protein synthesis through the enhancement of growth hormone secretion and to assist weight loss by increasing the basal metabolism. It is also known that L-ornithine has the ability to enhance immunity, liver function, and antifatigue.

"We are excited about having GRAS for L-ornithine, as this will expand the use of this important amino acid into traditional food and beverages," said Dr. Toshikazu Kamiya, CEO and president of Kyowa Hakko USA.

Research supported by Kyowa Hakko Bio suggests that L-ornithine has an antifatigue effect by increasing the efficiency of energy utilization and promoting the excretion of ammonia.[1]

The GRAS affirmation includes L-ornithine, L-ornithine monohydrochloride, and L-ornithine L-aspartate. L-ornithine will be marketed by Kyowa Hakko USA as a food ingredient in the US for use at levels of 200 mg of L-ornithine/serving in various food products, such as beverages and beverages bases, grain products and pastas, milk products, and processed fruits and fruit juices.

Kyowa Hakko USA 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 L-Citrulline and other branded ingredients including Cognizin Citicoline, Lumistor L-Hydroxyproline, Pantesin Pantethine, Setria Glutathione, and Sustamine L-Alanyl-L-Glutamine. For more information, visit http://www.kyowa-usa.com.

Notes

1. Sugino T, Shirai T, Kajimoto Y, Kajimoto O. L-Ornithine supplementation attenuates physical fatigue in healthy volunteers by modulating lipid and amino acid metabolism. *Nutr Res.* November 2008;28(11):738–743. http://dx.doi.org/10.1016/j.nutres.2008.08.008.

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ICIM Offers $20,000 Prize to the Best Proposal to Advance Chelation Research for Cardiovascular Disease

The International College of Integrative Medicine (ICIM) is offering a grant of $20,000 to stimulate further research on chelation therapy to treat vascular disease and/or diabetic complications. The funds are to be used to plan a significant study. Applicants must submit an adequate explanation of their proposals to include 1) the likelihood of a successful outcome based on previous studies, 2) the possibilities for funding of the entire study, and 3) involvement of experienced researchers and clinicians.

Proposals should be no more than 2–3 typewritten pages. They can be submitted to wendy@icimed.com by email. The deadline for proposals is 31 May, 2014. The Grant will be called the James P. Carter Memorial Grant for EDTA Chelation Research.

The International College of Integrative Medicine is a community of dedicated physicians who advance innovative therapies in integrative medicine by conducting educational conferences, supporting research, and cooperating with other scientific organizations, while always promoting the highest standards of practice.

ICIM's Summit on the Future of Chelation Therapy, Washington, DC, March 2013

New Offerings from Pharmasan Labs and NeuroScience Inc. Assess and Address Hormone Imbalances

Pharmasan Labs, a CLIA-certified provider of high-quality laboratory services, and NeuroScience Inc., a national leader in personalized health-care solutions, have introduced enhancements to salivary hormone profiles, as well as new products that address hormonal imbalances through support of the nervous system.

NeuroScience's new hormone-focused products offer a multipronged approach that includes nervous system support to promote healthy hormone activity.

Pharmasan Labs' new hormone profile enhancements include:

- New test panels: Two new panels offer five key sex and adrenal hormones, specially priced for cash-pay and patients with high insurance deductibles.
- More reliable testing methodology: Saliva hormone tests now utilize a 4-point pooled saliva method for measurement of reproductive hormones and DHEA. This method better reflects overall physiologic hormone levels, improving reliability.
- More comprehensive data: Patient reports now include observed HRT ranges for patients on patches, creams, or oral therapies; cycle status (follicular, midcycle, or luteal); menopause status; and optional progesterone-to-estradiol ratio (Pg/E2).

Pharmasan Labs' wide-ranging services and comprehensive test menu are tailored to support the needs of research institutions and health-care businesses, including their practitioners and patients. Pharmasan Labs Inc. is certified by the Clinical Laboratory Improvement Amendments program (CLIA ID# 52D0914898) and New York State Department of Health (PFI# 7426). For more information: www.pharmasan.com.

NeuroScience is committed to delivering personalized health-care solutions. In conjunction with Pharmasan Labs Inc., NeuroScience provides licensed health-care providers with integrative clinical assessments and proprietary nutraceuticals to identify and target neurological and hormonal imbalances. Through its Assess & Address approach, NeuroScience empowers forward-thinking clinicians to better understand patients' unique biochemistry and guide them toward optimal health through personalized, highly effective treatment recommendations. For more information: www.neuroscienceinc.com.

