WOMEN'S HEALTH

TOWNSENDLETTER.COM

Townsend Letter

The Examiner of Alternative Medicine

Feb/March 2020
Issue #439/440
$10.99

Rubidium for Depression

Defending Homeopathy

Best Natural Gynecology Rxs

Progesterone Myths and Facts

Gabby Reece's Program for Success

JUMP TO TABLE OF CONTENTS

Thank you for purchasing this issue of *TOWNSEND LETTER*

On the cover (next page) you will find a button that will take you directly to the table of contents. Once there, you can click page numbers that take you directly to articles. Click on "return to table of contents" at the bottom of each page to take you back to the TOC.

Most web and email addresses are clickable within the articles and in the calendar. We do not guarantee the accuracy of each address/URL, or that it is clickable.

Please don't overlook our advertisers, without their support *Townsend Letter* would not exist. Take the time to discover companies you might not be familiar with, many of whom offer special pricing for *Townsend Letter* subscribers. An advertiser list is printed on page 80 with clickable page numbers that will take you directly to their ad(s).

Subscription Rates and Options

Prices valid through 12/31/2020

Name _____ Email/Phone _____

Address _____

City/State/Zip _____

Payment accepted in US funds, payable by check / money order / credit card / or billed via PayPal

Payment by: Visa/MC/AMEX/Discover # _____ Expiration date: _____

Signature _____

Click here to subscribe online

	Description	Print Version	E-Edition	Combined
US Addresses (except WA state)	1-year Domestic US	$76.99	$66.99	$91.99
	2-year Domestic US	136.99	116.99	166.99
	6-month Domestic US	45.99	41.99	–
	1-year Student Domestic US	56.99	41.99	66.99
Washington State Residents	1-year Washington state (w/tax)	86.99	74.99	99.99
	2-year Washington state (w/tax)	146.99	127.99	183.99
	6-month Washington state (w/tax)	33.99	46.99	–
	1-year Washington Student (w/tax)	56.99	46.99	66.99
1st Class	1-year First Class Domestic US	96.99	66.99	111.99
	2-year First Class Domestic US	176.99	116.99	206.99
International Rates	1-year International (US$)	105.99	66.99	120.99
	2-year International (US$)	202.99	116.99	232.99
	6-month International (US$)	63.99	41.99	–
	1-year International student (US$)	76.99	41.99	93.99

SPECIAL RECEPTION ROOM OFFER:
Purchase a 2nd subscription for your waiting room

$57.99 US addresses – $87.99 International
Offer valid with current existing subscription

E-Edition Single Issue: $15.00

E-Edition Single Issue WA State (includes tax): $16.00

Single Print Issues: cover cost (for each issue), plus shipping charges, applicable taxes, and $3 per-order handling fee.

Townsend Letter

911 Tyler Street | Port Townsend WA 98368

info@townsendletter.com

360.385.6021 | 360.385.0699 (fax)

www.townsendletter.com

BioDisrupt®

Triple Action Support

3 Mechanisms of Action

- Promoting a healthy extracellular matrix*
- Supporting ideal cellular communication*
- Reinforcing normal microbial balance*

BioDisrupt® supports the healthy immune system's ability to target the sophisticated self-defense mechanisms of unwanted extracellular organisms. These organisms have developed a series of advanced mechanisms which allow them to evade immune detection. As part of this system, these organisms assemble into clusters, surround themselves with protective physical matrices and communicate among themselves.

Each 2 capsule serving contains:

- ✓ **EnzymeDisrupt™** - Lysozyme, Serratiopeptidase, Beta-glucanase, Lipase, Protease, Celllulase, Hemicellulase
- ✓ **HerbDisrupt™** - Cranberry fruit extract, Beberine, Rose-mary extract, Peppermint oil powder
- ✓ **N-acetyl cysteine**

Researched Nutritionals®
solutions for life

+1.800.755.3402

Tel: 805.693.1802 • Fax: 805.693.1806 • CustomerService@ResearchedNutritionals.com
www.ResearchedNutritionals.com | *Available only through healthcare professionals*

Promote Healthy Mast Cell Function*

Dual Mechanisms of Action

- *Promotes healthy mast cell function**
- *Supports healthy histamine receptor blocking**

In response to exposure to a perceived pathogen, mast cells set off a rapid biological response to foreign invaders and/or harmless triggers. Included in this response are the release of cytokines and other chemical messengers.

HistaQuel® is a researched-based formulation to promote a healthy response during this process. Each capsule contains:

Mast Cell Secure™

Fisetin, Luteolin, Perilla frutescens, Quercefit™ (highly absorbable quercetin)*

HistaCheck™

Stinging Nettle

"I can see a role for this in all levels of reactivity, from simple allergy support to promoting healthy mast cell function.

Joseph Burrascano Jr., MD

"Researched" - the first word in our company name, was chosen to communicate our research-driven culture.

RESEARCH IS ALWAYS IN PROCESS...

INTERNATIONAL CONGRESS OF REGENERATIVE MEDICINE

Spring 2020

Sangeeta Pati, MD FACOG
Leading expert in Bio-identical Hormone Therapy

Michael T. Murray, N.D.
One of the world's leading authorities on Natural Medicine

Mitch Ghen, DO
International lecturer on oral and IV nutrition and stem cell transplantation

John W. Apsley, MD(E), ND,DC
30 yrs specializing in Integrative Regenerative Medicine

Jenny Wilkins, NMD, CRA
Specialist in the Endocannabinoid System

JUNE 12-14, 2020 | CAPTIVA ISLAND, FL | REGISTER NOW!

13.5 credits of CME and Naturopathic CE applied for

How YOU Can Optimize the Immune System for Chronic INFECTIONS and CANCER: Protocols and Cases!

Whether you are in the business of treating chronic infections and cancer or not, every one of us is now faced with **1 out of every 3** of our patients, family, and friends battling the epidemic of immune failure. Join us as we dive into how to address teeth toxicities, adrenal/ thyroid insufficiency, oxygen status, phase angle, chronic stress response, pH and nutrition.

Do you want to leave in-hand with protocols that you can apply in your clinic the very next day? **Are you interested in having >85% reversal of disease rate?** This workshop aims to put practitioners just like YOU in the driver's seat with basic methods that have helped hundreds of patients regain immune function to combat cancer and chronic infections. **We are looking to empower leaders in the field of Regenerative Medicine!**

Healthcare Providers Special:

Purchase $100 Value on MDPrescriptives.com
using this code: **TOWNSEND**
and receive $100 SPECIAL OFF our upcoming
REGENERATIVE CONFERENCE!

REGISTER at ICRMConference.com
info@mdprescriptives.com
(877) 963-7737

Regenerate With Us & Leave Empowered!

From the Publisher

Bitten: The Secret History of Lyme Disease **by Kris Newby**

Ninety-five million years ago the brontosaurus and T. rex ruled the earth. A much smaller creature harried these dinosaurs sucking their blood – the tick. When the asteroid(s) collided with the planet 60 million years ago turning the climate into an ice age, the dinosaurs faced a catastrophic species extinction, but not the tick. It continued to evolve over the eons adapting itself to the terrain, weather, fauna, and flora. Trillions if not quintillions of generations later, the tick has become a ubiquitous predator capable of siphoning blood from all animals. The tick has evolved to efficiently sense changes in temperature, carbon dioxide, and ammonia identifying the approach of an animal through its forelegs. While some ticks await direct proximity of a host from a grassy stalk, the Lone Star tick hunts its prey. Once the tick has established a suitable location to seek its meal such as underneath the nape of the neck, it lowers its three-prong jaw, bites through the epidermis and injects an anesthetic substance into the animal. Burying and anchoring itself into the underlying tissue, it emits a cementing agent and a blood thinner ensuring that clotting ➤

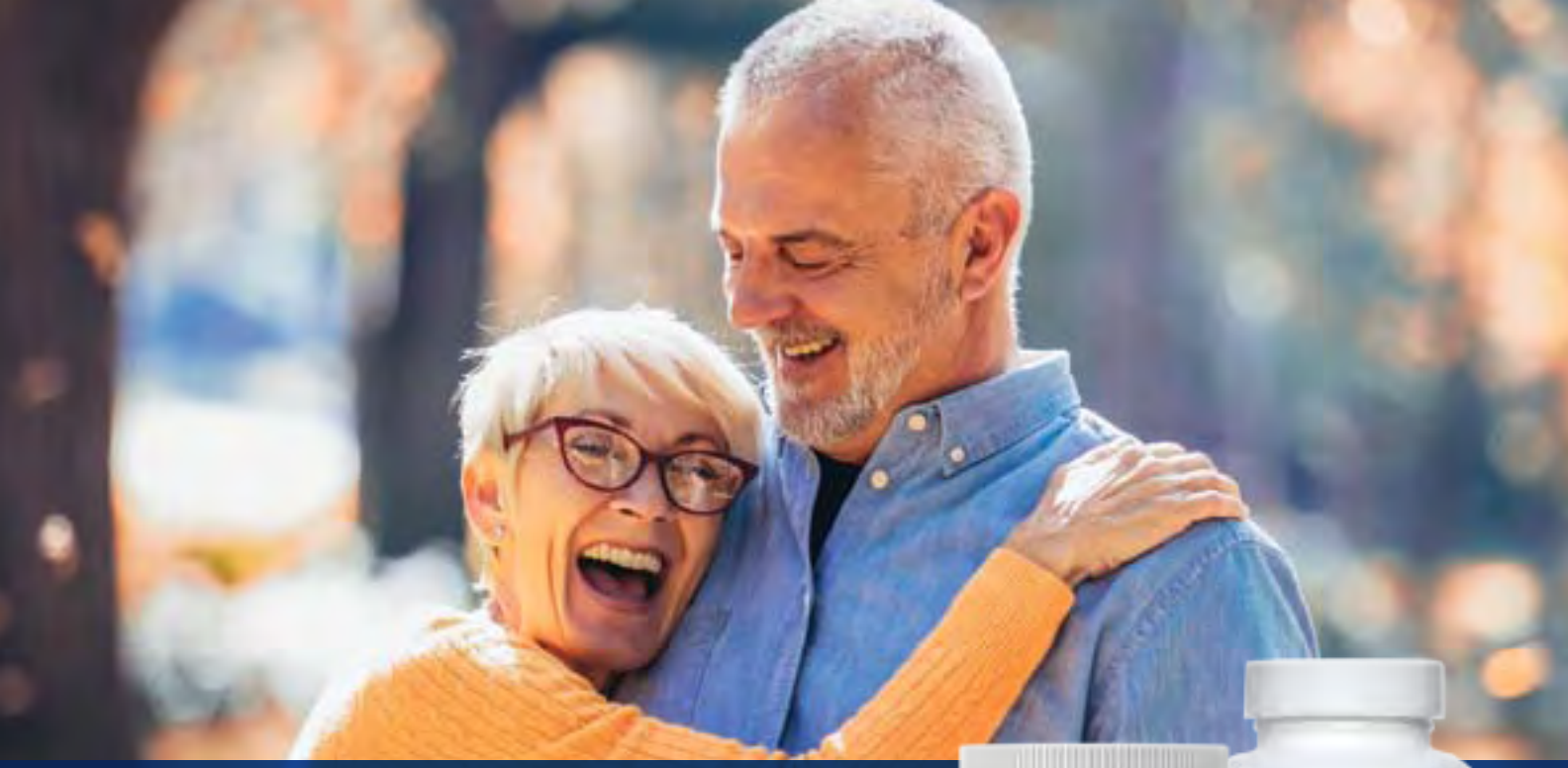
➤

will not interfere with blood extraction. As it sucks away blood, the tick injects a myriad of microorganisms, bacteria, parasites, viruses, worms, and more into the host. These tick-borne pathogens share a symbiotic relationship with the tick facilitating the tick's physiology. Unfortunately, these pathogens can cause a variety of diseases, some of which cause low-grade flu symptomatology, but others are far more severe and can persist indefinitely. Meanwhile the tick drops off after becoming engorged and then deposits a clutch of several thousand eggs repeating the cycle of tick development and predation.

After nearly one hundred million years, the tick has figured out survival; and its vampire activity has led to millions of humans becoming sickened with a diverse group of illnesses that have largely stumped the medical profession. The disease that most of us are concerned with is Lyme disease thought to be due to infection with a spirochetal bacterium, *Borrelia burgdoferi*, named after tick expert, Willie Burgdofer. Yet, the tick is just as likely to carry many other microorganisms, not the least of which are very tiny bacteria, *Rickettsia*, one of which, *Rickettsia rickettsii*, named after the investigator who first identified them, Ricketts, causes Rocky Mountain spotted fever. When Mormon settlers travelled through the Rocky Mountains in the mid to late 1800s it was not infrequent for them to be bitten by a tick and be infected with spotted fever. More than a century later tick bites have become associated not just with a Rickettsial infection, but one caused by a spirochetal bacterium. In Africa, a tick-borne Borrelial spirochete is responsible for infection with relapsing fever. In fact, ticks are well adapted to carry multiple bacterial and parasitic organisms. However, in the US, tick bites up until the 1970s were generally limited to Rocky Mountain spotted fever. How did the tick suddenly become the vector of a very new disease, Lyme disease, localized to Connecticut, New York, and New England?

In Kris Newby's fascinating book, *Bitten*, the new disease seemed to begin with an outbreak of babesiosis caused by the malarial-like parasite, babesia, that occurred on an island off of Massachusetts coast, Nantucket, in 1968. Where did this organism come from? In 1972 a cluster of individuals on eastern Long Island developed Lyme disease arthritis, Rocky Mountain spotted fever, and babesiosis. However, neither the CDC nor

continued on page 6 ➤



METABOLIC AND DIGESTIVE SUPPORT*

Essential-Biotic® HEART

with LRC™ and CoQ10

Lactobacillus reuteri NCIMB 30242 (LRC™) supports normal, healthy cholesterol metabolism and vitamin D levels in the blood.*

LRC™ encourages normal digestive system function and improved elimination.*

Coenzyme Q10 enhances production of cellular energy and supports overall cardiovascular health.*

LRC™ is a trademark of UAS Laboratories, LLC and used under license.

Ox Bile

Essential for Fat Digestion*

Supports absorption of dietary fats and fat-soluble vitamins, a healthy balance of flora in the gut, and normal bowel motility and regularity.*

Bile acids interact with nuclear and cellular membrane receptors to help regulate metabolic balance.*

Tested to ensure the product is free of antibiotic, pesticide, herbicide, and hormone residues.

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

AllergyResearchGroup®
Innovative Nutrition

NSF GMP Registered

emerson QUALITY PROGRAM

emerson ecologics | wellevate

natural partners

Call or order online today.
www.allergyresearchgroup.com
800.545.9960

Letter from the Publisher

➤ *continued from page 4*

regional health authorities understood the tick-based causes of these outbreaks despite intensive investigation through the mid-1970s. Burgdofer, who grew up and was educated in Switzerland, was hired by the Rocky Mountain Laboratory, in Hamilton, Montana, in the mid-1950s to study ticks and other arthropods causing parasitic disease. He became adept at going out in the woods and capturing thousands of ticks, fleas, lice, mosquitoes, as well as other insects, bringing them back to the laboratory for study under the microscope as well as on the lab bench. He used a "glass" knife to be able to carefully dissect the tick to study the organisms contained within. Willie was noted to be fastidious in his research and spent hours and hours researching ticks and identifying the tick's symbiotic organisms, some pathogenic, some not so.

In the early 1960s the US government transformed Burgdorfer's mission not to study ticks, but to learn how the tick could be used in biological warfare. Could the tick carry more aggressive illness-inducing organisms that could be dropped on an enemy force incapacitating them? This was the mission that Burgdorfer agreed to do – not just in Hamilton, Montana, but also at Ft. Dietrick in Maryland, where the armed forces conducted bio-weapon testing during the 1950s-60s until Nixon terminated the program in 1968. The testing was intensive and exhaustive. Willie wanted to know if one could manipulate hormone physiology to cause tick fertility to dramatically increase – that experimentation failed. Much more rewarding was experimenting with a variety of different organisms to determine if ticks would carry a pathogen successfully enabling new diseases to be transmitted after a tick bite. A variety of viruses, bacteria, and parasites were tried. Burgdorfer's work revealed that individual tick species would adapt symbiotically, hosting certain microorganisms but not others. One of the experiments authorized by Ft. Dietrick was an attempt to drop crates carrying massive numbers of ticks like an airborne bomb. Although it was never determined how successful the ticks were in infesting bombed areas, the airmen conducting such experimentation developed tick-borne illness. Perhaps the most insidious experimentation was conducted with aerosolized pathogens that were released like insecticide spraying from airplanes. Burgdorfer witnessed a prototype of this being done on a large animal herd with all animals becoming ill after inhalation of the pathogen.

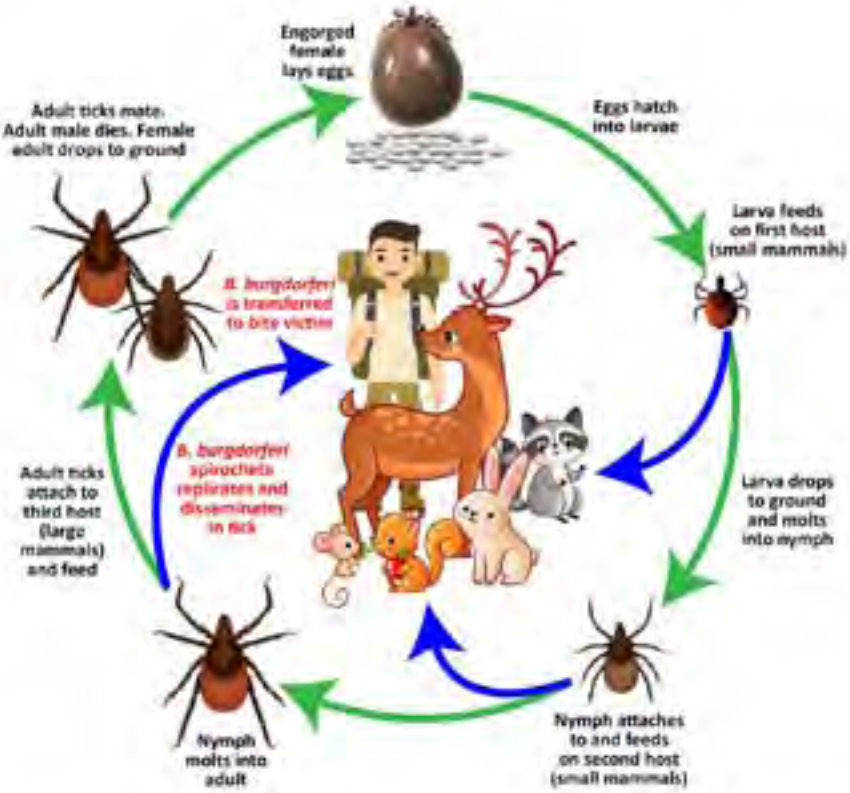
What Newby's book attempts to prove but never develops absolute proof for is that the tick bio-weapon research may have gone awry and ticks infected experimentally with pathogens may have inadvertently escaped into our ecosystem. Newby suggests that the epicenter for such experimentation that went awry could have been on the Atlantic seaboard over

continued on page 8 ➤

Multi-Peptide ELISA is the most comprehensive method for the detection of Lyme disease and other tick-borne diseases.

(US Patent 7,390,626 B2)

Inaccurate testing for Lyme can result in unneccesary treatment with antibiotics, leading to gut-to-brain abnormalities.



Untreated Lyme disease can turn into chronic Lyme disease, which in turn can lead to Lyme arthritis and neuroborreliosis.

IMMUNOSCIENCES LAB., INC.

CALIFORNIA-LICENSED, CLIA-CERTIFIED, CAP-APPROVED

Contact our Client Services Team at (310) 657-1077, or e-mail us at immunsci@gmail.com. Visit us at www.immunoscienceslab.com.

Letter from the Publisher

➤ *continued from page 6*

eastern Long Island and Nantucket. Burgdorfer's research in the late 1970s focused on a Rickettsial organism that was quite different from the *R. rickettsii*, *R. montanensis*, and most other Rickettsii. The new organism had a similarity to an organism observed in sheep in Europe – it was labelled in his work as the *Swiss agent*, a rickettsial organism resembling *R. montanensis*. Burgdorfer's research in 1980 took a major turn after his careful microscopic work found a spirochetal organism in the tick, which was associated with patients having Lyme disease. After careful antibody studies confirmed that the spirochete was the causative organism, Burgdorfer wrote a paper in *Science* detailing his findings. His work shocked the world as no one had associated a spirochete with Lyme disease, and he became an instant sensation with academicians and the public in 1982. For reasons that have never been explained the Swiss agent disappeared from Willie's work as well as the scientific literature. Researchers currently studying Rickettsiae do not have any information about the Swiss agent and it is not discussed in medical reports about Lyme disease.

Newby, an individual who together with her husband were bitten by ticks and subsequently developed Lyme disease, investigated Burgdorger, bio-weapons research, and tick disease. Her disease led to debilitating symptoms, which were never seriously treated by her specialist physicians but eventually were treated with several courses of antibiotics enabling her to recover. Her early work led to a documentary explaining how Lyme disease is not a simple infection that is easily treated as the infectious disease society has claimed. The interviews she had with Burgdorfer, examination of his hundreds of papers, interviews with major Lyme disease investigators from the universities and the CDC over six years led her to hypothesize that the bio-weapons program was responsible for unleashing a new tick-borne pathogen responsible for the devastating disease that Lyme disease and its co-infections have become. She suspects it is the Rickettsial organism termed the Swiss agent. In 2016 a newspaper investigative report made the case that Lyme disease may be caused by an unknown pathogen developed by the military during secret bio-weapon testing. Unfortunately, the research done by Ft. Dietrick remains classified and the papers documenting the Swiss agent are hidden. No whistleblower has stepped forward. Burgdorger, who passed away several years ago, informed Newby that the full story had not been disclosed but it's real.

Should we consider the Swiss agent Rickettsial organism as the cause of our Lyme disease woes? Moreover, rather than conceptualizing a tick bite as Lyme disease with co-infections, should we be rethinking a tick bite as a rickettsial infection with Lyme disease co-infection?