Metagenics Launches D3 10,000 IU with K2

D3 10,000 IU with K2 is an exciting new product designed for patients with demonstrated increased nutritional needs for vitamin D. It is ideal for patients with deficient or insufficient 25(OH)D levels (under 30 ng/ml). Each soft gel also contains 90 mcg of vitamin K2, composed of MK4 and MK7. Collectively, vitamin D and K protect bone health and may help support cardiovascular health.*

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

Metagenics.com • 800.692.9400 US • 800.268.6200 Canada

Two Clinical Studies Support Efficacy of Pure Encapsulations Resveratrol

Pure Encapsulations, a leading manufacturer of hypoallergenic nutritional supplements, announces the findings of two studies utilizing Pure Encapsulations Resveratrol. Conducted by academic researchers, these independent clinical investigations diverged from prior research studies on resveratrol by evaluating the product at a once-daily dose.

Since the 1990s, scientists have known that resveratrol moderates nuclear factor-kappa B (NFκB), a master switch of cytokine gene expression in cell culture. Dozens of studies have since attributed this mechanism to its cardioprotective and neuroprotective effects. However, these clinical studies used high doses, typically 100 to 500 mg per day, leaving questions about the ability of resveratrol to provide support at a lower dose.*

"While the clinical value of resveratrol is widely recognized, health-care professionals must navigate an overwhelming array of formulations and doses," stated Kelly Heim, PhD, a pharmacologist at Pure Encapsulations. "The new studies on Pure Encapsulations' Resveratrol allow the practitioner to select and apply our product with confidence. This research is among many examples of Pure Encapsulations' alignment with evidence-based medicine."

For more information on PureHeart Probiotic, or to request a copy of *The PureHeart Protocol: Screening + Supplements = Success* brochure, please contact Bryanna Charbonneau at bcharbonneau@PureEncapsulations.com or visit www.PureEncapsulations.com.

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

Douglas Laboratories Introduces PMS Support with BioResponse

Douglas Laboratories, the trusted choice of health-care professionals for superior-quality, science-based nutritional supplements for more than 50 years, is proud to introduce PMS Support with BioResponse DIM. Codeveloped by Shelena C. Lalji, MD, a well-known keynote speaker, medical expert, and knowledgeable trainer for fellow integrative practitioners, the PMS Support formula promotes healthy hormone levels and reproductive function in women while supporting normal premenstrual syndrome ("PMS") symptoms.†

"Douglas Labs is pleased to partner with women's health expert Dr. Lalji to offer this advanced female-focused product," said Andrew Halpner PhD, vice president, Product Development and Technical Services at Douglas Laboratories. "The addition of BioResponse DIM makes this formula unique from other PMS formulas, and helps to meet the need of women who suffer from PMS."

For further information on the PMS Support with BioResponse DIM formula, visit douglaslabs.com. BioResponse DIM is a registered trademark of BioResponse LLC, Boulder, CO. US Patent 6,086,915.

† These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure, or prevent any disease.

Essential Formulas' Line of Chia Omega Formulations Receives Respected NSF Certified for Sport Product Certification

Essential Formulas Incorporated's line of award-winning Chia Omega formulations recently earned the NSF Certified for Sport designation (http://www.nsfsport.com) from NSF International, one of the most respected independent product-testing and certification organizations.

Scientists at NSF International tested Essential Formulas' Chia Omega products (www.chiaomega.com) to verify that these products comply with strict standards of NSF/ANSI 173, the only American national standard for dietary supplements which was developed through a consensus process involving input from regulatory, industry, sports, and consumer groups. This included testing to verify label accuracy and that the product did not contain any harmful levels of contaminants.

Additionally, to earn NSF Certified for Sport certification, Chia Omega products were screened for more than 180 banned substances such as narcotics, steroids, stimulants, and hormones along with diuretics and other masking agents. Essential Formulas' manufacturing facility also was inspected to verify compliance with NSF's current Good Manufacturing Practices (cGMP) facility registration program.

"This distinguished certification helps athletes as well as general consumers make more educated decisions when choosing dietary supplements," said Michael Schoor, president and CEO of Essential Formulas. "Our company was founded on the principles of transparency, education and product integrity and we are proud to earn the highly respected NSF Certified for Sport designation for our Chia Omega products."

"Many professional athletes and sports organizations rely on NSF International's Certified for Sport program because it is the most rigorous testing and certification program available for sports nutrition and dietary supplement products," said Lisa Thomas, general manager of NSF's Dietary Supplement programs. "Essential Formulas' participation in the program demonstrates their leadership and commitment in developing products of high quality and safety."

The National Football League (NFL), Major League Baseball (MLB), National Hockey League (NHL), Ladies Professional Golf Association (LPGA), PGA, and Canadian Centre for Ethics in Sport (CCES) utilize the NSF Certified for Sport program to protect athletes from prohibited substances.

Athletes and consumers can find Essential Formulas' NSF certified products on NSF International's listings (www.nsfsport.com/listings/certified_products.asp) or by downloading the NSF Sport app (www.nsfsport.com/sport_app.asp).

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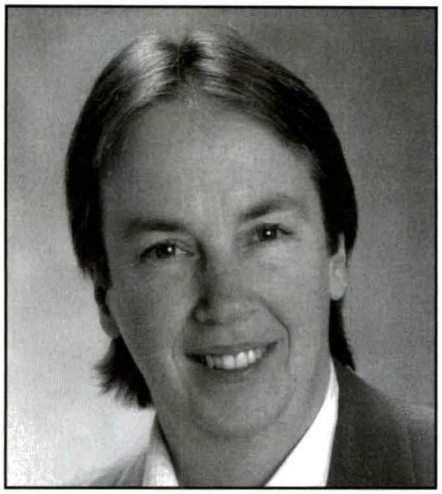
Dallas-based Essential Formulas Incorporated (EFI) was established in 2000 as the sole US distributor of world-renowned microbiologist Dr. Iichiroh Ohhira's award-winning probiotic dietary supplements. A family-owned and -operated business, EFI was founded on the philosophy of providing high-quality preventative, supportive, and comprehensive prohealth products for the entire family. Pledging to provide premium all-natural supplements and exceptional customer care, EFI continually strives to lead the industry in customer and retailer education in the use and efficacy of its innovative products, which include Dr. Ohhira's Probiotics formulations and the newly introduced Chia Omega line of omega-3 formulations. Both Dr. Ohhira's probiotic formulations and Chia Omega dietary supplements are available at Vitamin Shoppe, Whole Foods Market, and other health food stores across the country. For more information, visit www.essentialformulas.com, or call 972-255-3918. ◆



Women's Health Update

by Tori Hudson, ND
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Cardiovascular Tidbits

For Your Heart: Don't Forget the Flaxseeds

Because the incidence of cardiovascular disease significantly increases in postmenopausal women, alternative and conventional options to improve lipid profiles, lower blood pressure, and lower other cardiovascular risk factors are on the minds of clinicians and health-conscious women.

Among the many functional foods that have been evaluated for their effects on improving lipids, reducing insulin resistance, lowering blood pressure, and reducing atherogenic properties, flaxseed has shown some optimistic potential for its ability to reduce the progression of atherosclerotic lesions. Its lignans, alpha-linolenic acid, and soluble fiber all have positive influences. Flaxseeds have been shown to reduce serum cholesterol in humans.[1,2]

A flaxseed supplement consisting of three slices of flaxseed-containing bread and 15 g of ground flaxseed was studied in 15 hyperlipidemic patients, and total and low-density lipoprotein cholesterol levels were reduced significantly, 18 mg/dL and 19 mg/dL respectively. Triglycerides fell only slightly.[3] A study specifically in postmenopausal women found that 40 g/day of flaxseeds resulted in a small reduced serum total cholesterol and increased high density lipoproteins greater than that compared with the same amount of wheat germ.[4] In another study, 55 Native American postmenopausal women were divided into 3 groups over 3 months. Group 1 was the control group, group 2 received 30 g/day of flaxseeds, and group 3 30 g/day of flax plus additional oat-bran fiber. Dietary flaxseed supplementation lowered total cholesterol by approximately 7% and low-density lipoprotein cholesterol by approximately 10%.[5]

Not all results are positive when it comes to flaxseeds and lipids. In 2002, 40 g/day of flaxseeds did not improve the cholesterol profile in hypercholesterolemic menopausal women although it did improve mild menopausal symptoms and lowered glucose and insulin levels.[6] A study in postmenopausal women demonstrated no effect of a flaxseed component on lipids or any antioxidant properties.[7]