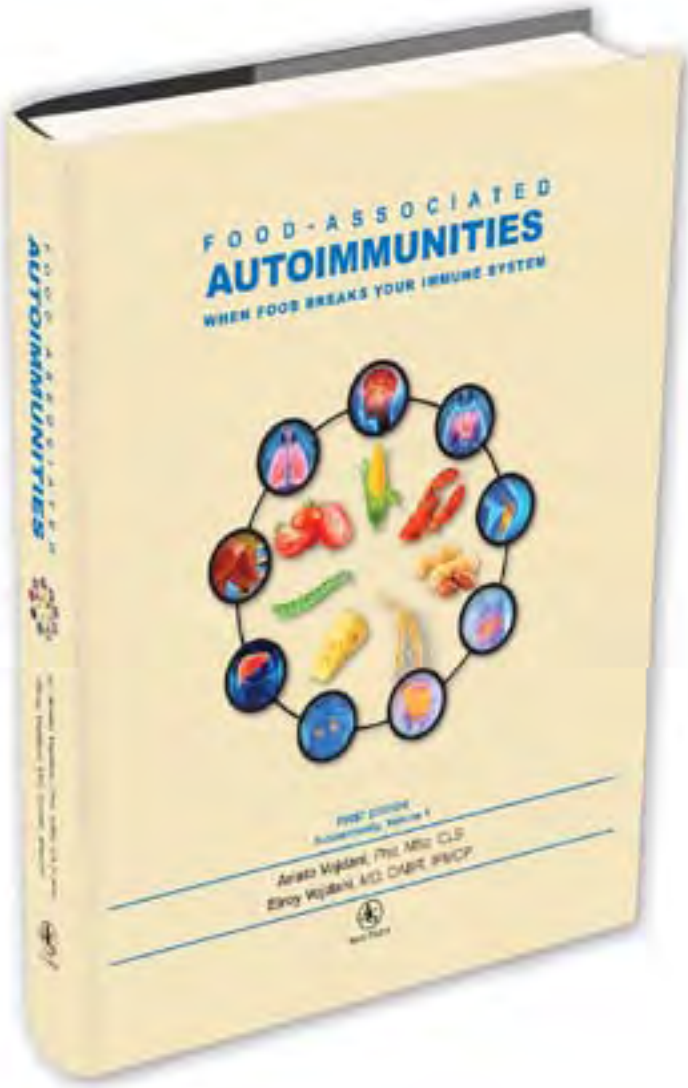
continued on page 10 ➤

Dr. Aristo Vojdani's Latest Book!

FOOD-ASSOCIATED AUTOIMMUNITIES

WHEN FOOD BREAKS YOUR IMMUNE SYSTEM

Now available online
at Amazon and Barnes & Noble!



The original inventor of food IgG testing breaks decades of silence regarding the prevalence of innacurate food testing and reporting in many laboratories.

This ground-breaking book redefines the standards for reliable reporting of food antibody test results.

In this book, the father and son team of Aristo Vojdani, PhD, MSc, CLS and Elroy Vojdani, MD, DABR, IFMCP, reveal new discoveries and information regarding the relationship between food proteins and autoimmune disorders.

The growing scientific interest in the interaction between diet and autoimmune disorders has created the new field called immunodietica, which is the subject of this book.

Letter from the Publisher

➤ *continued from page 8*

Cover Story: World-Class Athlete Gabby Reece

There are a great many endurance and performance sports that I have never participated in. Iron-man competitions and deep-water cave diving come to mind as do mountain climbing and back country helicopter skiing. But before one engages in extreme sports, an athlete trains hard for lengthy periods of time, often in adverse conditions, out in the elements, in the dark, deprived of sleep, not necessarily eating well, under deadline, often when physically or mentally not functioning well, and while injured. For Gabby Reece, a star volleyball player, such routines led to injury after injury to her knee. Despite numerous approaches to repair and rehabilitate it, she ultimately required a total knee replacement. Yes, she did try protein-rich plasma (PRP), physical therapies, acupuncture, laser, muscular work, nutritional supplementation, and more; but, unfortunately, the knee degeneration was too advanced and so she had surgery. The good news is that she has adapted to the prosthetic knee well and she is now engaged in high performance athletics as well as optimized training and instruction.

How does Reece do it? Karina Gordon interviews her in the cover article for the February/March issue focusing on women's health. Gabby contends that training involves both physical as well as mental regimens. As her husband puts it, the folks in the gym need to do yoga and those doing yoga need to go to the gym. She likes to do "dynamic and explosive" workouts in the pool – one of the routines she instructs her students involves lifting weights under water. For Gabby, water serves important roles in any training program; she likes using the sauna and cold-water baths. Why use prescription pain medication when magnesium and turmeric help to reduce inflammation and acupuncture abates muscle soreness? Reece is impressed with the importance of deep breathing, particular nasal breathing and meditation. Why not run on grass to experience grounding? For nutrition, make sure the food consumed adds to one's cellular repair process rather than burdening the system with high glycogen carbohydrates. And at the end of the day take a moment to reflect and acknowledge the physical workout accomplished.

Gary Huber, DO, on Progesterone Hormone Replacement

An issue featuring women's health would not be complete without some discussion about hormone replacement therapy (HRT). Many of us have made such treatment a primary part of our practice and have done considerable study of HRT. Nevertheless, mastering one's understanding of hormone physiology and replacement should be subject to refinement and reconsideration especially if our thinking has missed or ignored some important science. Gary Huber, DO, who has devoted much of his practice to studying the literature regarding hormone replacement therapy, finds that there is considerable misunderstanding regarding progesterone therapy. His article in this issue examines those myths, facts, and solutions.

Myth number one in endocrinology and gynecology is that progestins, such as Provera®, and compounded progesterone are the same. Most integrative physicians know that this is not true, but the same is not the case about the use of oral versus topical progesterone. Unfortunately, gut and liver metabolism of oral progesterone converts it into different "pregnanes," which do not offer the same level of cancer protection for endometrial and breast tissue as progesterone itself. Topical progesterone circulates through the body establishing high tissue levels in endometrium and breast affording excellent anti-cancer effect. Huber also challenges the notion that we can prescribe estrogen replacement for most of the month but only offer progesterone for the final third or half. As estrogen does exert pro-carcinogenic activity might it not be appropriate to administer progesterone concurrently with the estradiol? Huber graciously offers his own teaching resources for those wanting additional information and training.

Richard Moskowitz, MD, on Homeopathy

If you have been following the news, homeopathy has been facing a blistering rebuke worldwide over the past decade. England upended its long-standing utilization of homeopathic medicine by its National Health Service in the past year. In similar fashion numerous European medical societies have debased homeopathic prescribing. Australia and Russia have followed suit. (India remains steadfast in supporting homeopathic medicine.) Not to be left out, the US Food and Drug Administration has been under pressure to ban homeopathic medication and over-the-counter supplementation. In October, the FDA announced its intentions to begin regulation of homeopathic products. Despite the fact that homeopathy is recognized to be infinitesimally low-dosed, the FDA wants to base homeopathic safety on allopathic drug dosing. Homeopathic nosodes are generally not prepared from infectious materials or biological toxins, yet they may be outlawed despite the fact that there is no measurable toxin. Homeopathic opium has long been prohibited.

In this issue Richard Moskowitz, MD, makes the case for homeopathy. As Moskowitz states, "the fact that homeopathy is based on a phenomenon as yet unexplained…is far from proving that the phenomenon doesn't exist…It almost embarrasses me to have to point out the entire argument of those who make a point of ridiculing it still boils down to the same defective syllogism that even the eminent Dr. Holmes couldn't improve upon: "Homeopathy can't possibly work; therefore, it doesn't work!"

For those who find themselves stuck with this logic, I would highly recommend reading Moskowitz's article. His reasoning is exactly what we need to express when we encounter the homeopathic skeptic.

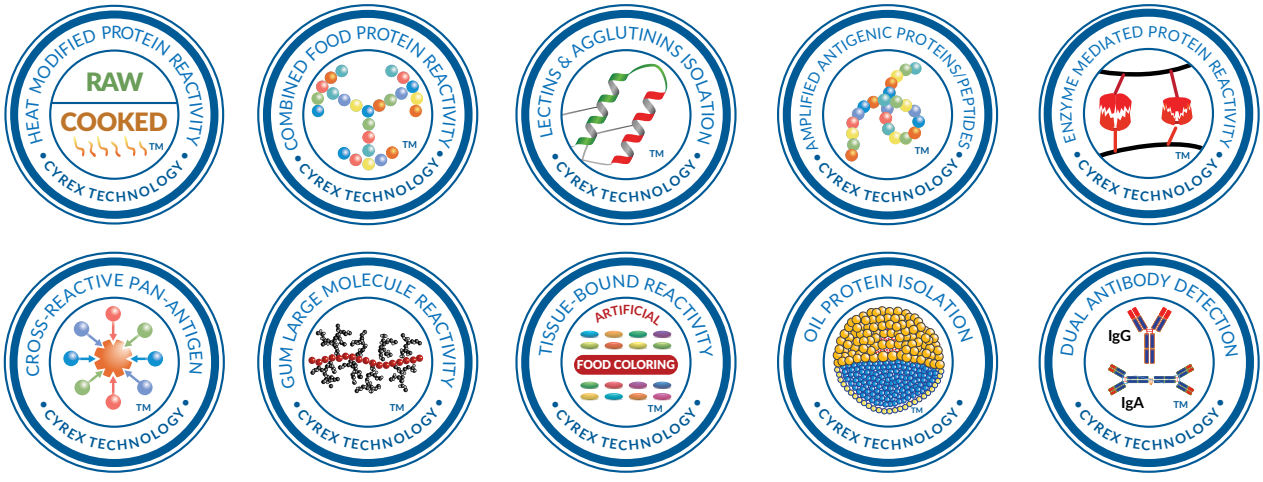
Jonathan Collin, MD

Reduce the Possibility of Missing Reactivity to Common Foods

Not all foods are consumed raw, in fact, the majority of our food is consumed modified in some way. Whether boiled, fried, baked or processed.

The revolutionary **Array 10 – Multiple Food Immune Reactivity Screen™** measures reactivity to **180 real-world food antigens** in cooked, raw and modified forms and features ten advanced proprietary technologies.

30 Years of Scientific Development
Ten Proprietary Technologies



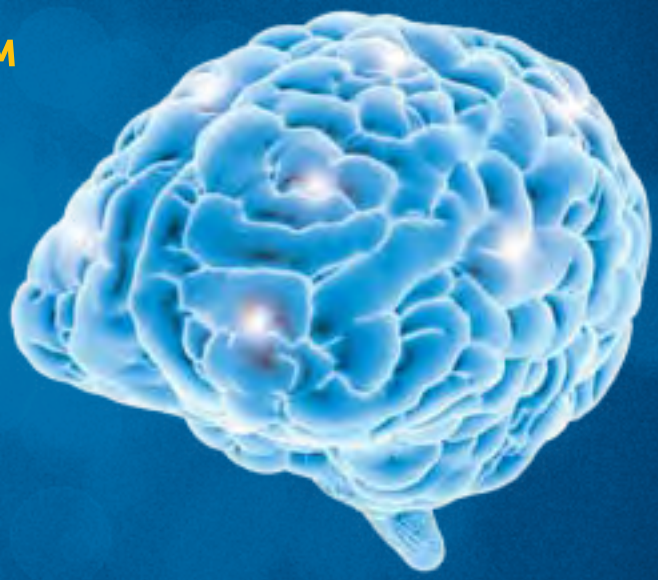
Test Foods the Way They are Consumed

Cyrex® Laboratories

1 (877) 772-9739 • www.JoinCyrex.com

BDNF Essentials™

Promote Healthy Brain Function



New research demonstrates the adult brain is capable of reorganizing its neural network by forming new connections —— and this is known as neuroplasticity. Neuroplasticity means the brain continues to generate new neurons & synapses throughout life, helping the brain heal from injuries.

KEY ACTIVITIES TO INCREASING NEUROPLASTICITY INCLUDE:

- ✓ Physical Exercise
- ✓ Learning New Skills
- ✓ Increase BDNF (Brain Derived Neurotrophic Factor)
- ✓ Good Nutrition
- ✓ Sleep
- ✓ Intermittent Fasting

Brain Derived Neurotrophic Factor (BDNF) is one of the key proteins that promote the survival, development and function of neurons. BDNF promotes neuroplasticity, the repair and generation of new neurons as well as supporting healthy telomerase activity.

BDNF ESSENTIALS™, formulated to promote healthy BDNF levels, neuroplasticity and healthy cytokine function, includes the following researched-based nutrients:

- ✓ **NeuroCyto Protect™ Blend:**
  Lions Mane Mushroom, Skullcap, Bilberry, Bacopa, Ashwagandha
- ✓ **Cognition Blend:**
  CDP Choline, Phosphatidylserine

Joseph Burrascano Jr., MD

"I am impressed with the formula of BDNF Essentials™ - it has all the things I look for when recommending this type of product."

Researched Nutritionals®
solutions for life

+1.800.755.3402

Tel: 805.693.1802 • Fax: 805.693.1806 • CustomerService@ResearchedNutritionals.com
www.ResearchedNutritionals.com | *Available only through healthcare professionals*

*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.

In this Issue

Feb/March 2020 | #439/440

On the cover: Gabby Reece's Program for Success (pg. 34); Defending Homeopathy (65, 78); Rubidium for Depression (pg. 62); Progesterone Myths and Facts (pg. 38); Best Natural Gynecology (pg. 58)

Snow Dragon by our webmaster, Joy Reuther-Costa

See our new website: www.townsendletter.com

MUSHROOM WISDOM®

SCIENCE COMPLEMENTING ANCIENT WISDOM

Unique, Research-Based Mushroom Extracts

Your choice for the best mushrooms nature & science has to offer.

Mushroom Wisdom has been offering mushroom products combining the best knowledge of nature with the latest science for almost 3 decades.

Our mushroom fruiting bodies are extracted, making them more bioavailable.

MW has been in the forefront of research on mushrooms and health since 1991 and continues this commitment to research today.

Super Mushroom and Mushroom Extracts

Subscribe to the Mushroom Wisdom newsletter for Special Offers & Updates
MushroomWisdom.com or Call 800-747-7418

* 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.

In Memoriam:
James "Jim" Sensenig

James Sensenig was born in Lancaster, Pennsylvania, on April 17, 1948. He was raised by Robert Sensenig and Pearl Sensenig and was the older brother to Tom and Joan Sensenig. His lifelong dedication to helping others began early as a boy scout and continued in the Coast Guard. He served as an intelligence officer in the US Army during the war in Vietnam.

In 1974, he enrolled in the National College of Naturopathic Medicine and began one of the brightest careers our profession has seen. He became Dean of Academics upon graduation and began teaching and practicing medicine. Teaching naturopathic philosophy, practicing naturopathic medicine, and being a leader in the profession were among his greatest joys.

Jim founded and was elected the first president of the American Association of Naturopathic Physicians, and was instrumental in the development of a national accreditation board for our schools (CNME), a national licensure examination that was uniform and fair (NPLEX), a peer-reviewed journal to develop increased credibility for our medicine (*JNM*), a definition of naturopathic medicine not based upon modalities that could be used for licensure as well as academic efforts, and a continuing education conference to fulfill licensure requirements and generate income for the Association. In five years, all of this had been accomplished, and the profession had a functional national association to work toward expanding licensure, based upon solid and legitimate standards and institutions.

Part of his genius was to pick other leaders and assign them the tasks that needed doing, then work with them to accomplish these goals: Alan Gamble, Joe Pizzorno, Bill Mitchell, Carlo Calabrese, Ed Hofmann-Smith, Peter D'Adamo, Cathy Rogers, John Weeks, Teri Davis, Thom Kruzel, Jared Zeff, Pamela Snider, and so many others. But he was the universal ingredient.

Like naturopathic founder, Dr. Benedict Lust, Jim was at legislative hearings all around the country to testify in favor of naturopathic licensure. He created a licensing "strike force," with Bob Timberlake and Harry Swope. He maintained a leadership role in the AANP through the turn of the century, and the candle lighting ritual at every AANP conference was initiated by him. He was one of the four doctors who established the Foundations of Naturopathic Medicine Institute (FNMI) and its textbook project to codify, preserve, strengthen and advance naturopathic medicine's unique philosophy, principles and theory of practice, and was one of eight senior editors. He also co-created the Institute for Natural Medicine (INM) to engage philanthropy and advance public awareness, and established the Naturopathic Medicine Institute (NMI) to sustain and further the teaching of vitalism in our profession and to call the profession back to its roots.

Jim also maintained, from the time of his graduation, a teaching role in our colleges. He not only served as Dean at NCNM but also taught courses: gastroenterology and naturopathic philosophy at first. For at least two decades he taught naturopathic philosophy at Southwest College in Scottsdale. He served as the founding Dean at UBCNM, where he also taught philosophy. He developed a comprehensive presentation of naturopathic medical philosophy that infused and inspired many young doctors. He testified incisively against tough political opponents and was a frequent speaker at many naturopathic medical conferences in the US and Canada. He was honored on many occasions with the profession's most prestigious awards, including an honorary Doctor of Naturopathic Philosophy degree from CCNM, the Beacon Award from the naturopathic medical students' gathering, the Dr. Kenneth Harmon Award from the Northwest Naturopathic Physicians Convention (NWNPC), and the 1988 Physician of the Year award from the American Association of Naturopathic Physicians.

Jim saw himself as a link in the chain of advocates for naturopathic medicine in the United States, beginning with Benedict Lust and continuing with Jim's teachers and mentors who included Drs. John Bastyr, William (Bill) Turska, Harold Dick, Robert Broadwell, and many others. He was a man of prodigious memory and sharp intellect, and able to speak in great factual detail without

➤

any notes, spontaneously, as needed. His ability to recall and accurately quote from keystone naturopathic and homeopathic texts was legendary and a powerful way of making everyone aware of the living legacy of healing knowledge provided by our vitalistic naturopathic predecessors.

With Drs. Letitia Dick, Thomas Kruzel, Harry Swope, Aviva Wertkin and Jared Zeff, he set out to restore the core of naturopathic education through a post-graduate organization, the Naturopathic Medicine Institute (NMI). Then along came Dr Eli Camp, who created and launched the NMI's Vital Conversation. The Vital Conversation began as a weekly call/interview, with a few doctors listening in on a conversation with Dr Sensenig, discussing naturopathic philosophy and clinical medicine. Many people often remarked that they wished they had recorded their conversations, any conversation with Dr Sensenig. It's no surprise that this weekly call quickly grew to 800 listeners each week. His determined effort to preserve the philosophy of naturopathic medicine and provide education in the knowledge and skills any good naturopathic doctor should possess led to the development of NMI's VNMI curriculum, creating a growing cohort of vitalistic practitioners throughout the profession and internationally. This was his final structural gift to the profession.

Through all of this, he maintained a full-time practice in Hamden, Connecticut, where he not only worked his medical miracles but also mentored many new doctors directly in his clinic. More of our colleagues had him as a mentor than anyone else in our profession.

He loved Rumi's poetry, dancing, hiking and escaping to the Oregon coast. He was a deeply spiritual man. Jim died early Saturday morning, November 30, peacefully in his sleep. He left behind many friends and colleagues who cherish him, people with whom he had worked, influenced, and directed. His legacy, in this regard, and in regard to the institutions he developed and his accomplishments in gaining licensure and similar efforts, is unparalleled in this generation, and comparable only to the example of Dr. Benedict Lust. He also leaves behind a grieving family, three children (Laura, Matthew and William), four grandchildren, his mother, his siblings and others, including four decades of patients for whom he worked the clinical miracles that he used to point out were taken for granted in the daily practice of naturopathic medicine.

Jim will forever be a giant in this medicine, respected and beloved by many, a teacher of many, a guide and friend for many. More than any other individual in our time, he is responsible for the resurrection of naturopathic medicine in the latter 20th century.

◆

Dr. Iichiroh Ohhira: A Pioneering Genius in Probiotic Science


Malaysian Mystery – 'Drinking Fermented Elixir'


Advanced Research – Okayama University

Founded BioBank


Discovery Lab TH-10


Testing Foods for Peak Nutrition


Exclusive 5-Year Fermentation


Nature's Perfect Probiotic w/POSTbiotics


Patented Encapsulation


Offering "Long Life and Good Health to All!"

Dr. Ohhira awarded GUSI Peace Prize

Developed Natures 'Perfect Probiotic' over 40 Years ago!

Dr. Ohhira has proven to be one of the world's most influential researchers in the history of probiotic science as his discoveries continue to be confirmed. He intrinsically understood restorative timeline when developing a 5-year natural temperature fermentation method that produces herculean strains of probiotics as well as therapeutic **Postbiotics Metabolites**, recently proven to be the most beneficial aspect of probiotic supplementation. Recent research on Dr. Ohhira's Probiotics revealed that his formula contains over 400 kinds of these health-promoting postbiotic metabolites!

Discover the Dr. Ohhira's Difference!™

ESSENTIAL FORMULAS®

www.EssentialFormulas.com • (972) 255-3918

* 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.

Highest quality & most effective Far Infrared Sauna in the world !

Relax® Far Infrared Sauna

Advanced technology, better results, safe, durable, convenient to use

Relax Sit-up Sauna
1500 watts

Relax Sauna Generators

Patented semi-conductor chip converts electrical energy into 95% PURE Far Infrared Energy.

Relax Lie Down Sauna
1000 watts
(Fits on a massage table, bed or floor)

ONLY Resonating Far Infrared Energy Pulsates the Water Molecules

creating a Dynamic Cascading effect of causing profuse sweating and...

- **Increasing Core Temperature**
  (killing Lyme Spirochetes, pathogens, viruses, etc)
- **Mobilizing the lympathic System**
  (detoxifying heavy metals, Dioxins, Phylates, metabolic waste)
- **Activating the Parasympathetic Nervous System**
  (producing deep Profound Relaxation)
- **Activating Mitochondria to produce ATP & Nitric Oxide**
  (enhancing oxygenation of body)
- **Increasing Microcirculation**
  (ameliorating diabetic ulcers, scar tissue, neuropathy, Reynaud's)

Why Thousands LOVE and prefer the Relax Sauna

- *Only takes 20 seconds (not 30 min) to warm up and feels great!*
- *Even distribution of healing light (reflective tent mirrors the light)*
- *People love having their head outside the tent so they can breathe*
- *Very effective with your clothes on for 5-10 minute treatments*
- *Produces a very profuse sweat in 20 to 30 minutes. NOT 40 to 60*

It took Relax Sauna 10 years to develop the technology, giving a Hot Springs effect.

The Relax Sauna is a $2000 sauna
This is NOT a $300 Amazon or $850 portable sauna.
It is more effective than $4000-$5000 wood infrared saunas.

At www.RelaxSaunas.com
use discount code: ***town202*** to get an additional $125 off
(until March 31st) **the $1300 Relax Sauna internet price.**

Listen to Amazing Miracles!

OVER 800 Testimonials
see: relaxsaunas.com/youtube

CALL 626.200.8454 phil@relaxsaunas.com

For a review of the Relax Sauna go to:
www.relaxsaunas.com/townsend

Pathways to Healing

by Elaine Zablocki

Discovering Healing After Trauma

As human beings, we all experience trauma. In his latest book, *The Transformation: Discovering Wholeness and Healing After Trauma*, James S. Gordon, MD, writes, "Trauma comes sooner or later, to all of us." He notes that while we see headlines for people who experience war and natural disasters, we all cope with trauma in our daily lives: illness or disability, the loss of a job, losing loved ones, the natural process of growing old. He writes, "the good news is that all of us can use tools of self-awareness and self-care to heal our trauma and, indeed, to become healthier and more whole than we've ever been."

Under Presidents Clinton and G. W. Bush, Gordon served as the chair of the White House Commission on Complementary and Alternative Medicine Policy. In 1991, he founded the Center for Mind-Body Medicine (CMBM), a community of healers who aim to make self-awareness, self-care, and group support central to all healthcare. For more than 25 years, he has led CMBM teams relieving psychological trauma throughout the world. In this book he draws upon years of experience in many different situations: after hurricanes and tornadoes, during and after wars, in communities affected by school shootings, and with active-duty US military and veterans. "If you want to help an entire traumatized population, you need to be able to rely on many people, not just the few available psychiatrists, psychologists, and clinical social workers," he writes. "Intelligent people of goodwill – rural high school teachers – could, with supervision by experienced clinicians, use our approach as skillfully as any MD or PhD."

In this book Gordon describes many different methods people can use to heal from trauma, such as active meditations and mental imagery, connecting with animals, slow deep breathing, or participating in a healing circle. Many of these methods have been used for millennia in the great spiritual traditions.

James S. Gordon, MD

The Biology of Trauma

Gordon explains the biology of trauma in a way that gives us all a more vivid understanding of how modern stress affects our bodies. The fight-or-flight response, which increases heart rates and blood pressure, helps us successfully challenge a wild animal, like a wolf or a tiger. Or, it helps us run away. It is a helpful response to a crisis situation. Our nomadic ancestors experienced the fight-or-flight response for short periods of time during acute emergencies.

Nowadays, we may find ourselves living with a long-term crisis. War. A failing marriage. Someone with an abusive household or an ominous medical diagnosis lives with stress for months or years. This long-term trauma exhausts the adrenal gland, diminishes the immune system, and damages vital brain connections. "These responses can persist even when the actual trauma is long over," Gordon writes. "The gazelle grazing on the plain and the mouse retreating to her mouse hole forget what has happened. We humans can carry

➤

➤

[traumas] with us. Our large complex brain may replay an endless loop of traumatic memories."

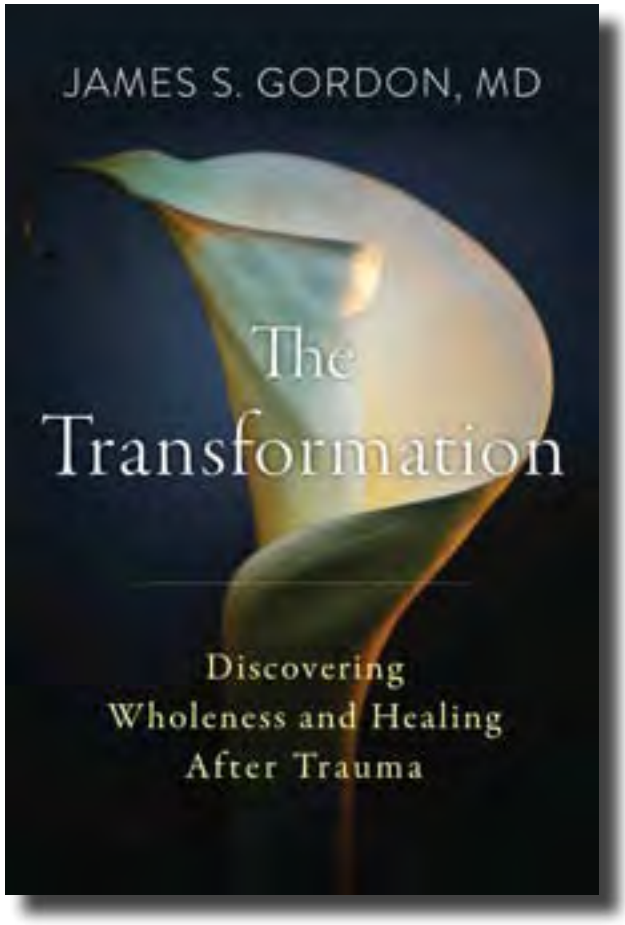
Gordon describes his visit with Kosovo Albanians who had fled Serbian ethnic cleansing. They remembered how they had seen their family members massacred before their eyes. Their hearts have been racing; they cannot sleep. Gordon leads the group in "an expressive meditation that includes dancing and shaking, pausing to relax and breathe, and then moving again." "Our ancestors," Gordon says, "shouted and danced and whirled and jumped when something terrible happened. They moved their bodies and let go of their tensions."

The Trauma-Healing Diet

After discussing the various ways trauma damages people, Gordon offers a chapter on "The Trauma-Healing Diet." This largely organic, whole food, plant-based, high-fiber diet will be familiar to most *Townsend Letter* readers. "This chapter tells you what you need to know to reverse the damage and heal yourself," he writes. "Everything we eat – and I mean everything – can either enhance or hinder trauma healing. If you've been self-medicating with comfort foods the first few days of healthy eating can be difficult.... after five or six days however, your gut will be calmer...you will be more focused and energetic, better able to sleep."

This chapter is particularly valuable because Gordon discusses many specific foods and supplements and connects their healing effects to the specific biology of trauma. He recommends using a high-dose multivitamin supplement, vitamin D, selenium and zinc. "Sometimes you'll quickly feel the benefits of the trauma healing diet," he writes. "Sometimes the effects will be gradual and subtle. You can know that it's providing a firm foundation for your comprehensive trauma-healing program."

This book includes so many different healing methods that every person who reads it will find new ways to support their own healing, growth, and recovery from trauma. Gordon closes it with a ritual to celebrate what we've learned from listening to and practicing these suggestions. He invites us to spend some time writing on two pieces of paper. The first one lists everything we want to leave behind, and how it feels to let go of it. The second piece is for everything we've learned that we want to remember and bring with us. We burn the first piece of paper. "Take a little time to choose the place," he writes. "It will become like the places that indigenous people have always chosen for ritual and ceremony, special to you, dedicated to the changes, the transformation that you're experiencing and will continue to experience." We keep



the second piece of paper and review it when we need to remember the tools that work best for us and support us as we meet our daily challenges.

Resources

The Transformation: Discovering Wholeness and Healing After Trauma, by James S. Gordon, MD

Gordon's website at https://jamesgordonmd.com includes interviews, videos, and his schedule of future public events.

Gordon is the founder and executive director of The Center for Mind-Body Medicine (CMBM), which has trained thousands of clinicians, educators and community leaders in the skills of self-care and group support. For more information about CMBM programs, go to https://cmbm.org

Elaine Zablocki is the former editor of CHRF News Files.

◆

Environmental Medicine Update

by Marianne Marchese, ND
www.drmarchese.com

Merging Women's Health and Environmental Medicine – Clinical Case Examples

Introduction

Every day, women are exposed to hormone-disrupting compounds through food, personal grooming and cleaning products, plastics, drinking water, hobbies and air pollution. These compounds can alter estrogen, progesterone, testosterone, and thyroid hormone leading to numerous women's health conditions. Conditions such as fibroids, breast cysts, endometriosis, PCOS, fibroadenomas, and thyroid disorders are all linked to endocrine-disrupting compounds (EDCs).[1] Physicians are tasked with recognizing when these conditions are due to exposure to EDCs, identifying the source of exposure through a detailed environmental exposure questionnaire, educating the patient on avoiding exposures, and trying to detoxify the body from these compounds.

Examples of endocrine-disrupting compounds that disrupt women's hormones include parabens, bisphenol-A (BPA), and other bisphenols, phthalates, pesticides and herbicides, polychlorinated bisphenols, PCBs, dioxins, polyaromatic hydrocarbons, and metals such as mercury, lead, cadmium, and arsenic. Food, water, the air, and personal care and grooming products are the main source of exposure.[1] An environmental medicine treatment approach to women's health conditions includes taking an environmental history, exploring ways to remove sources of exposure of EDCs, testing for the presence of chemicals in the body, and detoxification. Detoxification, also called cleansing, refers to the processes of both eliminating environmental toxicants from the body and neutralizing their adverse effects on health. Through the following clinical case examples, the results of this approach will be demonstrated.

Hypothyroidism

A 34-year-old woman was referred for evaluation of a heavy metal test result that was done by another doctor. The patient had hypothyroidism, fatigue, weight gain, and her left eyebrow and eye lash recently turned blond. The only medication she was on was Nature-Throid (one grain), and she stated she would love to get off it. A recent TSH blood test was 3.92 on this dose of Nature-Throid, and she did not have Hashimoto's disease. Even before reviewing the heavy metal test results previously done, I did an in-depth environmental history specifically looking for sources of exposure of metals. She had significant environmental exposure growing up in the Chicago area near factories and plants. She swam as a child in a local lake that was close to these factories. Both her parents worked in a machine shop, but she had no occupational or lifestyle exposures other than everyday living in a city with air pollution. She grew up drinking unfiltered tap water, which was later deemed to have high lead content due to an investigative report in Chicago years later.

Earlier that month another doctor ordered an unprovoked first morning urine metal test, which showed aluminum elevated at 39, cadmium 0.7, cesium 12, mercury 1.3, lead 0.4, and nickel 7.2. A provoked urine test using a body weight dose of DMSA was done the same day as the unprovoked urine collection, and it showed aluminum at 4.5, cesium 9.5, lead 6.8, and mercury 9.0. By giving a dose of DMSA the doctor essentially pulled some metals out of the body, called chelation. The provoked urine test cannot be used to tell the patient she had a high body burden of stored chemicals as the lab's reference ranges for the unprovoked and provoked urine were identical. There are no published reference ranges for provoked urine metal testing, and there is very little research linking a provoked urine to true body burden of metals the way a fat biopsy might reflect body burden.[2]

The unprovoked urine shows what was currently circulating in the body at the time of collection and showed elevated levels of metals. According to the National Health and Nutrition Examination Survey (NHANES) 4th report, her unprovoked urine showed very elevated aluminum, cadmium was above the 90th percentile, cesium was above the 95th percentile, mercury was above the 80th percentile, and lead was normal. According to Mayo Clinic and the Agency for Toxic Substances and Disease Registry (ATSDR), the best method of testing aluminum is blood or a 24-hour urine. A 24-hour urine level above 10 mcg indicates exposure.[3] Most urinary aluminum reflects leaching from a prosthetic implant, but she had none. Her kidney function was normal thus eliminating renal failure or dialysis as an explanation for the aluminum elevation. We deemed her very high aluminum was from her diet, water, and air pollution and possibly buffered aspirin she took occasionally. The cadmium and mercury elevations were also most likely from food exposure, and she had no recent vaccines or dental amalgams. She had been living in Phoenix Arizona, for 15 years at the time of her metal test and not using a

➤

water filter at home or work. The Phoenix area is known for higher than average levels of cesium and uranium in the drinking water.

I put her on an eight-week chelation plan with a body weight dose DMSA three days in a row with an 11-day break and repeated the sequence twice. I also placed her on a supplement that provided cofactors to support liver phase one and two metabolic reactions and an herbal product to cleanse the liver and gall bladder. which consisted of milk thistle, beet root, dandelion, burdock. and artichoke. The cofactor support product contained the following: vitamin A, vitamins D3, K1, B1, B2, B3, B5, B6, B12 (as methylcobalamin), C, and E; biotin; folate (5-methyl-tetrahydrofolate); calcium, chromium; copper; iodine; magnesium; manganese; molybdenum; potassium; selenium; zinc; choline; inositol; boron; vanadium; green tea extract; and turmeric.

Along with the DMSA and two supplements, she did four sessions of colon hydrotherapy and ten sessions of sauna therapy; and I educated her on avoiding EDCs in her diet, home, and work environment. At the end of eight weeks, she had more energy, could think more clearly, and the eyebrow and lash returned to dark color. We retested the metals using unprovoked urine, and the levels were now normal via the labs reference ranges and the NHANES percentiles. The aluminum lowered from 39 to 2.6, cadmium lowered from 0.7 to 0.3, cesium was 12 and now 4, lead was 0.4 now 0.2, mercury was 1.3 and now 0.5. Her Nature-Throid dose was eventually lowered to 1/4 grain from 1 grain, and her TSH has been stable and runs between 1-2. She was very happy she was able to lower medication dose and that she felt better overall.

Uterine Fibroid and Ovarian Cyst

A 47-year-old woman presented for her well woman exam. She had some pelvic bloating and sense of something firm in her uterus on self-palpation. Her menses were regular, 28 days, with normal flow and mild cramps. She had a past medical history of asymptomatic primary biliary cirrhosis and had been on ursodiol 300 mg since 2014. Her supplements included fish oil, vitamin D, probiotics, milk thistle, curcumin, glucosamine, and a B-complex. Her family medical and environmental history was unremarkable. The well women exam revealed an enlarged uterus with palpable mass. A subsequent pelvic ultrasound showed multiple fibroids, the largest being 7.5 x 5.4 x 4.2 cm in right anterior body and two other smaller fibroids 3 cm and 2.5 cm. She also had a 3 x 3.2 cm left ovarian simple cyst. Initial labs were normal and included CBC, CMP, estradiol, TSH, and a lipid panel. Her environmental exposure history was unremarkable for past and current living and work environment; she had no occupational exposure to toxicants, nor did she have any hobbies that may have exposed her to EDCs. As with most women, she was exposed through her food, water, air, and products to low-dose parabens, phthalates, BPA, pesticides, and dioxins. Her history of primary biliary cirrhosis could affect her liver's ability to detoxify EDCs. She required a lot of education about avoiding exposure to EDCs and healthier alternatives to her regular personal care products. She had been drinking and cooking with unfiltered tap water and did not use a HEPA-type air filter at home. Her diet was fairly healthy, but she did consume tuna two-to-three times a month and other forms of sushi. Based on her diet and drinking unfiltered water in the Phoenix area, blood mercury, cadmium, and lead testing was done as well as urinary arsenic. Blood lead was less than 1.5, cadmium was 0.3, and mercury was 6. This level of blood mercury is elevated based on NHANES ranges and most likely due to her fish intake. Based on knowledge of the links between EDCs and fibroids and ovarian cysts, she was started on a detoxification and naturopathic treatment program.

The initial treatment plan included education on avoiding endocrine-disrupting chemicals in her food, air, water and personal care products. She got a reverse osmosis water filter and small room air filter. The nutritional plan included avoiding dairy, red meat, gluten, and sugar along with adding flax seed, psyllium husk and cruciferous vegetables to the diet. She did not want to do chelation to lower the mercury and instead opted to avoid all fish and work on shrinking the fibroids and ovarian cyst. She was placed on a supplement designed to give cofactors to support the enzymatic reaction involved in liver phase one and two detoxification pathways. The ingredients are listed in the case above. She was also placed on a product to support the metabolism of estrogen through the liver that included methyl B12, methyl folate, N-acetylcysteine, NAC, calcium-D-glucarate, diindolyl-methane, DIM, and alpha lipoic acid. She was started on Turska's revised formula, which is a botanical tincture composed of vitex, arctium, ceanothus, chamaelirium, serenoa, baptisia, gelsemium, iris, phytolacca, zanthoxylum, zingiber, and aconite. Turska's formula or versions of it have been used for decades for fibroids and cysts. She completed five 30-minute sessions of frequency specific microcurrent designed to shrink fibroids.

After following the combined environmental and women's health treatment plan for eight weeks, she felt amazing and felt the uterus was softer. A repeat pelvic ultrasound showed all the fibroids and the ovarian cyst shrank by 1 cm. At this point, a day 20 blood progesterone and estradiol was drawn and the mercury retested in the blood. The mercury dropped to 2 without the use of a chelator, and she was found to be very low in her luteal phase progesterone, which is common for her age. Her estrogen level was normal. She was placed on progesterone cream 20 mg BID every day. Another very recent pelvic ultrasound show the fibroid and cyst continue to shrink and she remains asymptomatic. She continues to follow a healthy anti-inflammatory and detoxification diet and practices avoidance of EDCs at home and work.

Breast Mass

A 34-year-old woman found a right breast mass on self-breast exam. She came to see me, and on clinical breast exam I confirmed the presence of a small, 0.5 cm, mobile mass in right breast in the upper outer quadrant. She also reported breast pain that was non-cyclical for the past three months. Her maternal aunt had breast cancer in her 30s. She was not on any medication and was only taking a fish oil and multivitamin. She was currently very stressed with work and family issues. Three months prior she started the HCG diet that included injectable HCG and had lost 15 pounds. Her environmental exposure history was unremarkable for current occupational exposures, current home and work environment, and hobbies. She only ate organic and had been avoiding EDCs in her personal care and cleaning products, food, air and water for years. In the past she had significant toxicant exposure living in Iran. She was born in Karaj, Iran, in 1975 and lived there until age four. Karaj is a town 40 km west of Tehran. Prior to her birth, a large factory opened near where she lived. According to her mother it was some type of factory or plant that emitted air pollution, and neighbors started to develop cancer. In fact, the patient's older brother developed leukemia while living there, and the factory was the main reason her family left Iran and moved to Queens, New York. Karaj was known as an industrial town in the mid-1970s.[4]

After confirming the presence of a breast mass via palpation, a diagnostic mammogram and ultrasound were ordered; and I asked her stop the HCG injections. The imaging showed a 6 mm nodular

mass in the right breast and very dense breast tissue. The radiologist gave the imaging a BIRADS 0 and recommended a biopsy. She didn't want to do a biopsy and wanted first to try and improve the density and health of breast tissue. We agreed to an eight-week treatment plan and a biopsy. She scheduled the biopsy 10 weeks out and started taking modified citrus pectin in preparation of the biopsy. Citrus pectin can keep cancerous cells from spreading from a primary tumor.[5] She was placed on a product to support the metabolism of estrogen through the liver that included methyl B12, methyl folate, N-acetylcysteine, NAC, calcium-D-glucarate, diindolyl-methane, DIM, and alpha lipoic acid. She also started a supplement to cleanse the liver and gall bladder that consisted of milk thistle, beet root, dandelion, burdock, and artichoke. She completed 10 sessions of sauna therapy in seven weeks and maintained her healthy organic diet. She had been very stressed prior to the breast pain and mass and also worked on stress management and sought out counseling for emotional support.

She completed the treatment plan and returned to the imaging center for a biopsy of the breast mass, but it was no longer present via mammogram or ultrasound. Her breast pain had resolved, and she felt good. Six months later, she had a repeat mammogram and ultrasound, which were normal and showed no mass, BIRADS 2. She decided to repeat the treatment plan for another eight weeks as a preventive measure due to her family history of cancer and past environmental exposures in Iran. At age 38 she had another mammogram and ultrasound, which again were normal. At age 40, 42, and 44, she had both mammogram and ultrasound combined and all imaging has been normal.

Environmental Medicine

Summary

Numerous women's health conditions can be linked to endocrine-disrupting compounds in the environment. Women are exposed to these through the air we breathe, water we drink and use for cooking, food we eat, personal care and cleaning products, carpet, furniture, paint, and so much more. Even low-dose exposure to these compounds can over time cause hormonal disruption contributing to health conditions. It is important physicians learn how to connect the dots through an in-depth exposure history and testing, educate patients on avoiding EDCs, and integrate an environmental treatment approach when addressing women's health conditions. Many times, patient come to see practitioners for an alternative and integrative treatment approach, which needs to include environmental medicine to truly address the root cause.

References

1. Marchese, M. *8 Weeks to Women's Wellness*. Petaluma, CA; Smart Publications: 2011.
2. Marchese, M. Heavy metal testing controversies: the post-provocative urine test. *Townsend Letter.* 2016 Jan:90-92.
3. ToxGuide for Aluminum. Agency for toxic substances and disease registry. https://www.atsdr.cdc.gov/toxguides/toxguide-22.pdf. Accessed 11/01/2019
4. Mashayekhi A. The 1968 Tehran master plan and the politics of planning development in Iran (1945–1979), *Planning Perspectives.* 2019;34(5):849-876
5. Glinsky VV, Raz A. Modified citrus pectin anti-metastatic properties: one bullet, multiple targets. *Carbohydr Res*. 2009;344(14): 1788–1791.

Dr. Marianne Marchese is the author of the bestselling book *8 Weeks to Women's Wellness* about the environmental links to women's health and how to detoxify from toxicants. She maintains private practice in Phoenix, Arizona, and is adjunct faculty at Southwest College of Naturopathic Medicine, teaching both environmental medicine and gynecology. She lectures throughout the US and Canada on women's health, environmental, and integrative medicine topics. Dr. Marchese recently helped develop three supplements for Priority One Vitamins. www.drmarchese.com

◆

Improving eye health

For centuries European herbalists have been using bilberry, most famous for its long use as a medicine for eye and vision problems. Our unique formula acts as a micro-circulation enhancer that helps strengthen the capillaries while acting as a powerful anti-oxidant to inhibit damage to the eyes caused by free radicals.

Strix® Billberry Extract
improves night vision and overall eye health.

- Helps relieve eye overuse
- Bilberries have been prescribed since 1945 to improve vision
- High in flavonoids, with anti-oxidants to fight against eye disease

The information presented is not intended to be prescriptive or to replace the care of a licensed health professional in the diagnosis and treatment of illness.