However, a recent animal study also showed that a diet of 15% and 22.5% flaxseeds significantly reduced lipoprotein (a) and ApoB.[8] In other research, 13.7 g/day of flaxseed in healthy individuals significantly reduced inflammatory markers, including tumor necrosis factor-alpha, interleukin-1 beta, thromboxane B5, and prostaglandin E5.[9] Other studies have shown a reduction of inflammatory markers and adhesion molecule production, which suggests some antioxidant properties of flaxseeds.[10-12]

Overall, it seems that there is enough evidence that including flaxseeds into the diet can modify cholesterolemia. This is especially important in postmenopausal women, as their lipid levels begin to change in an unfavorable direction due to the decline in endogenous estrogen, and their cardiovascular risks increase.

Red Yeast Rice: Still a Player

Red yeast rice formulations have been a common strategy to improve lipids among alternative-minded practitioners, as well as consumers in self treatment. This approach, along with lifestyle changes, has provided a reasonable solution for those who have mild to moderate abnormal lipids. Red yeast rice is produced by culturing the yeast *Monascus purpureus* on rice. This results in a mixture of monacolins that inhibit hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase, which then inhibits the synthesis of cholesterol in the liver. Monacolin K is identical to lovastatin in its chemical structure. While these red yeast rice products are widely available as a dietary supplement, the monacolin levels per gram of active product are not standardized and this variability leads to variability in efficacy of products.

In the current study, physicians and spouses were participants in a randomized, double-blind, placebo-controlled trial. Those with a total

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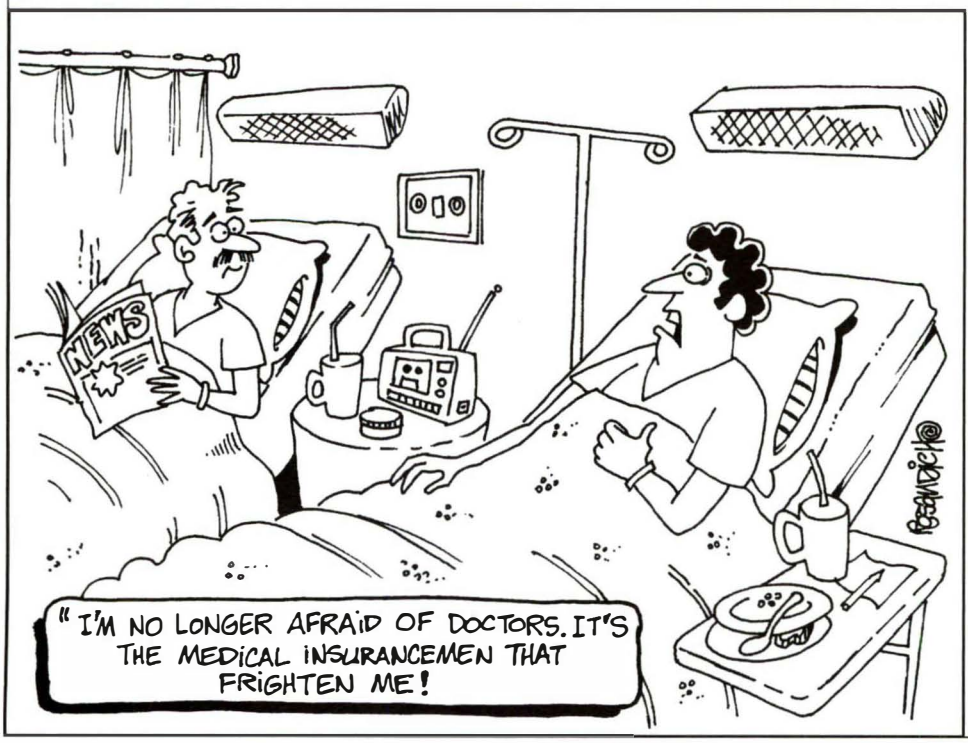
cholesterol >200 mg/dl were randomly assigned to receive red yeast rice (RYR) extract or placebo for 8 weeks. Participants were excluded if they were on statins, had a triglyceride level >400 mg/dL, or had changes in medications or food supplements that are known to affect lipid levels. A product was used that contained 1.5% monacolin K (5025 mg of monacolin K per capsule) along with coenzyme Q10 30 mg, procyanidins 20 mg, and lecithin 100 mg. A dose of 2 capsules per day of active product or placebo was given each evening for 8 weeks to the 54 participants, with 31 in the active group and 23 in the placebo group.