Available from major distributors such as *Threshold, Emerson Ecologics, and Super Natural.*

Scandinavian Formulas

Sellersville, PA 18960 • **P:** 215-453-2507 800-688-2276
F: 215-257-9781 • scandinavianformulas.com

Shorts

briefed by Jule Klotter
jule@townsendletter.com

Children and Aluminum Safety Questions

Two recent studies examine aluminum exposure and possible safety issues that result when following the current CDC pediatric vaccine schedule. Aluminum (Al) stresses endoplasmic reticula, the organelles responsible for lipid biosynthesis, calcium storage, and protein folding and processing; they reside in most cells in the body. Endoplasmic reticulum stress can produce the unfolded protein response and can lead to autoimmune conditions and neurotoxicity. Aluminum also impairs mitochondrial function and the Golgi apparati in the kidneys, which reduces the body's ability to excrete the metal.

Aluminum compounds, such as aluminum oxyhydroxide and aluminum hydroxyphosphate, are used in *some* vaccines to stimulate an immune response to the vaccine antigen. In their 2018 study, James Lyons-Weiler and Robert Ricketson state, "The dosing of aluminum in vaccines is based on the production of antibody titers, not safety science." The federal adult dose limit is 850 µg Al/dose by assay.

In 2011, the Joint Expert Committee on Food Additives set the Provisional Tolerable Weekly Intake for Al as being 2000 µg Al/kg of bodyweight, derived from studies with adult rodents. The Agency for Toxic Substances and Disease Registry uses 1000 µg Al/kg as its Minimal Risk Level. These guideline levels are for *consumed* aluminum, found in foods and water, not *injected* aluminum. Animal experiments show that far less ingested aluminum, compared to injected, is absorbed. The only safety guideline for injected aluminum is for people with renal dysfunction, set at 4-5 µg Al/kg/day. Many premature babies have impaired kidney function.

Lyons-Weiler and Ricketson applied Clark's rule to these guidelines. Clark's rule is used to evaluate pediatric dosage, based on the child's weight, when only adult recommendations are available. The Hep B vaccine, which the CDC recommends be given to all newborns, contains 250 µg Al, 17 times more aluminum than would be allowed if the dosage were adjusted for body weight using Clark's rule.

Lyons-Weiler is senior author of a 2020 study that compares vaccine aluminum exposure and the estimated chronic Al retention caused by three different vaccine schedules: the CDC schedule, the CDC schedule when using available low- or no-aluminum vaccines, and Oregon pediatrician Paul Thomas's "Vaccine Friendly Plan." The authors used the Priest model to estimate Al clearance.

Priest injected a single dose of a soluble aluminum isotope into an adult male and took periodic mass spectrometry measurements over 12 years. The Priest model cannot, of course, provide direct information about Al clearance in infants who weigh considerably less than an adult and whose kidneys' glomerular filtration rate (GFR) is less than an adult's. Children's GFR does not reach adult level until about age two. As the study authors explain, Priest's model is overly optimistic about Al clearance when applied to young children. It does not account for the child's weight, kidney function, genetic variations that may affect aluminum clearance, or synergistic toxicity with fluoride, mercury, or other toxic metals in the environment. But it is all we have right now.

Using Priest's equation, if the Hep B vaccine is given at birth (as CDC recommends), between eight and 12 percent of the 250 µg Al in that vaccine remains in the body when a baby receives the next set of CDC-recommended vaccines at two months. The CDC schedule at age two months consists of a second dose of HepB (250 µg Al), DTaP (diphteria-tetanus-acellular pertussis; 625 µg Al) Hib (Haemophilus influenae type b; 225 µg Al), and PVC13 (pneumococcal conjugate;125 µg Al), totaling 1225 µg Al. Between eight and 12 percent of that total will be in the body when the infant receives more vaccines at age four months.

The modified CDC schedule uses a low-aluminum DTaP (330 µg Al) and ActHib, which contains no aluminum – totaling 705 µg Al for the same four vaccines. (In addition to these aluminum-containing vaccines, CDC recommends rotavirus, and inactivated polio vaccines at age 2 months.) Dr. Thomas does not recommend the hepatitis B vaccine for babies whose

➤

➤

mothers are not infected with the virus. At age two months, he recommends the low-aluminum DTaP and ActHib (no aluminum).

At four months, babies on the CDC schedule get another dose of DTaP, Hib, and PVC13. Dr. Thomas gives second doses of low aluminum DTaP and ActHib and a first dose of PVC13. CDC recommends boosters of HepB, DTaP and PVC13 at age six months, Hib, PVC13, and a first dose of HepA (250 µg Al) at 12 months, and another dose of DTaP and HepA at 18 months.

With the CDC vaccine schedule, children receive 4925 µg Al by 18 months, compared to 3037 µg Al on the modified schedule and 1820 µg Al on Dr. Thomas's schedule. Using Priest's equation, 4% of the aluminum from that first HepB vaccine remains somewhere in the child's body tissue two years later. Given the regular introduction of more aluminum-containing vaccines during the first 18 months of life, it is easy to see that aluminum clearance and possible toxicity could be an issue for young children.

The authors "strongly recommend that the US FDA update their *modus operandi* to consider data from studies from injected forms of aluminum in infant mice, and that the FDA establish age-specific monthly limits of aluminum exposure *in toto* (all sources), including 1 or more [aluminum-contain vaccines] administered in the same month."

Lyons-Weiler J, Ricketson R. Reconsideration of the immunotherapeutic pediatric safe dose levels of aluminum. *J Trace Elements in Medicine and Biol.* 2018;48:67-73.

McFarland G, et al. Acute exposure and chronic retention of aluminum in three vaccine schedules and effects of genetic and environmental variation. *J Trace Elements in Medicine and Biol.* 2020.

Priest ND. The biological behaviour and bioavailability of aluminium in man, with special reference to studies employing aluminium-26 as a tracer: review and study update. *Royal Society of Chemistry.* 2004;6:375-403.

Time-Restricted Eating and Metabolic Effects

Intermittent fasting has been studied as a way to lose weight and improve cardiometabolic health. It can take several forms such as alternate-day eating, eating during the week and fasting on the weekend (the 5:2 diet), and eating only within a four- to 10-hour time period (time-restricted fasting). A 2018 study, led by Elizabeth F. Sutton, sought to determine whether the metabolic improvements – including better insulin sensitivity, reduced glucose and/or insulin levels, improved lipid profiles, lower blood pressure, and improvements in inflammation and oxidative stress biomarkers – were due to weight loss alone or to fasting.

In looking at four previous human trials that used time-restricted fasting (TRF), Sutton et al observed that results appeared to vary according to eating time. Eating during the middle of the day reduced body weight, body fat, fasting glucose and insulin levels, insulin resistance, hyperlipidemia, and inflammation. When eating time was in late afternoon or evening, the positive effects largely disappeared and, in some cases, postprandial glucose levels, β cell responsiveness, blood pressure, and lipid levels worsened. (β cells in the pancreas make and secrete insulin and amylin.) Sutton et al attributed the difference to circadian rhythms, which regulate glucose, lipid, and energy metabolism as well as sleep: "…insulin sensitivity, β cell responsiveness, and the thermic effect of food are all higher in the morning than in the afternoon or evening, suggesting that human metabolism is optimized for food intake in the morning." They decided to conduct a five-week randomized, crossover, controlled feeding trial to test the effect of restricted eating that started early in the day.

Eight overweight men with prediabetes were randomized to a time-restricted feeding (TRF) program during which they ate three meals within a six-hour period (with breakfast between 6:30-8:30 am, lunch three hours later, and dinner three hours after lunch) or to a control program (three meals within a 12-hour period) for five weeks. After a seven-week washout period, each participant followed the alternate pattern. They were given enough food to maintain their weight. Study staff monitored the meals to ensure that participants ate all three meals.

Time-restricted fasting improved insulin sensitivity and β cell responsiveness and lowered insulin levels; those with the highest insulin levels at baseline showed the largest reductions. However, one participant's insulin levels actually worsened on the TRF program; this man also had a long history of overnight shift work. The authors say, "Given that circadian rhythms are altered in adults who perform overnight shift work, it will be important to determine whether some subpopulations have altered circadian rhythms and would benefit more from alternative meal timing interventions."

In addition to insulin sensitivity, TRF produced a reduction in morning blood pressure (11 ± 4 mm Hg [systolic] and 10 ± 4 mm Hg [diastolic]) and a 14% decrease in 8-isoprostane (a marker of oxidative stress), compared to the control program

The men did not experience increased hunger during the longer TRF fast: "…on the contrary, eTRF decreased the desire and capacity to eat and increased feelings of fullness in the evening." The participants' main complaint involved having to eat three meals within six hours!

This study was quite small; larger trials that include women are needed. The authors also recommend that lipid levels, glucose levels, and blood pressure be measured throughout the 24-hour day.

Sutton EF, et al. Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes. *Cell Metabolism.* 2018;27:1212-1221.

Another Retracted Study

Using data from the National Health and Nutrition Examination Survey (NHANES), Gayle DeLong tested the hypothesis that the human papillomavirus vaccination might be one of the factors involved in the recent decline in US birth rates. She focused on data that represents 8 million 25-to-29-year-old women living in the US between 2007 and 2014, collecting information about age, income, education, race/ethnicity, marital status, pregnancy, and whether or not the woman received the HPV vaccine (number of doses and dates). NHANES did not have consistent birth control information for

continued on page 28 ➤

Let's Face It… Successful Aging is More than Just Hormones

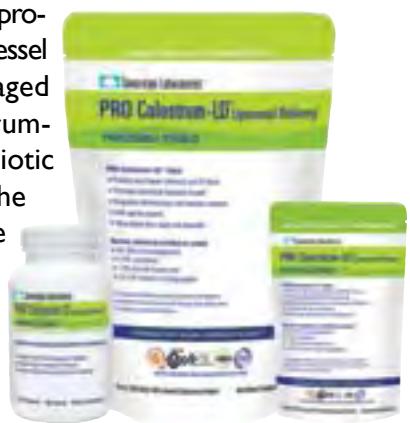
While it's the case that many menopausal women find themselves contemplating hormone replacement therapy, there are new and equally important supplement considerations. Offsetting chronic disease – which impacts physical health and mental well-being – is a top priority, especially if you want to live a long life with vitality and mental clarity and without pain or disability. Exciting new research is fueling our growing understanding of the gut microbiome and how these microorganisms can regulate gene transcription, translation, and human metabolic processes. Aging is associated with reduced microbial diversity, and healthy aging correlates with increased microbial diversity. Simply put, take good care of your gut bugs, and they'll take care of you.

Preventing intestinal hyperpermeability ("leaky gut") goes hand-in-hand with a healthy microbiome. Tight junctions in the G.I. lining are essential to gut integrity. An unremediated leaky gut leads to chronic inflammation and autoimmunity as the immune system attacks foreign material – food proteins, pathogens, chemical and environmental toxins – when they cross into the bloodstream. Bovine colostrum helps heal G.I. tissue and return permeability levels to normal. Along with healthy lifestyle behaviors, bovine colostrum supplementation is likely the best defense against potentially deleterious effects of advancing age.

The far-reaching benefits of colostrum supplementation include:

- Remediation of intestinal hyperpermeability
- Strengthening of tight junctions for gut integrity
- Regulation of excess or inappropriate inflammation
- Elimination of many gut-based pathogens
- Assistance for the immune system to fight viruses
- Accelerated tissue healing and recovery from injuries and wounds
- Increased lean muscle mass and bone density
- Enhanced mental focus and improved mood

PRO Colostrum-LD® is an all-natural source of growth factors, including IGF-1, IGF-2, TGF-α, TGF-β, EGF, FGF, PDGF, and VEGF. Growth factors play an important role in maintaining the body's tissues, including repair of leaky gut epithelia, bone remodeling and maintenance, fracture repair, wound healing, cellular migration and proliferation, collagen production, and blood vessel growth into damaged areas. PRO Colostrum-LD® serves as a prebiotic and helps maintain the ideal microbial balance to improve the overall health of the gut microbiome.



Sovereign Laboratories

Contact our Professional Sales Office for more information at (480) 553-7768.

➤ *continued from page 26*

the women in this age group, so she could not use that as a cofactor. DeLong reported, "Results suggest that females who received the HPV shot were less likely to have ever been pregnant than women in the same age group who did not receive the shot." Overall, about 35% of women who had the vaccine became pregnant at least once, compared to about 60% of the unvaccinated group. A similar disparity was found when looking just at married women: 50% of the vaccinated group had conceived compared to 75% of the unvaccinated group. This study was peer-reviewed by three researchers, and the editors of the *Journal of Toxicology and Environmental Health, Part A* made the study available online at no cost.

In the paper, DeLong clearly stated that this study showed an association but *could not* and *did not* prove causation. She pointed to other studies that have indicated that environmental pollutants, endocrine disrupters, and pesticides are able to decrease fertility, saying that these may also be contributors to declining rates. Multiple reports of premature ovarian failure in young women who received Gardasil (Merck's HPV vaccine) are in the literature, however; and in January 2016, the American College of Pediatricians voiced concern about the possibility that the vaccine might affect ovarian function in some young women.

In the long-honored practice of scientific debate, A. Shibata and Y. Kataoka publicly critiqued DeLong's study in a letter to the editor, published in *Human Vaccines & Immunotherapeutics.* DeLong refuted their criticisms in the same publication and offered data from Spain, Italy, the United Kingdom, Australia, and Romania. Romania, which had a very low HPV vaccine uptake, "showed a substantial increase in birth rates for all but the youngest age groups." The other four countries, all of which have strong HPV vaccine programs, have experienced clear declines in birth rates among younger women. She concluded "The correlation between the HPV vaccine and lowered fertility could be spurious, but not for the reasons that Shibata and Kataoka offer."

In October 2019, DeLong was informed that an investigation had been opened due to "'several public and private expressions of concern about flaws in analysis.'" She was given two weeks to respond to comments from four post-publication reviewers and did so. One of these reviewers agreed with DeLong that an open debate about the possibility that the HPV vaccine is contributing to infertility needs to take place. Nonetheless, her article, "A lowered probability of pregnancy in females in the USA aged 25-29 who received a human papillomavirus vaccine injection," was retracted – although it will remain online "to maintain the scholarly record," according to the editors in their statement of retraction.

In her response to the retraction, DeLong wrote: "A basic principle of medical ethics holds that if there is evidence that a treatment, drug or vaccine may be dangerous, even if that evidence is not conclusive, we must investigate those possible problems until we have settled the question one way or another."

DeLong G. Author Response to Journal of Toxicology and Environmental Health Retraction of "A lowered probability of pregnancy in females in the USA aged 25-29 who received a human papillomavirus vaccine injection." December 16, 2019.

DeLong G. Letters to the editor; Response to : a possible spurious correlation between human papillomavirus vaccination introduction and birth rate change in the United States. *Human Vaccines & Immunotherapeutics.* 2019;15(10):2503-2504.

DeLong G. A lowered probability of pregnancy in females in the USA aged 25-29 who received a human papillomavirus vaccine injection. *J Toxico and Environmental Health, Part A.* 2018; 81(14).

Field SS.New Concerns about the Human Papillomavirus Vaccine. American College of Pediatricians. January 2016.

Removing Access to Sugary Beverages

Banning workplace sales of sugar-sweetened beverages (SSBs) decreased consumption of these health-harming drinks and produced improvements in waist circumference and insulin resistance among 214 study participants who worked at the University of California at San Francisco (UCSF). In 2015, UCSF stopped selling sodas, sports or energy drinks, "fruit" drinks, and sweetened bottled teas and coffees in cafeterias, vending machines, hospital food services, and retail outlets. People could still bring these types of drinks to work. Sugar intake from beverages is more detrimental to metabolic health than sugar in foods, according to meta-analyses, and considered a strong risk factor for obesity and cardiometabolic disease.

Elissa S. Epel and colleagues surveyed 2556 employees about their daily beverage intake before the ban. They then conducted a randomized study with 214 survey participants who reported drinking 12 fl oz or more of sugar-sweetened drinks each day; 109 met with a health educator for a 15 minute motivational interview in which they were given information about the sugar content of these drinks, the effect on health, and how to reduce sugar intake. The remaining 105 acted as the control.

Simply banning the sale of sugar-sweetened beverages nearly halved consumption: "They reported a mean daily intake of 1050 mL (35 fl oz) of SSBs at baseline and 540 mL (18 fl oz)" six months after the ban began. Those who took part in the motivational interview had a significantly greater response compared to the control: a mean (SD) reduction of 25.4 [2.8] fl oz vs 8.2 [2.8] fl oz. In addition, improvements in insulin sensitivity, measured by Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), correlated to SSB intake reductions, particularly in participants with higher body mass index (BMI); and mean (SE) waist circumference decreased by 2.1 (2.8) cm. Removing access to these beverages appears to be an easy way to decrease consumption.

Epel ES, et al. Association of a Workplace Sales Ban on Sugar-Sweetened Beverages with Employee Consumption of Sugar-Sweetened Beverages and Health. *JAMA Intern Med.* October 28, 2019.

◆

Literature Review & Commentary

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

Vitamin D for Osteoporosis Prevention: More Is Worse, Not Better

Three hundred thirty-one adults in Calgary, Canada, (53% male, 47% female; mean age, 62 years) who did not have osteoporosis were randomly assigned to receive, in double-blind fashion, 400, 4,000, or 10,000 IU per day of vitamin D for three years. Calcium supplements were given, if needed, to bring total calcium intake to around 1,200 mg per day. The mean serum 25-hydroxyvitamin D level at baseline was 31.5 ng/ml, indicating normal vitamin D status. The primary outcome measures were changes in total volumetric bone mineral density (BMD) at the radius and tibia, assessed by high resolution peripheral quantitative computed tomography, and bone strength (failure load) at the radius and tibia, estimated by finite element analysis. Ninety-two percent of the participants completed the study. At the end of the trial, mean serum 25-hydroxyvitamin D levels with 400, 4,000, and 10,000 IU per day of vitamin D were 31 ng/ml, 53 ng/ml, and 58 ng/ml, respectively.

Compared with baseline, the mean change in BMD at the radius was -1.2% with 400 IU per day, -2.4% with 4,000 IU per day, and -3.5% with 10,000 IU per day ($p < 0.001$ for 10,000 vs. 400 IU per day; $p < 0.05$ for 4,000 vs. 400 IU per day). Compared with baseline, the mean change in BMD at the tibia was -0.4%, -1.0%, and -1.7% for 400, 4,000, and 10,000 IU per day, respectively ($p < 0.001$ for 10,000 vs. 400 IU per day; $p > 0.05$ for 4,000 vs. 400 IU per day). Mean bone strength decreased to a greater extent in both high-dose groups than in the low-dose group, but the differences were not statistically significant.

Comment: In this study of healthy adults with a mean 25-hydroxyvitamin D level in the normal range at baseline, treatment with 4,000 or 10,000 IU per day of vitamin D, as compared with 400 IU per day, significantly decreased BMD of the lower radius, and significantly (10,000 IU per day) or nonsignificantly (4,000 IU per day) decreased BMD of the tibia. There was also a nonsignificant trend toward reduced bone strength with the two higher doses of vitamin D. The adverse effect of high-dose vitamin D would probably have been even greater if it had been compared with 800-1,000 IU per day, rather than with 400 IU per day. That is because previous studies have shown that 800-1,000 IU per day is effective for preventing fractures[1] and decreasing bone loss,[2] whereas 400 IU per day is not effective.

In previous randomized controlled trials, high-dose vitamin D was either nonsignificantly less effective or similarly effective for preventing bone loss, when compared with moderate-dose vitamin D (such as 800 IU per day). I am not aware of any studies that found high-dose vitamin D to be more effective than moderate doses. Based on the available evidence, high-dose vitamin D (such as more than 2,000 IU per day) should not be recommended for osteoporosis prevention unless there are extenuating circumstances such as malabsorption.

Burt LA, et al. Effect of high-dose vitamin D supplementation on volumetric bone density and bone strength: a randomized clinical trial. *JAMA*. 2019;322:736-745.

Pregnant Smokers Need More Folic Acid

Three hundred forty-five cigarette-smoking women in Tampa, Florida, who were pregnant at less than 21 weeks of gestation, were randomly assigned to receive 0.8 mg per day or 4.0 mg per day of folic acid. All women were given smoking cessation counseling. Small for gestational age (SGA) was defined as below the 10th percentile of birth weight for

➤

➤

gestational age. Fetal growth restriction (FGR) was defined as less than 85% of the expected mean birth weight for gestational age. The overall incidence of SGA and FGR was 23.7% and 29.2%, respectively. Mean birth weight was significantly higher by 140 g with 4.0 mg per day of folic acid than with 0.8 mg per day. The incidence of FGR was significantly lower by 35% with 4.0 mg per day than with 0.8 mg per day (p value not stated). The incidence of SGA was 31% lower with 4.0 mg per day than with 0.8 g per day (borderline statistical significance; p value not stated). The higher dose of folic acid was not associated with an increased risk of adverse events.

Comment: Serum and erythrocyte folate levels are lower in women who smoke cigarettes than in nonsmokers.[3] Low maternal folate status, in addition to increasing the risk of neural tube defects, may lead to a reduction in fetal weight. The results of the present study suggest that pregnant women who smoke cigarettes have a higher folic acid requirement than pregnant nonsmokers.

Yusuf KK, et al. Comparing folic acid dosage strengths to prevent reduction in fetal size among pregnant women who smoked cigarettes: a randomized clinical trial. *JAMA Pediatr*. 2019;173:493-494.

Is a Gluten-Free Diet Beneficial for Autoimmune Thyroiditis?

Thirty-four women (aged 20-45 years) with autoimmune thyroiditis and an incidental finding of positive IgA anti-tissue transglutaminase antibodies (which is strongly suggestive of celiac disease) were assigned, based on patient preference, to follow a gluten-free diet (n = 16) for six months or to serve as controls (n = 18). At the end of the study, 10 of 16 patients in the diet group and none of those in the control group tested negative for anti-tissue transglutaminase antibodies. (According to Mayo Clinic Laboratories, these antibodies should begin to decrease within 6-12 months after starting a gluten-free diet). The mean titer of thyroid peroxidase (TPO) antibodies decreased by 24% in the diet group and increased by 3% in the control group ($p < 0.05$ for the difference in the change between groups). Similar results were seen for thyroglobulin antibodies.

Comment: In this study, consumption of a gluten-free diet for six months resulted in a moderate decrease in thyroid antibody titers in women with autoimmune thyroiditis and probable celiac disease. Presumably, the antibodies produced in response to gluten ingestion were cross-reacting with thyroid tissue. It is not known whether a gluten-free diet would also decrease thyroid antibodies in patients with non-celiac gluten sensitivity, although there are anecdotal reports of such.