In the active group, low density lipoprotein (LDL) was lowered by 36 mg/dL (22%) and total cholesterol by 37 mg/dL (15%), a statistically significant effect compared with no reduction seen in total cholesterol and LDL in the placebo group. There were no reported side effects.

Comment: The study dose of 10,050 mg of monacolin K is a higher dose than most commercially available RYR products. Given the political and legal climate of dietary supplements, and the particular history of RYR products in this regard, it can be very difficult to get a good answer from a supplement company on the precise amount of monacolin K in its products. This makes prescribing RYR challenging. The manufacturer of this particular product used in this study added coenzyme Q10 to the formulation with the purpose of aiming to reduce myalgia side effects. Coenzyme Q10 deficiency has been proposed to have a role in HMG-CoA reductase–inhibitor induced myopathies that can be seen with prescription statins, and occasionally RYR as well.

Lowering total cholesterol and LDL is one thing, but reducing cardiovascular disease is another. This can be seen as an advantage of the prescription statins by some, due to studies that have been done with cardiovascular disease outcomes. However, there is also some evidence regarding RYR and secondary prevention from a large multicenter, randomized, double-blind, placebo-controlled study in almost 5000 Chinese patients with a history of myocardial infarction and moderate hypercholesterolemia.[13,14] Over a duration of 4.5 years, a one-third reduction in cardiovascular deaths and the need for coronary revascularization was seen, and in those with diabetes and hypertension, a reduction in coronary events was also seen.

Verhoeven V, Hartmann M, Remmen R, et al. Red yeast rice lowers cholesterol in physicians-a double-blind, placebo controlled randomized trial. *BMC Comp and Altern Med*. 2913;13:178



Lowering Lipids in Women: How Effective Is It in Treating Heart Disease?

One of the most important issues to be reminded of in the common focus on addressing lipids is that over 50% of patients who have heart attacks did not have any prior known risk factors. For women, the first symptom of coronary heart disease (CHD) is in fact a heart attack. Treating cholesterol numbers reduces CHD by about 50%, but targeting regular exercise, good nutrition with a Mediterranean diet, weight reduction, smoking cessation, and perhaps even a little red wine can reduce cardiovascular disease by about 80%. New guidelines from the American Heart Association and the American College of Cardiology have, in my mind, basically admitted that lipid targeted strategies are limited in risk reduction. The new guidelines have changed the focus from LDL and total cholesterol levels to focusing on other risk factors, with the only lipid number still relevant for the indication of a cholesterol-lowering medication being an LDL > 190 mg/dL.

Women have significantly different mechanisms underlying their CHD symptoms. Symptoms in women are more related to microvascular angina and stress cardiomyopathy and are more likely to be upper back pain or neck pain, dyspnea, palpitations, indigestion, and/or fatigue. Women also are most likely to have the symptom of sweating if they are having a heart attack.

Approximately 40% of women have no chest pressure, discomfort, or pain. Using statins in women is also less effective than in men.

In addition, the usual treadmill test is not very useful in women, especially in those under 50 years old. It is more predictive in women >65 years old (68%), but overall, in all ages, it is only a predictive value of 51%. A stress echo and nuclear medicine testing are more helpful tests in most women.

For women, a specific tool can define risk for coronary heart disease. It is a scoring system developed by physicians at the University of Texas Southwestern Medical Center, and published in the *American Journal of Cardiology* in 2013. A scoring system of seven independent factors predictive of CAD in women is used in those with abnormal stress test findings:

- 55 years old or older
- body mass index > 30 kg/m^2
- smoking
- low HDL
- family history of premature CAD
- lateral abnormality on stress imaging
- exercise capacity

One point is assigned for each variable. A score under 2 indicates little risk of CAD; a score of over 2 signals concern. If the score is <2, then the treadmill stress test has a negative predictive value of 80%.[15]

For women, it is important to really understand the lesser role of lipid lowering and incorporate strategies that address vascular health, heart muscle health, circulation, inflammation, blood pressure, blood pressure, insulin resistance, and body weight.

Notes

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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 28 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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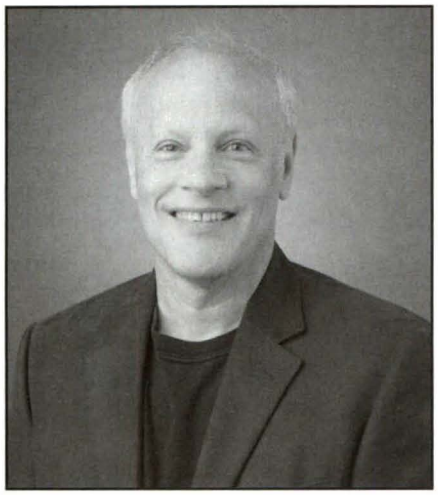

Reader Beware

As scientists and health-care practitioners, we depend on the reliability of the research published in biomedical journals. For that reason, reputable journals have a peer-review process, in which experts review submitted papers to determine their suitability for publication. In recent years, thousands of open-access journals have been created in many different fields of science and medicine. The articles published in these journals are available online to the public without charge, and the journals are supported by publication fees paid by the authors.

Journals that employ this business model have an inherent conflict of interest, because rejecting studies of poor or questionable quality decreases their revenue. By the same token, authors or companies that are willing to pay to have their research published might have a vested interest in the substances that they are researching. Some open-access journals appear to operate with a high degree of integrity and have an adequate peer-review process, whereas others might not.

To investigate the quality of the peer-review process of open-access journals, a researcher named John Bohannon recently submitted a bogus paper to 304 such journals, describing the purported in vitro anticancer effects of a compound extracted from a lichen.[1]

According to Bohannon, the experiments were so hopelessly flawed that any reviewer with even a rudimentary understanding of chemistry and data presentation should have recognized that the results were meaningless. For example, the "anticancer" molecule was dissolved in a high concentration of ethanol before incubating it with the cancer cells, whereas the control cancer cells were not exposed to ethanol. Therefore, the molecule's reported effect on cancer cell growth was nothing more than the well-known cytotoxic effect of ethanol. The study also purported to show that the molecule augmented the inhibitory effect of radiation on cancer cell growth. However, the control cancer cells were not exposed to radiation, so the experiment showed nothing more than the fact that radiation inhibits cell growth.

Of the 304 journals that were sent the paper, 157 accepted it, 98 rejected it, and the remaining 49 were either still reviewing it or were no longer in existence. In 36 cases, the peer reviewers commented about the serious scientific flaws of the study; however, 16 of those 36 submissions were accepted for publication by the editors anyway. Bohannon noted that many open-access journals hide their true geographic location, to make it appear that they are Western academic publications. For example, the *American Journal of Medical and Dental Sciences* is published in Pakistan, and the *European Journal of Chemistry* is published in Turkey. Both of those journals accepted the bogus paper.

Open-access journals do not have a monopoly on poor peer review. Over the years I have seen many papers in subscription-based journals that should not have been accepted for publication. For example, one study claimed to show that a particular treatment was

effective because the improvement was statistically significant in the active-treatment group but was not significant in the placebo group. However, the magnitude of the improvement was actually greater in the placebo group than in the active-treatment group. Another study included 5 patients in the active-treatment group and 4 in the placebo group. In that study, the baseline characteristics differed so greatly between groups that the groups could not be considered comparable. Both of those studies were funded by the company that owned the patent on the product being studied.

However, because of their inherent conflicts of interest, open-access journals are much more likely than standard subscription-based journals to publish studies that have not been adequately peer reviewed. One must therefore view these publications with a certain degree of skepticism. Is the abstract of the paper consistent with the results in the body of the paper? Are only the positive results emphasized in the abstract and discussion section, while the negative results are glossed over? Are the data described in the text consistent with the findings shown in the tables and figures? Did the authors emphasize positive results that were not statistically significant? If there was no control group, could the results be explained by a placebo effect or spontaneous remission? Did the researchers or the funding source have real or potential conflicts of interest?

Practitioners often think that they do not have the time needed to get to the truth behind the headlines and abstracts of research studies. However, when considering papers that will affect your clinical practice, it is important to spend that extra time and effort. And the editors and owners of open-access journals should understand that their credibility and ultimately their future depends on maintaining a legitimate peer-review process.

Alan R. Gaby, MD

Notes

1. Bohannon J. Who's afraid of peer review? *Science*. 2013;342:60–65.

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