Krysiak R, et al. The effect of gluten-free diet on thyroid autoimmunity in drug-naïve women with Hashimoto's thyroiditis: a pilot study. *Exp Clin Endocrinol Diabetes*. 2019;127:417-422.

Iron Fortification of Infant Formula: How Much Is Too Much?

Four hundred five infants from low- to middle-income neighborhoods in Santiago, Chile, who had normal iron status were randomly assigned at six months of age to consume iron-fortified (12 mg/L) or low-iron (2.3 mg/L) formula for six months. The children subsequently underwent tests of cognitive function at an average age of 16.2 years. Compared with the low-iron group, the iron-fortified group had lower mean scores on eight of nine tests of cognitive function, three of which were statistically significant (visual memory, arithmetic achievement, and reading comprehension achievement).

Comment: The American Academy of Pediatrics Committee on Nutrition recommends that formula-fed infants aged 6-12 months receive iron-fortified infant formula that contains 10-12 mg/L of iron. In contrast, the Committee on Nutrition of the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition has no specific recommendation for infants in that age group, and the Committee concluded that it is unclear whether fortification at a level of 10-14 mg/L has any advantages.[4]

In the present study, teenagers who had previously received infant formula containing iron at a concentration recommended by the American Academy of Pediatrics had worse cognitive function, compared with teenagers who had received a low-iron infant formula. It is important to maintain adequate iron status during early childhood because iron plays a key role in brain development. However, excessive iron intake appears to have adverse effects. Further research is needed to determine the optimal level of iron intake for infants.

Gahagan S, et al. Randomized controlled trial of iron-fortified versus low-iron infant formula: developmental outcomes at 16 years. *J Pediatr*. 2019;212:124-130.e1.

Vitamin B6 Neurotoxicity: Some People Can Tolerate Large Doses

A 30-year-old woman with homocystinuria who had been taking 1,250-1,750 mg per day of pyridoxine for 20 years developed progressive sensory neuropathy with ataxia and impaired sensation in the extremities. Electrodiagnostic testing revealed abnormal sensory nerve potentials, and the patient was diagnosed with sensory ganglionopathy. The pyridoxine dosage was reduced to 500 mg per day, which resulted in the disappearance of sensory symptoms and ataxia, and normalization of sensory nerve potentials.

Comment: There have been a number of case reports of severe peripheral sensory neuropathy developing in people taking large doses of vitamin B6. Most of these patients improved within two months after discontinuing pyridoxine, although subtle neurological dysfunction persisted in some cases for years. The neurotoxicity of vitamin B6 is dose-related. The lowest dose that has clearly been shown to be neurotoxic in humans is 500 mg per day. In some patients with schizophrenia, homozygous homocystinuria, or primary hyperoxaluria, dosages greater than 500 mg per day appear to be needed to achieve optimal clinical results. Many patients tolerate these large doses and do not develop neurotoxicity.

In the present case report, pyridoxine neurotoxicity developed after long-term use of 1,250-1,750 mg per day, but the condition resolved when the dosage was decreased to 500 mg per day. Patients taking large doses of vitamin B6 should be advised to watch for early warning signs of neurotoxicity (such as hypoesthesia or unsteadiness), and they should be given periodic neurological examinations.

Echaniz-Laguna A, et al. Regressive pyridoxine-induced sensory neuronopathy in a patient with homocystinuria. *BMJ Case Rep*. 2018;2018:bcr-2018-225059.

Questionable-Research Department

Eighty-six Iranian women with polycystic ovary syndrome (PCOS) were randomly assigned to receive, in double-blind fashion, 200 mg per day of coenzyme Q10 (CoQ10), 400 IU per day of vitamin E, both treatments, or placebo for eight weeks. All 86 women were taking 500 mg of metformin three times a day at baseline. Compared with placebo, CoQ10 (with or without vitamin E) significantly improved insulin resistance, as determined by homeostasis model assessment. Compared with placebo, all three active treatments significantly decreased the mean total testosterone level ($p < 0.001$). One might conclude from this study that CoQ10 improves insulin resistance and that CoQ10 and vitamin E each improve testosterone levels in women with PCOS.

Comment: In an editorial in the July 2019 issue of the *Townsend Letter*, I expressed concern that a large and growing number of papers from Iran and some other countries have left me wondering whether the research was fabricated. Several aspects of the present study raised my eyebrows. First, there are no clear biochemical mechanisms by which CoQ10 or vitamin E would be expected to improve insulin resistance or testosterone levels in women with PCOS. Second, it is unusual for researchers to invest money in an expensive double-blind trial before there is preliminary evidence of efficacy (such as case reports or uncontrolled trials). The only previously published research that examined these effects of CoQ10 and vitamin E in women with PCOS came from another Iranian researcher whose work was the main focus of my July 2019 editorial. The present study appears to have been rather expensive, since it included 172 measurements each of serum insulin, sex hormone-binding globulin, luteinizing hormone, follicle-stimulating hormone, progesterone, and estradiol.

Third, although the use of metformin was not one of the inclusion criteria, all 86 women in the study were taking 500 mg of metformin three times a day. Metformin has a high incidence of gastrointestinal side effects, and as many as one-third of women taking a similar dose of metformin discontinue it because of these side effects.[5] Therefore, it is difficult to believe that none of the women had discontinued metformin treatment and none had been advised to try a lower dose (side effects often improve when the dosage is lowered).

Fourth, the CoQ10 and vitamin E supplements used in the study were manufactured by a US company, whereas the placebos were manufactured by an Iranian company. It is unusual for a company to attempt to manufacture an identical placebo for a product produced by another company.

Izadi A, et al. Hormonal and metabolic effects of coenzyme Q10 and/or vitamin E in patients with polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2019;104:319-327.

Vitamin C Deficiency Is Common in Hospitalized Patients

Of 149 patients hospitalized in Australia, 77% had a low serum vitamin C level. The median age was significantly higher in patients with vitamin C deficiency than in those with normal vitamin C levels (73 vs. 65 years; $p = 0.04$). As compared with patients with normal vitamin C levels, those with low levels had higher C-reactive protein concentrations and their median length of hospital stay was two days longer ($p = 0.02$).

Comment: This study is consistent with previous research demonstrating that low vitamin C status is common in hospitalized patients. Vitamin C plays a key role in a number of physiological processes (such as immune function and wound healing) that are important for patients recovering from surgery or illness. In addition, a randomized controlled trial found that vitamin C supplementation (500 mg twice a day) significantly improved mood in hospitalized patients. In that study, 66% of the patients had a low plasma vitamin C level prior to treatment. Since vitamin C is safe and inexpensive, supplementation should be considered for most hospitalized patients.

Sharma Y, et al. Vitamin C deficiency in Australian hospitalised patients: an observational study. *Intern Med J*. 2019;49:189-196.

Fiber Supplement Improves Gastroesophageal Reflux Disease

Thirty-six patients (mean age, 35 years) with non-erosive gastroesophageal reflux disease (GERD) whose diet was low in fiber (less than 20 g per day) were advised to continue their usual diet and to take 5 g of psyllium three times a day. Each psyllium dose was consumed as a suspension in 150 ml of water and was followed by an additional one cup of liquid. The proportion of patients who experienced heartburn decreased from 93% at baseline to 40% at the end of the study ($p < 0.001$), and the mean score on the GERD symptom questionnaire improved by 45% ($p < 0.001$). The total number of reflux episodes decreased by 38%. The mean value for the minimal lower esophageal sphincter pressure increased significantly, from 5.41 mm Hg at baseline to 11.3 mm Hg at the end of the study ($p < 0.03$).

Comment: Low dietary fiber intake is associated with decreased gastric motility and delayed gastric emptying, each of which may contribute to gastroesophageal reflux. In the present study, increasing fiber intake by supplementing with psyllium was associated with an increase in lower esophageal sphincter pressure, a decrease in heartburn, and a reduction in the number of reflux episodes in patients with GERD whose diet was low in fiber. Controlled trials are needed to confirm these findings.

Morozov S, et al. Fiber-enriched diet helps to control symptoms and improves esophageal motility in patients with non-erosive gastroesophageal reflux disease. *World J Gastroenterol*. 2018;24:2291-2299.

References

1. Gaby AR. Osteoporosis. In Gaby AR. *Nutritional Medicine*, 2nd Edition. 2017, Concord, NH, https://doctorgaby.com, chapter 166.
2. Macdonald HM, et al. Hip bone loss is attenuated with 1000 IU but not 400 IU daily vitamin D3: a 1-year double-blind RCT in postmenopausal women. *J Bone Miner Res*. 2013;28:2202-2213.
3. Witter FR, et al. Folate, carotene, and smoking. *Am J Obstet Gynecol*. 1982;144:857.
4. Kleinman RE. Introduction: Recommended iron levels for nutritional formulas for infants. *J Pediatr*. 2015 Oct;167(4 Suppl):S1-2.
5. Fleming R, et al. Ovarian function and metabolic factors in women with oligomenorrhea treated with metformin in a randomized double blind placebo-controlled trial. *J Clin Endocrinol Metab*. 2002;87:569-574.

◆

Vendor Highlights: British Columbia Naturopathic Association Conference 2019

by Jacob Schor, ND

Perhaps I've attended one too many conferences in recent years. I used to be so thrilled to step into the vendor halls at conferences and couldn't wait to see what new products or services they were promoting. It was the ideas, the ability to translate new science into practical and pragmatic actions that was so exciting. The supplement makers seemed to be ahead of the rest of us in reading the science and translating it into practice. One can learn a lot having a smart sales representative explain complicated chemistry. In fact, often one learns more from the vendors than from the speakers. I should probably cut that line out lest someone takes offense. The excitement seems to have worn off of late, and now I approach the various vendors with a hesitancy; too often it boils down to a transactional equation of "you can make lots of money; buy this and sell it to your patients." Whether it will improve their health doesn't seem to be as important.

It also used to be that companies gave away better free stuff. What happened to the hats, the t-shirts, the phone chargers? Stuff that was worth something? The best prize I carried home from Vancouver was a stainless-steel thermos from AOR (which I like).

On Sunday morning, the last day of the British Columbia Naturopathic Association's annual conference, I was packing my suitcase, trying to decide what to keep. I took time off to hammer off this article. Dirty laundry takes up more space than clean clothes and my suitcase had shrunk in size. How much of this stuff could I squeeze in? I remembered how a few years back I shared a room with Torrey Smith, ND, from Alaska, at the AANP conference in Oakland, and was impressed that he had the forethought to bring a second empty suitcase with him just for the purpose of hauling samples home. He's always been a smart guy.

Few companies think about the hassle of getting through TSA lines with liquid samples and, of course, neither had I until the last moment. Are they worth the hassle of checking my carry-on? Thus, I spent precious time watching the clock, knowing that the best speakers are always saved for last, trying to figure out what to keep, what to trash.

The vendor table that most caught my attention in Vancouver had been a uniquely Canadian company called Canadian Pine Pollen. Founded by Burgess Andre and Saeid Mustagh, ND, the company markets extracts made from pollen that is wildcrafted from either Lodgepole or Ponderosa pine trees. Both of these guys were at the table enthusiastically and energetically talking about their endeavor. The idea of using pine pollen medicinally was totally new to me. It turns out that pollen is a traditional medicine in China and the subject of substantial published medical research (in Chinese). Who knew? I certainly hadn't. I have to commend Saeid for putting up with my wtf interrogation and patiently explaining the chemistry and clinical application of their products. I'd never thought about any of this before.

But think about it. Plants concentrate a major part of their lifetime focus on reproduction and these coniferous trees that are either female or male invest precious energy into their pollen that they hope will fertilize the ovaries on other trees. Pollen ends up loaded with plant hormones, growth factors, and other goodies that have parallel action in animals, including humans. Thus, it seems that these extracts have 'hormone'-like action when consumed by people. There are two uses that Dr. Mustagh seemed most excited about. For women, relief from hot flashes, the grand prize we are all always hoping to find that will work reliably. And for men, a response that sounds like their testosterone has increased. These effects aren't from taking estrogen or testosterone exactly but from complexes of plant hormones that appear to have a parallel synergistic effect. On top of the utility of these products, this company deserves a gold star for supporting all of the naturopathic high notes: wildcrafted, sustainable, organic agriculture that has put an economic value on living trees beyond clearcutting them for lumber.

I invested a few minutes searching the medical literature and quickly found strong hints that pine pollen might be useful in treating diabetes[1,2] and its side effects like retinal injury.[3] In fact, there is a 2019 clinical trial with rather promising results for treating diabetes. Sadly, it is in Chinese but thank God for Google Translate.[4] Pine pollen has also been shown useful in treating chronic arthritis in mice[5] and people.[6] Several papers elucidate why pine pollen inhibits cancer in chickens,[7] and possibly in humans.[8] Given that Dr. Mustagh promised that I'll see results in patients and feel them myself in less than a week, I did finally decide to check my luggage so I could carry them home and give them a try. Dr. Mustagh has summarized the pine pollen research at https://canadianpinepollen.com/pages/pine-pollen-research.

Of course, claiming a supplement relieves hot flashes is tricky as these symptoms typically respond well to placebo.[9] We've seen no end of supplements over the years that

worked in small trials but failed in larger more rigorous trials. Determining whether an intervention really reduces hot flashes is more complicated than one might guess.[10] Perhaps I need to temper my enthusiasm?

This is a timely reminder of how badly our profession needs to set up a system to run simple clinical trials of the supplements vendors are so certain work. Surely in the era of Survey Monkey there must be a way to conduct quick, cheap and effective clinical trials? Otherwise we are left to guess at a product's efficacy by the enthusiasm of those selling and the reputation of our colleagues endorsing a particular product. Burgess and Saeid were certainly enthusiastic. I'll give them that.

Tina Kaczor, ND, and Gurdev Parmar, ND

I detoured to a local pharmacy on Sunday morning on the way to the airport train with my dear friend Tina Kaczor, ND, to see if I could purchase Dukoral. I had to check the pharmacy to see if the rumors Dr. Kaczor had shared were true. And they are. One can walk right into a Canadian pharmacy and purchase Dukoral without a prescription and even pay cash. The price I was quoted was just $105 (CAD). Dukoral is a drinkable vaccine that provides protection against "traveler's diarrhea" or technically "heat-labile producing enterotoxigenic *E. coli*." A full immunization requires two oral doses taken at least one week apart, with the last dose taken at least one week before travel.[11]

Canadians like to travel. No one wants to get diarrhea especially far from home. It is made from chemically purified cholera toxin. Dukoral has been licensed in Sweden since 1991. Cholera is caused by *Vibrio cholerae*, which produce an enterotoxin, composed of five receptor binding subunits surrounding a single catalytic subunit. The binding subunits bind to GM1 ganglioside receptors in the small intestine and the catalytic subunit is released into the cell where it activates adenylate cyclase. This activation leads to a massive outpouring of fluid from the small intestine, overcoming the absorptive capacity of the bowels resulting in massive amounts of watery diarrhea. Cholera treatment requires rapid rehydration and antibiotics. Timely appropriate treatment can reduce mortality to less than 1% from as high as 50%.[12] Yet, it wasn't to prevent diarrhea that we were so interested in this vaccine.

Back in 2017, a paper was published in the journal *Gastroenterology* that suggested that use of this cholera vaccine was associated with a lowered risk of death in patients with colorectal cancer (CRC). The researchers identified patients diagnosed with colorectal cancer in Sweden between 2005 and 2012. Sweden has nationalized healthcare and so these patients' records of drug use could be checked in a national registry. Using Cox regression analysis, a hazard ration (HR) of death from CRC and overall mortality was calculated for CRC patients who had used the cholera vaccine against matched controls who had not. A total of 175 CRC patients were identified who had taken the vaccine after diagnosis. Their risk of death from CRC was 47% lower than the matched controls who had not received the vaccine (HR, 0.53; 95% CI, 0.29-0.99). In addition, overall risk of death decreased 41% (HR, 0.59; 95% CI, 0.37-0.94) irrespective of patient age, tumor stage, or sex.[13]

The same authors published a second study about cholera vaccine in 2018. In their second study they examined use of cholera vaccine and the risk of death in prostate cancer patients.

Again using data gathered in Sweden, in this case from 841 patients diagnosed with prostate cancer and who had used this vaccine, the authors concluded that those who used the vaccine had a 43% lower risk of death from their cancer (HR, 0.57; 95% CI, 0.40-0.82) compared to patients who had not used it. In addition, vaccine users had a 47% decreased risk of death overall (HR, 0.53; 95% CI, 0.41-0.69). Again, the decreased mortality rate was consistent, irrespective of patients' age or tumor stage at diagnosis.[14]

These are the sort of studies where one wants to ask, "What are you waiting for?" Granted, the evidence isn't definitive, but the risks are minimal. This vaccine is given to children without prescription. The specific vaccine used in Sweden isn't sold in the US; but as you may have guessed, it is sold in Canada and, as mentioned, it is sold over the counter without a prescription for about $80 US.

As I've mentioned before, one can learn a great deal of useful information by attending conferences in person and not always by sitting in the lectures.

References

1. Feng XT, Duan HM, Li SL. Protective role of Pollen Typhae total flavone against the palmitic acid-induced impairment of glucose-stimulated insulin secretion involving GPR40 signaling in INS-1 cells. *Int J Mol Med*. 2017 Sep;40(3):922-930.
2. Feng XT, et al. Pollen Typhae total flavone improves insulin resistance in high-fat diet and low-dose streptozotocin-induced type 2 diabetic rats. *Biosci Biotechnol Biochem.* 2014;78(10):1738-42.
3. Lei X, et al. Typhae pollen polysaccharides ameliorate diabetic retinal injury in a streptozotocin-induced diabetic rat model. *J Ethnopharmacol*. 2018 Oct 5;224:169-176.
4. (https://translate.google.com/translate?hl=en&sl=zh-CN&u=http://www.ahhdsw.com/index.php%3Fcase%3Darchive%26act%3Dshow%26aid%3D83&prev=search)
5. Lee KH, Choi EM. Effect of pine pollen extract on experimental chronic arthritis. *Phytother Res*. 2009 May;23(5):651-7.
6. Voloshyn OI, Pishak OV, Seniuk BP, Cherniavs'ka NB. [The efficacy of flower pollen in patients with rheumatoid arthritis and concomitant diseases of the gastroduodenal and hepatobiliary systems]. *Lik Sprava*. 1998 Jun;(4):151-4.
7. Wang Q, et al. Taishan Pinus Massoniana pollen polysaccharide inhibits the replication of acute tumorigenic ALV-J and its associated tumor growth. *Vet Microbiol*. 2019 Sep;236:108376.
8. Chu HL, et al. Effects of sulfated polysaccharide from Masson pine (Pinus massoniana) pollen on the proliferation and cell cycle of HepG2 cells. *Int J Biol Macromol*. 2013 Apr;55:104-8.
9. Mahon SM, Kaplan M. Placebo effect in hot flush research. *Lancet Oncol*. 2012;13(5):e188.
10. Sloan JA, et al. Methodologic lessons learned from hot flash studies. *J Clin Oncol*. 2001;19(23):4280-4290.
11. https://www.dukoralcanada.com/taking-dukoral
12. Lopez AL, et al. Killed oral cholera vaccines: history, development and implementation challenges. *Ther Adv Vaccines*. 2014 Sep; 2(5): 123–136.
13. Ji J, Sundquist J, Sundquist K. Cholera Vaccine Use Is Associated with a Reduced Risk of Death in Patients with Colorectal Cancer: A Population-based Study. *Gastroenterology*. 2017;0(0).
14. Ji J, Sundquist J, Sundquist K. Association between post-diagnostic use of choleravaccine and risk of death in prostate cancer patients. *Nat Commun*. 2018 Jun 18;9(1):2367.

◆

On the cover

Take-Home Message with Gabby Reece

by Karina Gordin, MSc

Total knee replacement hasn't stopped world-class athlete Gabby Reece from training harder, performing longer, and recovering faster. Her secret to athletic longevity? A healthy lifestyle and positive mindset. "We all have setbacks, that's reality," notes Gabby. "But strong comebacks are also reality. You don't have to be a super-elite fitness and nutrition expert – just stay proactive with your health and get others involved." So, with the support of her community, Gabby continues to challenge herself and nourish both her body and mind to ultimately achieve athletic longevity – even with a "fake knee."

KG: I understand you experienced chronic knee pain for close to 15 years, which culminated in a full knee replacement. What treatment options did you opt for before finally turning to surgery?

GR: Quite a few – I stayed very proactive. Traditional physical therapy was a fairly regular practice in my life. I received platelet-rich plasma. I worked with lasers. I did therapy localization. Before you get a knee replacement, particularly earlier in life, you try to exhaust all the options. As you mentioned, I dealt with the discomfort and decreased function for nearly 15 years, but it just got to a place where it really did not function.

KG: Considering the nature of your injury, alternative therapies like platelet-rich plasma (PRP) prolotherapy were not as effective?

GR: In my case, the injury was just too advanced. Generally, though, you'll hear people getting great results with prolotherapy and similar therapies like Synvisc and stem cell. I strongly believe those should be first-line treatment options. I made sure to exhaust all my options, and more importantly, stay proactive. I have tons of friends who received PRP and either got long-term relief or complete restoration. In my case, I had a lot of lateral damage. I was close to being bone on bone, so, I was simply not the right candidate. But like I said, I know a lot of athletes who are very hard on their bodies and see great success with those alternative therapeutic modalities. I'm a big advocate because, look, what's the worst that can happen? It doesn't work. PRP doesn't have any side effects, it's not cost-prohibitive, and it's not like you're taking these radical risks, so I do recommend it.

KG: How did you sustain the injury?

GR: I will say this – I always try to remind people, and it's even a reminder to myself, that my knee was *a symptom*. Yes, I incurred wear and tear playing volleyball, and I have long levers and I'm not naturally the most bendy person, but the truth of it is, my hips, ankles, and foot flexion were very tight – not adequately stretched – so I was inevitably prone to injury. Granted, I sustained repetitive trauma jumping, jumping, jumping, but my body wasn't able to adapt and move in a correct pattern because I had such tight muscles, so the load got redistributed disproportionately to my knees. Unless you have a catastrophic injury, the pain is often just a symptom of something else. And you know, part of my homework even now with a "fake knee" is stretching the fascial tissue on my quads. They're like rocks, so I constantly have to work at that.

KG: You're constantly challenging yourself, and today you're in top physical form. Over the years you have gained invaluable training experience, so what advice would you give your younger self?

GR: That's an interesting question – the problem with athletes is that our training and our sport beat us up. We train, train, train, and pound our bodies so we can prepare for competition. If I could go back, I would train and improve my performance without continuously pounding my joints. For example, the last ten years I've been training in water so now I do dynamic, explosive, ballistic exercises without hammering my joints. I'd tell myself that more isn't always more. Work smarter not harder. Also, I would really emphasize the connection between what I put in my mouth and my overall performance. In other words, better nutrition equals better performance, faster recovery, and athletic longevity. Food is fuel after all. But like I mentioned earlier, I would incorporate a much more diligent flexibility regimen into what I was doing. If you have full range of motion and your workload is getting distributed mechanically correctly, and every hinge is able to perform, our bodies can handle a lot for a long time. The interesting thing about athletes is, yes, we push ourselves and can do a lot, but we have a tendency to injure ourselves if we aren't prepared, since everything is accelerated. You're working harder, lifting heavier, jumping higher. In other words, *it's like going in the wrong direction really fast.*

KG: Whereas a more optimal training and lifestyle approach allows you to work harder, lift heavier, and jump higher – at an elite athletic level – without sustaining injury.

GR: That's the idea. My husband says, "The people at the gym should take yoga, and yogis should go to the gym."

KG: That would certainly achieve athletic longevity!

GR: Right, we have a tendency to just do things we're good at and one thing I'd say about athletic longevity is to explore the areas that are more vulnerable, that you're not as good at, because those are the ones that'll support you as a more wholistic, complete, moving being. Agility, strength, and balance are important in equal measure. People might shrug off flexibility and only focus on strength training or use age as an excuse to avoid developing strength. I don't buy into that. It's all about using your body correctly. Take runners for example – certainly as we age, running could become uncomfortable, but that's not an excuse to just stop. I suggest *running barefoot* (unshod) on a soft surface like sand or grass. It's just a little kinder with each step, but you can still challenge yourself.

KG: Speaking of shod versus unshod running – you were the first woman to design a signature shoe for Nike. So, how important is the style of shoe to the corresponding sport, and what are your thoughts on minimalist and barefoot shoes? Or running barefoot altogether, and training barefoot?

GR: There are so many factors that go into the formula. The more the foot can work to its fullest potential – whether you're walking, running, jumping, dancing – the longer you'll be able to walk, run, jump, dance. Sure, when running on the street you need foot protection. Preferably you should run on a soft environment like sand, so it's easier to say, "Hey, go barefoot!" If you read *Born to Run*, Tarahumara Indians run hundreds of miles in "naked shoes" along Mexico's Copper Canyons, all without rest or injury. The shoes are ultra-minimalist with just a thin layer of protection, and this really frees the foot and toes enough to work, to grip, to release. That's pivotal to develop your toe muscles, and not keep them in a cast essentially. I have a lot of friends who are basketball and tennis players that wear sneakers with the latest cushioning and arch support – their feet are just hammered. Imagine shoving feet into shoes and really working them to the max. Running barefoot also connects you to the earth, so that's another benefit – grounding. The earth is struck by lightning how many millions of times per day? It's basically a giant battery constantly being recharged by all the lightning strikes. So just by taking off the insulated sneakers and connecting to the earth barefoot, we also recharge. For me, movement and exercise have a lot to do with our overall well-being. It's more than exercising and getting really ripped. Those are all great parts of it, but not the whole.

KG: Thank you for bringing that up, what an important point. I am sure grounding also helps with athletic recovery and repair!

GR: I can say firsthand it does. Sure, you have your massage therapists and expensive supplements to help speed recovery, but grounding is simple, effective, and costs nothing.

KG: Speaking of recovery, can you please discuss your approach to recovery post-op? I understand you opted out of taking opioids, and in fact, took that as an opportunity to help spread awareness about the opioid epidemic. How did you manage postsurgical pain?

GR: I made the decision beforehand. It's like when you go to a restaurant and say, "Okay, when they put the breadbasket down, I'm not going to eat it." When you're not dealing with it in the moment, you are more prepared. I always acknowledge that pain is very personal, but I had gone in thinking opioids are not an option for me. I prepared myself for the discomfort, I was realistic about it and didn't expect to go into surgery and sleep comfortably. So, I went into it with that mindset. For me personally, they used a cream on the incision that gives you numbness for about the first 24 to 72 hours to help weather the "storm of pain." I also had liquid Tylenol, and in the hospital, they did give me Tramadol. But once I was discharged, I used Marc Pro – an electrical muscle stimulation device. You put it in X-patterns over places of pain in order to fatigue your neuroreceptors, and that gives you temporary pain relief. Icing is also good for temporary pain relief, but I mostly avoided it because you need the swelling as part of healing, and icing decreases circulation. When I was in enough pain I'd say, "Screw it, I'll take the ice," but I was always calibrating my pain and making informed decisions. And listen, there's nothing like a good old-fashioned cry in the closet. You know, "I feel miserable, I feel tired, I feel anxious, I don't know if my body will heal the

➤

➤

way I want it to," so let all that out. And really what people have to remember, especially when you have a major injury or surgery, half your anxiety is your fear. You have to separate and allow yourself to feel like that and work through the fear. Don't let fear get in the way of your dream.

KG: The fear would likely exacerbate the pain.

GR: Oh listen, big time! I think fear is the greatest component of the pain because it's connected so closely to our own fears and anxieties. It's totally normal and natural to feel fearful, but like the pain, take time to work through it, there are no easy, fast solutions. Support is key. My husband would remind me, "You know, it's going to be okay. You know, life is going to get better." Every once in a while, he would just sort of give me the heads up, to stay on the right side of the fence and stick to my beliefs. Your belief system is also part of your healing. Emotional therapy is just as important as physical therapy. Remember it won't happen easily, nothing is easy, but it'll happen.

KG: How about acupuncture for pain relief?

GR: Post-surgery, you're almost just paying your time, but there are ways to recover more efficiently, and acupuncture is one of those ways. It's safe, relatively inexpensive, effective. Great for pain relief, anxiety management, circulation, relaxation, sleep. Think about it, if you're not sleeping well, you're not recovering well. I'd also take magnesium to relax and sleep. My friend gave me an ashwagandha tincture and non-psychoactive CBD drops, and that really helped me adapt and relax. Also keep sugar out and load up on turmeric to help manage (not suppress) inflammation. The other thing I'm learning as I go – and it's funny because it's the most basic thing we do – breathing. Deep breathing is so important for recovery because it helps with everything from dealing with fear to sleeping more soundly. None of us really breathe, none of us are mindful of our breaths. My husband and I got into breathing a few years ago, and now we're really focusing on nose breathing and all the advantages of nose breathing. When you mouth breathe, you scrub your CO2. Your cells are not set up as well to absorb oxygen if you scrub your CO2. Nasal breathing is wildly uncomfortably for a lot of people in the beginning, but keep in mind, your sinuses emit nitric oxide, which helps you absorb more oxygen. Even your teeth and jaw are in better shape if you nose breathe and not mouth breathe. The book *The Oxygen Advantage* breaks it all down scientifically about what happens when you nose breathe. Did you know yawning and sighing are a way to get rid of CO2? So that's pretty cool.

KG: Deep breathing is definitely a major component of the wholistic recovery process. And as you suggested earlier, optimal nutrition is another key component. Can you address your dietary and lifestyle routine, including how you may fuel your day?

GR: Pea protein is one of the more bioavailable protein sources, and I go through cycles where I make smoothies every morning with pea protein, nut butter, sweetened almond milk, and maybe some frozen fruit. My husband Laird Hamilton has a superfood company and sells plant-based creamers, so around the age of 45 I actually started drinking coffee and adding plant-based creamers like the turmeric superfood creamer, unsweetened coconut cream, and even cocoa mint creamer, so I can get a lot of superfoods just in my cup of coffee. Even though I'm getting caffeine, I am balancing it with fat, which slows down the dumping of caffeine into my system. I'll even have a cup of coffee with a superfood creamer before training. There is definitely a synergistic effect between coffee and cocoa, so I can't complain.

KG: Speaking of fats, what are your thoughts on whole fat and even raw dairy versus, say, low-fat?

GR: First of all, I have no issue with anything raw. Milk, butter, cheese. If it hasn't been pasteurized or homogenized, I'll eat it. Laird doesn't like anything that's pasteurized or homogenized – we prefer as close to natural state as possible. In Hawaii, we're part of a co-op and buy food that's as least processed as possible. I'm not really a milk drinker, but I'd use raw milk that still has cream on the top. I prefer goat milk, but I'm not big on dairy. I am able to get a whole raw butter here, and it even has a different smell. It's so fresh we can even put it in a pan, and it doesn't turn brown. Fats are an important part of your diet; just make sure they're good quality and come from real sources like avocadoes, nut butters, eggs, coconut, unprocessed dairy. I eat quite a bit of fat and stay just as lean. I'm not jumping on the ketosis wagon, but I've noticed that my body performs better when I eat fat. I have a clean diet, I limit sugar and carbs, I tend to not overeat as much, and actually, fat helps me not overeat.

KG: Agreed, fat might have a bad rap, but fat keeps you thin!

GR: I've been talking to a guy named Dr. Andy Galpin, and I think that what he says about fat is very interesting. He studies muscle physiology and says that we should be as proficient at burning fat as we are carbs. And when it comes to carbs, we should stick with fruits, vegetables, whole grains. So that's what I try to eat. My biggest sugary drink indulgence is kombucha.

KG: Do you brew your own kombucha, and replace white sugar with, say, maple syrup or honey?

GR: If I had more time, I'd brew my own, but the reality is, I'd probably kill the poor scoby. Dr. Robert Lustig discusses sugar in his talk, "The Bitter Truth About Sugar," and you could even listen to the condensed version online. Dr. Lustig gives you the stripped-down science of sugar, and he really emphasizes the problem of sugary drinks in your diet. And it's not just soda, but pasteurized juices, which are pretty much just sugar.

KG: How about fresh-squeezed juices?

Katrina Gordin is a medical journalist and currently writes for a variety of commercial and peer-reviewed health publications. She would like to thank her father, Dr. Leonid Gordin, for advocating the importance of meditation and mindfulness, which has informed her writing and research.

Karina can be reached at Write@HealthWright.org.

GR: Like my husband says, when would you sit down and eat 12 oranges? But there is a place for juice, like fresh green juices, which you could cut with an apple and lemon, and that can help you meet your body's demand for macro and micronutrients. You can also give your digestion a break and only do liquids, and throw in a bone broth, so cycle in the juices. If you are having a crazy day or you're traveling, that's probably not the time to fast. If you're going to a dinner meeting at the best Mediterranean restaurant, that's not the day when you go, "Well, I'll just have bone broth." But if you make a plan to stay in, relax, and detox, juices and bone broth can be great. It shouldn't make you miserable, that's counterproductive.

KG: Do you have any favorite recipes for post-workout recovery?

GR: Well, it's interesting. More greens than one would think. If I need something quick and convenient, I will do a collagen whey protein. Again, very bioavailable. I'd drink that within 30 minutes following workout. If there's more time, salad with a protein like chicken or salmon, eggs. Healthy, whole-grain carbs replenish glycogen, so that's optimal for recovery. It's nothing glamorous or complicated, just practical.

KG: Do you include saunas as part of your post-workout protocol?

GR: I encourage people, if they're able to access a sauna, to use it at least twice a week, especially men. Recent studies show if men sauna two or three times per week, their risk of Alzheimer's decreases quite a bit. But generally, saunas relax muscles and joints after intense physical activity, and the heat helps improve circulation. That's why my husband and I include heat, and cold, as part of our training program – Extreme Performance training, or XPT.

KG: I look forward to trying XPT, how did it evolve?

GR: Laird and I have been performing extreme training for close to 12 years, and in some ways longer. That includes weight training in the pool, dynamic warmups, and super ventilation breathing, but also incorporating saunas, ice baths, and recovery breathing post-workout. Whenever Laird and I would train, 20 to 30 of our closest friends would join us and see great results and consistent impact. Inevitably, we created a curriculum that we can share, so that everyone can benefit, as a community. Ultimately, if you're talking athletic longevity, you need a support system. It's nearly impossible to train this way alone day in and day out, week in, week out. So, XPT encourages community, and working together to maintain motivation. But that doesn't just apply to XPT, it applies to any workout. Support is pivotal to accomplish your goals over the long run. The exploration of who you are, and what works for you, is as equally important as us giving you training suggestions. There are countless days when the encouragement and support of friends, family, and community, got me back up and training.

KG: Do you have any favorite exercises in the XPT program?

GR: The pool training is definitely the most profound. Swimming can get repetitive, so training with weights in the water gives you an opportunity to be ballistic and explosive. You never feel beat up, but you do feel exhausted. Beyond that, what I've learned is that the recovery aspects – deep breathing, heat, and ice baths – enhance your ability to perform. I designed a HIGHX curriculum, which is high-intensity interval training, but you're on a team. Listen, I have people that are 19 in my class, and people in their 70's in my class, and the point is to do the best you can and adapt the program to your goals and abilities. But you have to leave the ground if you can – impact is good for us if performed correctly. Just continue challenging yourself.

KG: What are some ways you continue to challenge yourself?

GR: I recently started meditating. People say it's not a challenge, but it's hard for me. I've started doing just ten minutes in the morning and following that up with stretching. It's like the onion that I can't figure out how to unpeel. It's like I tell people who are looking to lose weight – "It took you twenty years to get here, you can't lose it in a week." That applies to racing minds and stiff muscles (I'm not the most bendy person). So, in my case, it's like I wound my body for 30 years, it might take me a little while to unwind myself. When you go up a mountain, you don't look at the summit, you put your head down and put one foot in front of the other. Then you stop once in a while and look up and say, "Wow, I made some ground," and then keep going. It all starts with the heart, with the desire to take the first step. But the heart is emotional, so you have to get the brain involved and make a plan, strategize, and stay on track to ultimately reach your summit. ◆

Progesterone Use as Hormone Replacement Therapy: Myths, Facts, and Solutions

by Gary Huber, DO

Winston Churchill famously quoted, "Men occasionally stumble over the truth, but most of them pick themselves up and hurry off as if nothing had happened." Hopefully as scientists and academics, we are willing and able to identify truth when it shows itself. I want to share with you my soft stance on the use of progesterone. I resist hard stances because I never know what future research may reveal and I hope to remain flexible in my thinking. The purpose of the following discussion is to shed light on some of the myths related to hormone therapies and add facts to facilitate a confident and logical decision-making process in the discussion of endometrial cancer avoidance. Which hormone therapies best protect the endometrium from cancer risk? Given the complexity of hormone receptors, metabolites, and function, it is difficult to engage in discussion without including some related comment on breast cancer; but the primary target for this paper is endometrial hyperplasia and cancer. Interestingly, many of the conclusions arrived upon in this discussion will apply equally to breast cancer risk.

Here are the assertions I wish to demonstrate in this discussion:

1. Progestins differ greatly from progesterone in form and function, but both serve to protect the endometrium from estrogen stimulation and proliferation.
2. Progestins did not perform better than progesterone and carry far too much overall health risk to be considered for use in long-term therapies.
3. Topical progesterone has been shown to effectively reduce estrogen's mitogenic influence on endometrium.
4. Oral progesterone is also protective to the endometrium, but excessive oral progesterone is short lived and increases pregnanes and thus breast cancer risk.
5. Topical progesterone achieves higher cellular and blood levels of progesterone than oral progesterone.
6. The most efficacious and safest way to protect the endometrium is with topical progesterone.

Breast cancer will be diagnosed in one out of every eight women while uterine cancer occurs in only one out of every 3,700 women. Uterine cancer rates are currently 27 cases per 100,000 women.[1] A woman between the age of 45 to 65 years, is more than twice as likely to die from cancer than heart disease. Breast cancer is the leading cause of death in women 45-65 years old, while uterine cancer ranks much lower in the seventh position.[2]

Consequently, treating a woman with any modality to protect her endometrium that puts her breast at risk is not viewing the larger picture. I want to explore how we can best protect endometrium and breast tissue as we help women move through menopause.

Cause of death – Females, by age group.

Ages 45+ by Age Group – All Females

Rank	Age 45-54	Age 55-64	Age 65+
1	Cancer 31.7%	Cancer 37.1%	Heart disease 24.4%
2	Heart disease 15.1%	Heart disease 17.0%	Cancer 18.7%

Let's Be Clear

Progesterone is NOT progestin. It is alarming how many scientific articles confuse the two and even lump them into the same category as if they share the same physiologic effect. Let's compare:

- Progesterone is needed in order for a woman to conceive a child, maintain pregnancy, and is produced at exceedingly high levels, roughly 400 mg/day in the third trimester. By contrast, progestins cause birth defects and prevent pregnancy.[3]
- Progesterone is breast protective and reduces risk for breast cancer while use of progestins increases risk of breast cancer by 26%.[4-12]
- Progesterone promotes cognitive function and calming neuro-steroids (allopregnanolone) while progestins increase risk of Alzheimer's by 100%.[3,13]

- Progesterone benefits heart health while use of progestins increase risk of heart attack by 28% and adversely affects coronary function in young women.[12,14-16]

Let's agree that from a sheer physiologic standpoint these are very different elements and we need to be cautious in our vocabulary and thinking when reading medical literature that constantly confuses the two. We would hope that our endocrinology experts would know this distinction, yet endless articles published in endocrinology journals continue to list "progesterone/progestin" and speak of "progesterone" in the title when it was in fact progestins used in the studies. This generates tremendous confusion for both practitioners and patients. The following studies are just a small sampling of articles that make medical claims yet confuse progestins with progesterone; but any remedial search of the literature will expose hundreds more. In "Progesterone Action in Endometrial Cancer, Endometriosis, Uterine Fibroids, and Breast Cancer," the authors consistently list "progesterone/progestin" speaking of the two as interchangeable.[17] In "The impact of micronized progesterone on breast cancer risk: a systematic review" the authors state micronized progesterone in the abstract but then go on to discuss Provera and the PEPI trial without making a distinction.[4]

Hormone Physiology

A few basic physiology points need to be made clear, and I do believe the following points are universally agreed upon in the medical literature. Estrogen is the mitogenic factor leading to pathologies of the uterus and breast, including endometrial cancer, endometriosis, uterine fibroids, and breast cancer.[17] Estrogen stimulates, whereas progesterone inhibits, endometrial growth. Progesterone inhibits epithelial proliferation by blocking the production of mitogenic mediators in the stroma.[18] Progesterone can bind the receptor but also has paracrine effects whereby it has antiproliferative effects via "Hand2" to impact epithelial cells even without binding the progesterone receptor. Progesterone receptor expression is driven by estradiol presence and is expressed in both endometrial epithelial and stromal cells but not in all cells or all the time. In fact, as few as 30% of the cells may be expressing receptors at any one time. Progesterone antagonizes estrogen-driven growth in the endometrium, and insufficient progesterone action strikingly increases the risk of endometrial cancer.

In the adult mammary gland, the progesterone receptor (PR) is not expressed in all cells; rather, 7–10% of the epithelial cells are PR-positive, and these cells are usually not proliferating.[19-21] The majority of human breast cells that were proliferating were PR-negative.[22] Consequently, we know that autocrine and paracrine effects are in play when dealing with breast and endometrial physiology.

Oral vs Topical Progesterone

This question creates confusion for many clinicians. If we look at the simple physiology and metabolism of the two different routes of administration, then this confusion quickly clears. Orally administered progesterone is quickly and thoroughly metabolized by both the prehepatic gut microflora and then the hepatic first pass metabolism, such that very little unadulterated progesterone makes it to the breast and uterine tissues. In studies by Adlercreutz, Nahoul and Levine, we consistently see that oral progesterone is quickly converted to metabolites and that blood and tissue levels never reach significant levels.[23-25] Given that topical and vaginal delivery methods bypass the early gut and liver metabolism, true progesterone as measured in the blood stream by LC-MS is robustly present. Early studies of progesterone's movement utilized radio immune assay (RIA) techniques that have in recent years been shown to be inaccurate as these RIA techniques can't distinguish metabolites such as pregnenes and pregnanes from true progesterone.[24]

Chang showed that when radiolabeled progesterone was given topically and then measured in breast tissue biopsy that high levels had indeed been found despite little to none being seen in the blood stream.[8] In fact, he noted that only 0.1% of the injected dose appeared unmetabolized in the bile. Miles et al administered topical vaginal progesterone versus IM injections of progesterone, then measured blood and endometrial biopsy that showed superior tissue delivery using vaginal progesterone over IM prog.[26] The study by Levine and Watson is the most compelling evidence as he administered either 90 mg of vaginal progesterone or 100 mg of oral and then measured blood values by LC-MS.[24] The vaginal progesterone gel dramatically outperformed the oral, generating a C-max reading of 10.51 ng/ml compared to the oral progesterone's mere 2.2 ng/ml. Not only was the gel greater in peak concentration, it also produced a long-term effect lasting many more hours than the oral dose. The area under the curve was 133 ng-h/ml for the vaginal gel and only 3.46 ng-h/ml for the oral dose.

The most efficacious and safest way to protect the endometrium is with topical progesterone.

Based upon these findings, we have seen clearly that aggressive metabolism of orally administered progesterone could leave the uterus and breast tissue unprotected. Topical applications either to skin or vaginal mucosa have both proven to be effective delivery tools with satisfactory tissue levels. Only a neophyte to hormone replacement therapies would advocate that oral progesterone is needed to protect the endometrium. But let's review the voluminous studies to date to gain perspective here.[27-42]

We also have to acknowledge that there are dozens of studies exploring the use of oral progesterone to protect the endometrium during use of estradiol

➤

➤

replacement therapy. These studies range across a wide array of doses for both estradiol and progesterone, oral and topical, leaving us with a mixed picture of success. We will address those studies momentarily.[27-42]

Exploring Progesterone's Metabolites

We have already seen that using oral progesterone leads to rapid breakdown and poor tissue levels so the trend by some has simply been to increase the oral dose to create a larger pool of progesterone. This immediately creates a second problem as large doses of oral progesterone alter the natural metabolism of progesterone and generate increasingly large pools of pregnane metabolites. A review of Wiebe's work will offer a clear picture.[43-45] He has demonstrated that enzymes for progesterone's breakdown exist in all types of cells and tissues and is not limited to the gut and liver. The enzyme 5-alpha-reductase will rapidly metabolize progesterone to pregnanolone and pregnanediol, the "pregnane" metabolites. These pregnanes are known as neuro-steroids and do offer a calming influence to the brain; but when their production outpaces preg*nenes* then this ratio drives breast cancer risk. Studies using various breast cell lines have shown that 5aP (pregnane) and 3aHP (pregnene) have opposing actions in terms of cell proliferation and adhesion; 5aP stimulates cell proliferation (through increased mitosis and decreased apoptosis) and cell detachment, whereas 3aHP suppresses cell proliferation (through decreased mitosis and increased apoptosis) and detachment. This effect has been noted in multiple breast cell lines regardless of estrogen and progesterone receptor sensitivity or receptor presence. In breast cancer cell lines, we consistently measure pregnanes at high levels relative to low pregnene levels.

From my experience in over hundreds of hormone replacement cases, when urinary progesterone metabolites are measured it is rare that any women can tolerate more than 100 mg of oral progesterone without aggressively producing excess pregnane metabolites. This is a major concern as I pointed out above that pregnanes put the breast at risk and breast cancer is already thousands of time more likely to occur than endometrial cancer. It just doesn't hold up to logic that we would attempt to protect the endometrium with a strategy that places the breast at greater risk – especially when topical progesterone approaches work better and with less risk. For a simple video explaining interpretation of urinary hormone metabolites, please visit my website at www.huberpm.com to watch "Estrogen Lab Interpretation – Assessing Risk." Here is a link: https://www.huberpm.com/videolibrary.aspx.

Oral Progesterone Use in Endometrial Studies

There are dozens of studies exploring the use of oral progesterone to protect the endometrium, and we see a range of effects depending on dose; but a few consistent findings shine through.[27-42] First of all, oral progesterone can provide endometrial protection; but consistently the studies show that at lower doses such as 50 to 100 mg of oral progesterone there is still risk of endometrial proliferation. To be fair, even studies of progestins are not perfect and will display a small percentage of proliferative change. As doses ascend to 400 mg of oral progesterone, that risk expectantly decreases; but none of the studies employing these high progesterone doses extended their study to include examination of urinary metabolites. If they had, there is strong suspicion that we would have seen excessive pregnane:pregnene ratios, thus a risk to breast tissue which is unacceptable.

Another surprising trend in many of these studies is the use of excessive estradiol dosing. Let's look at the Jondet study from 2002 where 336 postmenopausal women were given 1.5 mg of topical estradiol daily for 24 days per month and then either a progestin (10 mg) or oral progesterone (200 mg) for 14 days per month.[35] Endometrial biopsy at the end of 18 months of treatment did not show any cases of hyperplasia but did reveal some proliferative endometrium in a small percentage from both groups. But I want to expose the fact that this is a huge and unusual dose of estradiol. We know that it is the stimulatory effects of estradiol that potentially drives endometrial change and proliferation, so why would a study choose to give a dose that is 10 times physiologic? In a normal cycling female, the amount of estradiol produced over four weeks is roughly 3 mg. In standard hormone replacement therapy, we often give an average dose of 250 mcg of estradiol daily for 24 days which equates to roughly 6 mg. So why would we offer 1.5 mg daily for 24 days netting a total of 36 mg!! That is an enormous estradiol burden. It's also puzzling why they would offer high-dose estradiol for 24 days yet only provide protective progesterone or progestin for a mere 14 days. That reflects the very definition of "estrogen dominance," a state in which we expect to see adverse effects from hormone replacement. It's not surprising that there was some breakthrough proliferative change seen; in fact, the surprise is that there wasn't a higher percentage.

By contrast, the Moyer study using more sensible lower dosed estradiol patches over five years didn't report any hyperplasia or carcinoma and showed reduced rates of endometrial growth by reducing rates of mitosis with lower dosed hormones.[37] DiCarlo et al used a 50 mcg estradiol patch with oral (100 & 200 mg) progesterone versus vaginal (100 & 200 mg) progesterone and reported no occurrence of hyperplasia.[46] Interestingly they also reported that there were fewer bleeding occurrences in those taking progesterone vaginally. This points again to the superiority of topical progesterone application as it avoids first pass breakdown. In a follow up study by DiCarlo, they applied the same topical estradiol patch but this time to women taking three different progestins versus oral progesterone (200 mg).[47] He followed 100 women through 12 monthly cycles; but again we see use of estradiol on a daily basis yet progesterone or progestin only

given for 11 days. Again, this represents estrogen dominance, not in daily dose but in imbalance in daily exposure, and they witnessed bleeding episodes as monthly predictable cycles 73.6% of the time. They also saw additional irregular bleeding 8.3% and spotting occurrence 10.2% of the time. This represents breakthrough bleeding of some type in >92% of the time. Personally, my patient base wouldn't tolerate this. It is not the intended goal of hormone replacement therapy to generate a monthly cycle. It's interesting that oral progestins failed at a higher rate than the oral progesterone at controlling endometrial proliferation. I have to point to the low usage of the progesterone/progestin treatment arm as it was only available 11 days out of 28 while estradiol was applied daily. Would these results be more acceptable if progesterone were more consistently available throughout the month rather than just 11 days? The evidence suggests that it would.

So many of the studies exploring this topic used high-dose estradiol, which is hopefully something we have come to learn is unnecessary and dangerous. The Darj study used oral estradiol 2 mg/day while the Holst study used 3 mg of topical estradiol gel.[29,34] It is common to see doses ranging from 1 to 3 mg daily for at least three weeks per month while limiting the progesterone to poorly absorbed oral doses given just 10 days per cycle. The general finding was that higher doses of oral progesterone were more protective than lower doses and more consistently produced an atrophic endometrium, but even doses of 400 mg orally did not completely halt proliferative changes from occurring. When compared to topical progesterone, there was no benefit seen and some assumed risk for breast pathology.

Endometrial Cancer

What factors consistently drive hyperplasia and proliferation of the endometrium?

- Excessive estradiol dose or excessive number of days of estradiol without the protective presence of progesterone.
- Lack of progesterone tissue levels due to rapid metabolism of oral dosing.
- Progesterone doses that are too low or too brief.

Other external factors that contribute to this paradigm are the non-hormonal factors such as obesity, plastics, and lifestyle. I feel that we all too often get caught up in our search for the perfect hormone regimen but overlook the obvious. Studies by Sjostrom & McCawley have shown that women who lost 20 Kg had a 38% reduction in cancer rates that included endometrial cancer.[48,49] Obesity creates a deepening state of unopposed estrogen.[50-52] Fatty tissue generates a greater amount of 5-alpha reductase converting more ➤

➤

of the testosterone in local tissue to estrogen. We also know that 5-alpha reductase converts progesterone into pregnane metabolites.

Lastly, we have to acknowledge that toxins within our environment are creating much of this cancer risk. Exposure to glyphosate, phthalates, BPA, and metals have all been identified as endocrine disruptors.[53-55] Every single hormone-related medical problem or fertility issue in both men and women can be generated or exacerbated by exposure to BPA and plastics. So, while you attempt to micromanage your patient's estradiol and pregnane level, she is guzzling soda pop from plastic bottles, choosing chips over cruciferous vegetables, and gaining weight. The battle has to be taken beyond the lab result and into the mind and homes of our patients.

FAQs

1. Do women need progesterone post hysterectomy? Absolutely. Progesterone plays a key role in brain, bone, and cardiac function. Progesterone is breast protective and any woman choosing to use estradiol post hysterectomy will be healthier with progesterone to counterbalance the effects of estrogen.
2. Topical progesterone use – vaginal vs oral troche vs topical. Progesterone applied to any mucosal membrane, oral or vaginal, will absorb with roughly twice the efficiency as skin application. Topical progesterone moves largely via diffusion and lymphatics so there will be a disproportionality high concentration of the hormone near the site of application. Skin application allows us to spread this effect over a broader area by applying it to different sites to allow distribution more evenly to brain, breast, and pelvic structures.
3. Typical dosing. Topical progesterone cream use can range from 10 to 80 mg depending on indication, age of patient, and personalized metabolism. For more information on this please feel free to contact my office for treatment protocols and guidance at help@huberpm.com or see our website for discussions at www.huberpm.com.
4. Is oral progesterone safe to use? Yes, but stick to lower doses of 50 to 100 mg as it is rare that women can tolerate a dose above 100 without producing excessive pregnanes. If you use higher doses, then be sure to monitor urinary pregnane and pregnene levels. I recommend monitoring urine metabolites in every hormone patient. See my discussion of quinone estrogens and management of estrogen metabolism on my website www.huberpm.com in the video section. I review estrogen metabolism and lab interpretation. https://www.huberpm.com/videolibrary.aspx.
5. Urine metabolites are great for assessing "risk and metabolites," but it is not the proper tool for assessing tissue levels or making dose adjustments. When assessing tissue levels, blood spot and saliva are the reliable approaches. Only a small amount of your hormones leaves the body by urine as the gut is the primary pathway of elimination so checking urine will not give you a reliable picture. It is similar to magnesium, which can be measured in the blood; but it only represents 2% of your total body burden of magnesium in the serum and so is not accurate for assessing body status.

I trust that this discussion has offered a rational insight to help your practice. If you have further questions then please feel free to contact me at help@huberpm.com. Allow me to close with another famous quote by Maslow who once prophetically stated, "If your only tool is a hammer, then every problem looks like a nail". My hope is that we can all remain flexible in our thinking and always leave the door open for new ideas. Our patients are counting on it.

Gary Huber, DO, spent 20 years as an emergency medicine physician before evolving his practice to integrative care. Dr. Huber is a professor for the American Academy of Anti-Aging Medicine as well as George Washington University's Metabolic Medicine Institute for integrative medicine. Dr. Huber serves as adjunct clinical professor teaching integrative medicine to medical students and residents at Ohio University's medical program as well as the University of Cincinnati College of Pharmacy. He lectures nationally on hormone replacement therapies, cardiovascular care, sports medicine, and other integrative medicine topics. Dr. Huber offers preceptorships to fellows in training or any physician looking to expand their integrative practice. Visit his YouTube Channel at Dr. Gary Huber, YouTube. Or visit his website at www.huberpm.com for articles and videos.

References

1. CDC – Uterine Cancer Incidence and Mortality — United States, 1999–2016 Weekly / December 7, 2018 / 67(48);1333–1338.
2. LCOD All Females by Age Group 2015 – Women›s Health – CDC. Centers for Disease Control and Prevention. https://www.cdc.gov/women/lcod/2015/all-females/index.htm. Accessed July 15, 2019.
3. Ross L. Prentice and Garnet L. Anderson. The Women's Health Initiative: Lessons Learned. *Annu. Rev. Public Health*. 2007. 29:131–50.
4. Stute P, Wildt L, Neulen J. The impact of micronized progesterone on breast cancer risk: a systematic review. *Climacteric*. 2018;21:2, 111-122.
5. Dinny Graham, et al. Hormone-Responsive Model of Primary Human Breast Epithelium. *J Mammary Gland Biol Neoplasia*. 2009;14:367–379.
6. Chlebowski RT, et al. Breast Cancer after Use of Estrogen plus Progestin in Postmenopausal Women. *N Engl J Med*. 2009 February 5; 360(6): 573–587.

7. Foidart JM, et al. Estradiol and progesterone regulate the proliferation of human breast epithelial cells. *Fertility & Sterility*. May 1998;69 (5).
8. Chang, Lee, et al. Influences of percutaneous administration of estradiol and progesterone on human breast epithelial cell cycle in vivo. *Fertility & Sterility*. April 1995;63 (4).
9. Paolo Muti. Is progesterone a neutral or protective factor for breast cancer? *Nature Reviews Cancer*. 2014.
10. Alkhalaf M, El-Mowafy A, Karam S. Growth inhibition of MCF-7 human breast cancer cells by progesterone is associated with cell differentiation and phosphorylation of Akt protein. *European Journal of Cancer Prevention.* 2002; 11: 481–488.
11. Wood CE, et al. Effects of estradiol with micronized progesterone or medroxyprogesterone acetate on risk markers for breast cancer in postmenopausal monkeys. *Breast Cancer Res Treat*. 2007;101:125–134.
12. John Eden. The endometrial and breast safety of menopausal hormone therapy containing micronized progesterone: A short review. *Aust NZ J Obstet Gynaecol*. 2017; 57: 12–15.
13. Schule C, Nothdurfter C, Rupprecht R. The role of allopregnanolone in depression and anxiety. *Progress in Neurobiology*. 2014;113:79–87.
14. Rosano GM, et al. Natural Progesterone, but Not Medroxyprogesterone Acetate, Enhances the Beneficial Effect of Estrogen on Exercise-Induced Myocardial Ischemia in Postmenopausal Women. *J American College of Cardiology*. 2000;36 (7).
15. Rossouw JE, et al. Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women. *JAMA*. 2002;288 (3).
16. Hulley S, et al. Randomized Trial of Estrogen Plus Progestin for Secondary Prevention of Coronoary Heart Disease in Postmenopausal Women. *JAMA*. 1998;280 (7).
17. Kim JJ, Kurita T, Bulun SE. Progesterone Action in Endometrial Cancer, Endometriosis, Uterine Fibroids, and Breast Cancer. *Endocr Rev*. 2013 Feb; 34(1): 130–162.
18. Li Q, et al. The antiproliferative action of progesterone in uterine epithelium is mediated by Hand2. *Science.* 2011; 331:912–916.
19. Ismail PM, et al. A novel LacZ reporter mouse reveals complex regulation of the progesterone receptor promoter during mammary gland development. *Mol Endocrinol*. 2002;16:2475–2489.
20. Shyamala G, et al. Cellular expression of estrogen and progesterone receptors in mammary glands: regulation by hormones, development and aging. *J Steroid Biochem Mol Biol*. 2002;80:137–148.
21. Silberstein GB, et al. Progesterone receptors in the mouse mammary duct: distribution and developmental regulation. *Cell Growth Diff* . 1996;7:945–952.
22. Graham JD, et al. Hormone responsive model of primary human breast epithelium. *J Mammary Gland Biol Neoplasia*. 2009;14:367–379.
23. Adlercreutz H, Martin F. Biliary excretion and intestinal metabolism of progesterone and estrogen in man. *J Steroid Biochemistry*. 1980;13:231-244.
24. Levine H, Watson N. Comparison of the pharmacokinetics of Crinone 8% administered vaginally versus Prometrium administered orally in postmenopausal women. *Fertility & Sterility*. March 2000;73 (3).
25. Nahoul K, et al. Profiles of plasma estrogens, progesterone and their metabolites after oral or vaginal administration of estradiol or progesterone. *Maturitas.* 1993;16:185-202.
26. Miles RA, et al. Pharmacokinetics and endometrial tissue levels of progesterone after administration by intramuscular and vaginal routes: a comparative study. *Fertil Steril*. 1994 Sep;62(3):485-90.
27. Bolaji II, et al. Clinical evaluation of near-continuous oral micronized progesterone therapy in estrogenized postmenopausal women. *Gynecol Endocrinol*. 1996;10:41–7.
28. Bolaji II, et al. Endometrial response in oestrogenised postmenopausal women after treatment with oral progesterone: results of a prospective analysis. *J Obstet Gynaecol.* 1992;12:412–17.
29. Darj E, et al. Clinical and endometrial effects of oestradiol and progesterone in post-menopausal women. *Maturitas.* 1991;13:109–15.
30. Dupont A, et al. Comparative endocrinological and clinical effects of percutaneous estradiol and oral conjugated estrogens as replacement therapy in menopausal women. *Maturitas.* 1991;13:297–311.
31. Gillet JY, et al. Induction of amenorrhea during hormone replacement therapy: optimal micronized progesterone dose. A multicenter study. *Maturitas*. 1994;19:103–15.
32. The Writing Group for the PEPI Trial. Effects of hormone replacement therapy on endometrial histology in postmenopausal women. The Postmenopausal Estrogen/ Progestin Interventions (PEPI) Trial. *JAMA*. 1996;275:370–5.
33. Hargrove JT, et al. Menopausal hormone replacement therapy with continuous daily oral micronized estradiol and progesterone. *Obstet Gynecol*. 1989;73:606–12.
34. Holst J, Cajander S, von Schoultz B. Endometrial response in postmenopausal women during treatment with percutaneous 17 betaoestradiol opposed by oral progesterone. *Maturitas*. 1986;8:201–7.
35. Jondet M, et al. Comparative endometrial histology in postmenopausal women with sequential hormone replacement therapy of estradiol and, either chlormadinone acetate or micronized progesterone. *Maturitas*. 2002;41:115–21.
36. Lane G, et al. Dose dependent effects of oral progesterone on the oestrogenised postmenopausal endometrium. *Br Med J* (Clin Res Ed). 1983;287:1241–5.
37. Moyer DL, et al. Prevention of endometrial hyperplasia by progesterone during long-term estradiol replacement: influence of bleeding pattern and secretory changes. *Fertil Steril.* 1993;59:992–7.
38. Prestwood KM, et al. Ultralow-dose micronized 17beta-estradiol and bone density and bone metabolism in older women: a randomized controlled trial. *JAMA*. 2003;290:1042–8.
39. Pelissier C, et al. Chlormadinone acetate versus micronized progesterone in the sequential combined hormone replacement therapy of the menopause. *Maturitas*. 2001;40:85–94.
40. Suvanto-Luukkonen E, et al. Insulin-like growth factor-binding protein-1: a biochemical marker of endometrial response to progestin during hormone replacement therapy. *Maturitas*. 1995;22:255–62.
41. Moyer DL, et al. Micronized progesterone regulation of the endometrial glandular cycling pool. *Int J Gynecol Pathol*. 2001;20:374–9.
42. Grady D, et al. Hormone replacement therapy and endometrial cancer risk: a metaanalysis. *Obstet Gynecol*. 1995;85:304-313.
43. Wiebe J. Progesterone metabolites in breast cancer. *Endocrine-Related Cancer*. 2006;13: 717–738.
44. Wiebe JB, Pawlak KJ, Kwoka A. Mechanism of action of the breast cancer-promoter hormone, 5a-dihydroprogesterone (5aP), involves plasma membrane-associated receptors and MAPK activation. *J Steroid Biochemistry & Molecular Biology.* 2016;155:166–176.
45. Wiebe JP, et al. Progesterone metabolites regulate induction, growth, and suppression of estrogen- and progesterone receptor-negative human breast cell tumors. *Breast Cancer Research*. 2013, 15:R38.
46. Di Carlo C, et al. Transdermal estradiol and oral or vaginal natural progesterone: bleeding patterns. *Climacteric.* 2010 Oct;13(5):442-6.
47. Di Carlo C, et al. Bleeding patterns during continuous estradiol with different sequential progestogens therapy. *Menopause*. 2005;12(5):520-525.
48. Sjöström L, et al. Effects of bariatric surgery on cancer incidence in obese patients in Sweden (Swedish Obese Subjects Study): a prospective, controlled intervention trial. *Lancet Oncol*. 2009;10(7):653–62.
49. McCawley GM, et al. Cancer in obese women: potential protective impact of bariatric surgery. *J Am Coll Surg*. 2009;208(6):1093–8.
50. Creasman WT. Endometrial cancer: incidence, prognostic factors, diagnosis, and treatment. Semin Oncol. 1997;24(1 Suppl 1):S1–140-S1–50.
51. Münstedt K, et al. Cancer of the endometrium current aspects of diagnostics and treatment. *World J Surg Oncol*. 2004; 2:24.
52. Sherman ME. Theories of endometrial carcinogenesis: a multidisciplinary approach. *Mod Pathol*. 2000;13:295–308.
53. Tarone RE. On the International Agency for Research on Cancer classification of glyphosate as a probable human carcinogen. *Eur J Cancer Prev*. 2018 Jan;27(1):82-87.
54. Pahigian JM, Zuo Y. Occurrence, endocrine-related bioeffects and fate of bisphenol A chemical degradation intermediates and impurities: A review. *Chemosphere*. 2018 Sep;207:469-480.
55. Monneret C. What is an endocrine disruptor? *C R Biol*. 2017 Sep - Oct;340(9-10):403-405.

◆

The Holistic Benefits of Nature-Based Therapy for Women with Breast Cancer

by Kurt Beil, ND, LAc, MPH

Spending time in nature is part of the timeless human experience and something most people appreciate and incorporate into their lives. Recently, empirical research has identified how beneficial this ancient experience is to our health and well-being. Many different nature-based therapies (NBT)* have demonstrated positive effects in a variety of health areas, ranging from mental health conditions like depression, anxiety, and concentration to positive alterations in biomarkers of physical health such as cortisol, blood pressure and heart rate variability.[1–3] These exciting findings are being applied across many different areas of health exploration.

One area of interest is the use of NBT for treating and supporting patients with cancer, one of the most common and most impactful diseases in healthcare. Breast cancer, in particular, is of interest as it is the most common form of cancer in women and second highest cause of female cancer mortality.[4] NBT is an especially appealing approach to assist women with breast cancer because it simultaneously addresses multiple aspects of health in a supportive, low-cost, low-impact way.[5-6]

*Note: No standardization or distinct demarcation of terminology has been identified to this author's knowledge for use in this new area of clinical techniques. Use of terms such as nature-based therapy, nature therapy, forest therapy, natural restorative experiences, ecotherapy, ecological medicine, environmental therapy, nature cure, biophilic medicine/therapy, etc... are often used interchangeably at the current time. The use of "nature-based therapy" in this article is not meant to connote preference for this term over any other, conceptually or otherwise.

Forest Therapy

The currently most talked about form of NBT is forest bathing (originated in Japan as *shinrin-yoku*) which has been written about in many academic and public media sources.[7,8] This full-sensory immersion in the forest environment has years of research demonstrating its physical and mental health benefits. Some studies of healthy female participants have investigated how forest bathing (aka forest therapy or FT) can provide women with psychological improvements in mood, anxiety, and quality of life (QOL), as well as physiological improvements in salivary cortisol, heart rate, heart rate variability (HRV), and lung capacity in exposures ranging from only 15 minutes to three full days.[9–12] And a few studies have provided evidence of FT's potential for specifically benefitting women with breast cancer.

Possibly the most famous FT study, published less than a decade ago, is one of these. It involved healthy participants and the impact that just a few hours in a forest environment, but not a "control" urban one, had on increases in their serum natural killer (NK) cells. These immune system cells are well-known for their ability to identify and reduce the size of cancerous tumors.[13] Elevated blood concentration of NK cells and their "cytotoxic arsenal" of perforin and granzyme enzymes[14] remained for more than 30 days after a single forest exposure, leading to much interest in FT as a complementary addition to cancer treatment and prevention.

Other studies have followed up these findings. In a Korean study published in 2015, eleven women with diagnosed stage I-III breast cancer participated in a two-week forest therapy immersion program outside of Seoul.[15] These women lived in a forest cabin during this experience and participated in daily two-hour forest walks every morning. Their afternoons were spent with free-time activities and group sessions discussing their experience of breast cancer treatments as well as other personal topics. Meals were standardized according to Korean nutritional health guidelines. Blood samples were collected from these women at the beginning (Day 1) and end (Day 14) of the forest therapy experience, as well as one week after returning home to regular life (Day 21), to measure concentrations of NK cells, perforin, and granzyme B.

For the women in this study, the results were substantial. Levels of NK cells increased 39% during the two-week FT experience and were still elevated 13% above baseline on Day 21, one week after returning home. Perhaps more impressively, NK cells' arsenal of cancer-fighting enzymes increased significantly throughout the study and continued increasing after the completion of the FT. The serum concentrations of perforin and granzyme B rose 59% and 155% (respectively) from Day 1 to Day

14 and continued a very notable rise to levels 114% and 359% (respectively) above baseline when measured after participants had returned home for a week on Day 21.

These findings show an intensive up-regulation of the tumor-fighting capacity of the immune system and suggest substantial benefits of FT to support women coping with breast cancer. These results should be taken with caution, as this was a preliminary feasibility pilot study with only 11 participants that included no control group. However, if these results can be replicated, this has large implications for the inclusion of FT as an adjunctive therapy for breast cancer and many other cancers and other health conditions benefitted by NK cell activity.

Supportive Well-Being and QoL

Of course, increasing NK cell activity is just one aspect of addressing cancer. More broadly-reaching studies have investigated FT and other NBTs' ability to support the whole person. One such study published in 2013 had 22 cancer-diagnosed individuals (Note: Only 18 of the participants were female and diagnoses were a mix of breast and lung cancer) participate in twelve weekly non-residential six-hour sessions of FT as well as horticulture therapy (gardening), yoga, and group counselling.[16] NK cell activity was assessed before and after the twelve-week session, as were extensive subjective measures of physical and mental well-being. At the end of the twelve-week session, all participants had increased NK cell activity (41.5% above baseline). In addition, pre-post subjective measures showed substantial benefits in areas of cancer-related fatigue, QoL, mood, anxiety, and well-being, all $p<0.05$ (see Fig 1). All participants reported highly positive feedback and indicated they would like to see this type of experience made more commonly available as part of routine cancer care.

These results are valuable because they remind us of the holistic, patient-centered reality of cancer. Fatigue, mood, anxiety, and sense of well-being are all issues that significantly impact the quality of life of individuals experiencing cancer and can be very difficult to address through conventional medical care alone. NBTs such as the ones in this study improve the life and reduce the difficulties of the person with cancer, more than just addressing the tumor.

Focus, Attention, Mental Health, and Stress

One of the most common sequelae of a cancer diagnosis is impairment of cognitive function, particularly mental acuity and the ability to focus attention. In addition to physical symptoms such as pain, other issues like navigating doctor visits, maintaining personal and professional responsibilities, avoiding social stigma, and fear of impending mortality can greatly impair attention. This often leads to distractibility, poor concentration and memory, and increased impatience. And these are all before considering the damaging cognitive effects of chemotherapy recognized as "chemo brain."[17] These all degrade quality of life for women diagnosed with breast cancer, beyond the challenges of the physical disease itself.

Fortunately, exposure to Nature helps with this too! Everyone has experienced the relaxing peace of mind that comes from taking a walk in the woods or stroll through a park. As noted by famed 19th century landscape architect Frederick Law Olmsted, "The enjoyment of [natural] scenery employs the mind without fatigue and yet exercises it; tranquilizes it and yet enlivens it; and thus, through the influence of the mind over the body gives the effect of refreshing rest and reinvigoration to the whole system"[18]

One study that effectively demonstrates this refreshing rest was conducted in Michigan with 157 women newly diagnosed with breast cancer.[19] These women were participated in a series of home-based natural restorative experiences (NREs) for a minimum of 120 minutes per week for an average of 36 days, from the time just after their diagnosis to a time after surgery but before beginning adjuvant therapy (e.g. chemotherapy, radiation). NRE were defined as any experience in nature fulfilling four criteria as originally defined by University of Michigan professor Stephen Kaplan's classic Attention Restoration Theory[20]:

1) Fascination: The NRE should easily capture one's interest.
2) Being Away: The NRE should mentally and/or physically remove one from typical daily routines, concerns, and/or locations.
3) Extent: The NRE should not be boring or become tedious.
4) Compatibility: The NRE should be personally enjoyable and/or pleasant.

Options to experience different NRE were provided and included but were not limited to (in participants' own

➤

Figure 1. Before/after results of a 12-week holistic program for patients diagnosed with breast or lung cancer (n=22).

Test	Measure	%Score Δ	p-value
Cancer Fatigue Scale (CFS)	Physical	-50.0%	.001
	Affective	-25.9%	.032
	Total Fatigue	-32.9%	.004
SF-36 (Quality of Life)	Physical Functioning	6.9%	.034
	General Health	9.4%	.035
	Vitality	11.9%	.007
	Mental Health	8.9%	.027
Profile of Mood States (POMS)	Tension-Anxiety	-29.9%	.030
	Confusion-Bewilderment	-35.8%	.002
State Trait Anxiety Inventory (STAI)	State Anxiety	-23.3%	.001
	Trait Anxiety	-13.1%	.011
FACIT (Well-Being)	Functional Well-being	14.1%	.027
	Spiritual Well-Being	14.2%	.039
NK Cell Activity		41.5%	<.001

➤

words): "tak[ing] care of my garden," "walk[ing] along the river," ""watch[ing] a beautiful sunrise," and "spend[ing] an hour with my plants." Multiple regression analysis demonstrated that women who engaged in NRE had significant improvements in standard measures of memory, focus, and concentration compared to no changes in the wait-listed control group (b= -0.872 (0.345), β= -0.158, p<0.01).

These benefits can be considered as part of NBT's ability to ease mental fatigue and reduce the significant impact of stress that a diagnosis of cancer can bring. Such effects are well-recognized in the cancer community, such that the field of "psycho-oncology" has been established to focus specifically on reducing the detrimental mental burden of cancer, including impacts on mood, concentration, and QoL.[21–23]

Various other NBT may be useful in addressing these issues in ways similar to other healthy and clinically affected populations, as shown by multiple reviews and meta-analyses.[3,24,25] The underlying effects are based on humans' inherent affinity and evolutionarily derived "biophilia" to respond positively to restorative natural settings.[26,27] This applies to both the psychological and physiological components of stress that influence mental and physical health.[2,28] Substantial evidence supports the concept that nature provides restorative, health-promoting, "salutogenic" experiences for all people,[29] and NBTs can be especially effective in providing this type of support to women with breast cancer.

Qualitative Nature Experience

Navigating life with breast cancer is of course more than just a collection of lab values and subjective quality of life scores. It is a daily experience that is challenging, frustrating, difficult, nonsensical, heartbreaking, and so many other mixed emotions. To address each of these, spending time in the "therapeutic landscapes" of the natural world can be incredibly valuable and supportive during this process. Nature is a source of inspiration, a place of refuge, an opportunity for distraction, and so much more. Some of the descriptive research on these topics has explored the common themes of nature exposure for women with cancer,[30] and found the most common reported benefit was the ability of nature to provide women with a sense of personal connection to something of value. For some women this was the land and natural features themselves, while in others it was cherished memories of time spent with loved ones or internal reflections on forgotten parts of the self. Other common ways nature has supported women through the challenges of breast cancer are as a place of emotional safety and strength during treatment, or as a place of refuge and escape from mental and physical difficulties.[31,32] Additionally, there are many symbolic and aesthetic aspects of being in nature that provide insight and joy to many women, in

ways that transcend cultures.[33] Other more extensive work from a feminist or eco-feminist lens are beyond this author's expertise to comment on and are referenced here for the benefit of readers that would like to explore these valuable topics further.[34,35]

Public Health Evidence

All of the benefits of NBT mentioned above exist for anyone spending time in nature, whether they are participants in a scientific study or not. As evidence of this, there are some large-scale epidemiological investigations that show proximity to nature may be preventive or protective against breast cancer. In one study in Spain, women (n=2,748) were found to have a 35% lower (OR 0.65, 95%CI 0.49–0.86) risk of having breast cancer if they lived in areas of high vs. low residential green space, defined as a forest, park, public garden, etc…within 300 meters of their homes.[5] These findings were significant after adjusting for other potential factors such as socio-economic status, menopausal status, number of children, family history of breast cancer, population density, level of physical activity, and amount of air pollution. These results are similar to another large-scale study in Japan using the entire National Health System data set of ~126 million people, which revealed a highly significant inverse correlation between residential proximity to a forest and a woman's risk of having diagnosed breast cancer (r=-0.530, p<0.0001).[6] Clearly, there are many benefits of being close to nature.

Conclusion

People have a timeless connection with the natural world as a source of sanctuary and solace from physical and mental ills and stresses. The challenges presented by breast cancer are significant and frequently difficult to manage, especially in the modern world. This article has detailed how the scientific method provides supportive evidence of the benefit of nature-based experiences (called various names such as nature-based therapy, forest therapy, horticulture therapy, natural restorative experiences, and more) to make these challenges easier and provide healing to mind and body. Many more years and research studies will be needed to establish clinical "best practices" of NBT regarding type of exposure and "dose/frequency prescriptions" for various conditions and personal individualized preferences. Long-term investigations will be needed to evaluate whether regularly visiting a forest affects breast tumor size, or exactly how much improvement in subjective well-being can be anticipated from these visits. However, we know that these ancient experiences of connection with our natural surroundings are well-tolerated, low-cost, low-risk interventions that can be incorporated into holistic breast cancer treatment programs to benefit women's experiences and lives.

References

1. Mygind L, et al. Immersive nature-experiences as health promotion interventions for healthy, vulnerable, and sick populations? A systematic review and appraisal of controlled studies. *Front Psychol*. 2019;10(APR).
2. Antonelli M, Barbieri G, Donelli D. Effects of forest bathing (shinrin-yoku) on levels of cortisol as a stress biomarker: a systematic review and meta-analysis. *Int J Biometeorol*. April 2019:1-18.
3. Kondo MC, Jacoby SF, South EC. Does spending time outdoors reduce stress? A review of real-time stress response to outdoor environments. *Health Place*. 2018;51:136-150.
4. CDC. Breast Cancer Statistics. https://www.cdc.gov/cancer/breast/statistics/index.htm. Published 2019. Accessed December 14, 2019.
5. O'Callaghan-Gordo C, et al. Residential proximity to green spaces and breast cancer risk: The multicase-control study in Spain (MCC-Spain). *Int J Hyg Environ Health*. 2018;221(8):1097-1106.
6. Li Q, Kobayashi M, Kawada T. Relationships Between Percentage of Forest Coverage and Standardized Mortality Ratios (SMR) of Cancers in all Prefectures in Japan. *Open Public Health J*. 2008;1:1-7.
7. Hansen MM, Jones R, Tocchini K. Shinrin-yoku (Forest bathing) and nature therapy: A state-of-the-art review. *Int J Environ Res Public Health*. 2017;14(8).
8. Beil K. Forest Bathing: Immersion in the Healing Power of Nature. *Townsend Lett*. 2018;(July #420).
9. Song C, et al. Effects of Walking in a Forest on Young Women. *Int J Environ Res Public Health*. 2019;16(2).
10. Yu YM, et al. Effects of forest therapy camp on quality of life and stress in postmenopausal women. *Forest Sci Technol*. 2016;12(3):125-129.
11. Lanki T, et al. Acute effects of visits to urban green environments on cardiovascular physiology in women: A field experiment. *Environ Res*. 2017;159(June):176-185.
12. Lee JY, Lee DC. Cardiac and pulmonary benefits of forest walking versus city walking in elderly women: A randomised, controlled, open-label trial. *Eur J Integr Med*. 2014;6(1):5-11.
13. Miller JS, Lanier LL. Natural Killer Cells in Cancer Immunotherapy. *Annu Rev Cancer Biol*. 2019;3(1):77-103.
14. Backes CS, et al. Natural killer cells induce distinct modes of cancer cell death: Discrimination, quantification, and modulation of apoptosis, necrosis, and mixed forms. *J Biol Chem*. 2018;293(42):16348-16363.
15. Kim BJ, et al. Forest adjuvant anti-cancer therapy to enhance natural cytotoxicity in urban women with breast cancer: A preliminary prospective interventional study. *Eur J Integr Med*. 2015;7(5):474-478.
16. Nakau M, et al. Spiritual Care of Cancer Patients by Integrated Medicine in Urban Green Space: A Pilot Study. *EXPLORE*. 2013;9(2):87-90.
17. Hermelink K. Chemotherapy and Cognitive Function in Breast Cancer Patients: The So-Called Chemo Brain. *JNCI Monogr*. 2015;2015(51):67-69.
18. Olmsted FL. Nature , Health & Well-being Health & Environment. 1865.
19. Cimprich B, Ronis DL. An Environmental Intervention to Restore Attention in Women With Newly Diagnosed Breast Cancer. *Cancer Nurs*. 2003;26(4):284-292.
20. Kaplan S. The restorative benefits of nature: Toward an integrative framework. *J Environ Psychol*. 1995;15(3):169-182.
21. Holland JC. Psycho-oncology: Overview, obstacles and opportunities. *Psychooncology*. 2018;27(5):1364-1376.
22. Pérez S, et al. Acute stress trajectories 1 year after a breast cancer diagnosis. *Support Care Cancer*. 2016;24(4):1671-1678.
23. Kang D-H, Park N-J, McArdle T. Cancer-Specific Stress and Mood Disturbance: Implications for Symptom Perception, Quality of Life, and Immune Response in Women Shortly after Diagnosis of Breast Cancer. *ISRN Nurs*. 2012;2012:1-7.
24. Houlden V, et al. The relationship between greenspace and the mental wellbeing of adults: A systematic review. *PLoS One*. 2018;13(9).
25. McMahan EA, Estes D. The effect of contact with natural environments on positive and negative affect: A meta-analysis. *J Posit Psychol*. 2015;9760(December):1-13.
26. Ulrich RS. Natural versus urban scenes: Some psychophysiological effects. *Environ Behav*. 1981;13(5):523-556.
27. Wilson EO. *Biophilia*. Cambridge: Harvard University Press; 1984.
28. Twohig-bennett C, Jones A. The health benefits of the great outdoors: A systematic review and meta-analysis of greenspace exposure and health outcomes. *Environ Res*. 2018;166(June):628-637.
29. Von Lindern E, Lymeus F, Hartig T. The Restorative Environment: A Complementary Concept for Salutogenesis Studies. In: Mittelmark MB, Sagy S, Eriksson M, et al., eds. *The Handbook of Salutogenesis*. Springer; 2016:1-461.
30. Blaschke S. The role of nature in cancer patients' lives: A systematic review and qualitative meta-synthesis. *BMC Cancer*. 2017;17(1):1-13.
31. English J, Wilson K, Keller-Olaman S. Health, healing and recovery: therapeutic landscapes and the everyday lives of breast cancer survivors. *Soc Sci Med*. 2008;67(1):68-78.
32. Pascal J. Space, Place, and Psychosocial Well-Being: Women's Experience of Breast Cancer at an Environmental Retreat. *Illness, Cris Loss*. 2010;18(3):201-216.
33. Liamputtong P, Suwankhong D. Therapeutic landscapes and living with breast cancer: The lived experiences of Thai women. *Soc Sci Med*. 2015;128:263-271.
34. Szumacher E. The feminist approach in the decision-making process for treatment of women with breast cancer. *Ann Acad Med Singapore*. 2006;35(9):655-661.
35. Lynch L. Rapture and the Volcano: A Special Issue on Women and the Natural World. *Ecopsychology*. 2010;2(3):121-123.

Kurt Beil, ND, LAc, MPH is a naturopathic and Chinese medicine practitioner with practices in Sandy, Oregon, and New York's lower Hudson Valley region. He is a research investigator at NUNM's Helfgott Research Institute, where he focused on biomarker and psychometric assessment of the restorative and therapeutic effect of natural environments. Dr. Beil is also an editor of the *Natural Medicine Journal*, the official journal of the American Association of Naturopathic Physicians, and writes a regular column reviewing papers on the healing power of contact with nature. He holds a master's degree in public health focused on the benefits of green space as a sustainable public health promotion tool, and speaks, writes, and peer-reviews regularly about these topics. Dr. Beil also maintains a regular public blog and Facebook group ("Naturopaths for Nature") on these topics, and gets out to walk his talk in nature as often as possible. He can be reached at drkurt@earthlink.net or www.drkurtbeil.com.

Reproductive Milestones Are Under Assault

by Dr. Devaki Lindsey Berkson

Mother Nature hard-wired humanity with specific milestones of reproduction. This means that for millennia the entire human race has had very specific times during specific years when women can start making babies or stop making babies.

Hormones flourish and initiate or diminish and halt. This has been the hormonal dance throughout the ages. Reproductive milestones are humanity's rhythms that have far reaching effects on entire life spans. Yet the timing of these milestones is under attack by our dirty planet and food.

"Time shifting" of reproductive milestones is threatening the health and survival of the human race. Modern humans have been around for about 180,000 to 200,000 years. Some scientists worry that *homo sapiens* may only have another several 100 years left, if timing of reproductive markers and overall human health continues to diminish.[1]

Let's get the timing terms straight.

Puberty is the age at which a girl is first capable of sexual reproduction and having a baby. Puberty has classically been regarded as a time of raging hormones and sexual maturation. But puberty is much more. Puberty's "timing" and "quality" affect health and well-being across the entire female adult lifespan.[2] During puberty, hormones nudge brain development that drives sociological and psychological behaviors that have lifelong influence.

Menarche marks the onset of fertility. It is the first time a girl gets her period.

Age of onset of both puberty and menarche have started to decline. Girls are sexually maturating and menstruating at younger and younger ages. Menarche had historically occurred between 15 to 17 years of age up into the mid-19th century.[3] Then, in the 1950s, girls started to menstruate earlier. This overlaps with the time Mother Earth started to become more polluted.

At the end of WWII, in 1945, about 80,000 chemicals began to be dumped into earth's environment. This was a few years before the menarche and puberty ages began to decline. Menarche and puberty started to occur at an average age of 12 years and remained stable at this younger age…for a while.

Newer studies are now demonstrating that both puberty and menarche ages are continuing to decline and get younger once again.[4] Younger girls are starting to show signs of sexual maturation or begin menstruation starting at 8 or 10 years of age. In Puerto Rico, reproductive toxicologists have consistently been reporting six-month-old infants showing sexual maturation signs of breast buds (the beginning of breast tissue sexual growth).[5] Analyzed food specimens from typical meals in Puerto Rico revealed significant levels of estradiol equivalents in some meat samples due to synthetic estrogens added to the feed lots of the animals to enhance growth and taste. The early sexual development is suspected to be due to exogenous estrogen contamination in the food ingested by the children and by their mothers.[5]

Many scientific studies have revealed a trend towards an earlier onset of puberty and have disclosed an increasing number of children that display precocious puberty. As an explanation, some authors have considered the action of endocrine-disrupting chemicals. Just one example of these many possible hormone-altering-chemicals is bisphenol A (BPA), an aromatic compound largely used worldwide as a precursor of some plastics and chemical additives. BPA is well known for its molecular estrogen-like and obesogenic actions.[6]

You can't fool Mother Nature and get away with it.

This disturbing trend[7] of young girls sexually developing precociously comes with a host of increased potential health problems. Girls who menstruate early and develop sexual characteristics early (like breasts buds or pubic hair) are more at risk, as they age, of obesity, heart disease, polycystic ovarian syndrome, and even breast cancer. They are possibly at risk of mood disorders and behavioral issues, like anxiety, depression, and substance abuse, but all these connect-the-dots are just starting to be researched.

Perimenopause age is changing, too. Perimenopause is the time when hormones start to yo-yo as cessation of reproduction looms. It's historically occurred up to 10 years before a woman goes into menopause. Menopause is when a woman has not had a period for a solid year demonstrating that her body is no longer capable of getting pregnant.

Gynecologists are reporting that some women are going into peri-menopause younger, even in their mid- to late-20s, decades earlier than females have historically done.[8] Earlier perimenopause also increases a woman's set of issues. The earlier a woman's hormones start to yo/yo and go south, the more her risk of anxiety, depression, fatigue and brain fog, as well as increasing vulnerability to diverse diseases such as heart disease,[9] obesity, type 2 diabetes, and even Alzheimer's disease.[10]

The typical *menopause* age is not immune from change. In the US the age of menopause has classically been 51.4 years old. But there is now a documented trend of some women, not all of course, going through menopause earlier,[11,12]

Menopause is partly hard-wired to occur when the number of eggs in the ovaries goes below a certain threshold. Endocrine-disrupting chemicals (whether from exposures while in the womb or as an adult) wind up affecting hormones in the reproductive system and set up genes to prompt the number of eggs to diminish *prematurely*. In this way, women go into menopause earlier.

Cosmetics have been linked to decreased egg counts and higher FSH levels (a hormone that rises in menopause).[13] Many household products that contain perfluorocarbons (PFCs) – found in stain resistant sprays for carpets and furniture, food packaging, and non-stick cookware – have been linked to earlier menopause.[14] These chemicals have also been linked to making fat cells nasty and almost impossible to shed, thus many of these chemicals have been dubbed by Dr. Bruce Blumberg as obesogens.

Abnormal timing of puberty, menarche, perimenopause, or menopause is associated with a huge host of problems: reduced span of fertility; increased risk of age-related diseases, including breast, endometrial, and ovarian cancer; heart disease; and bone loss (osteoporosis).[15,16] Infertility is on the rise in both men[17] and women,[18] possibly as a result of these hormonal changes. And cognitive decline, too.[10]

Men are not immune to hormonal change. Young men are supposed to be flush with testosterone (T). But replicated reports are demonstrating a disturbing trend of lowered T levels in younger males, similar to what used to occur mostly in the aging male.[19]

The times, milestones of reproduction times, they are a-changing.

What does this mean for your children and for the human race? That is a serious question I have been writing and lecturing about for several decades now. Scientific studies are informing us that hormone levels and functionality of hormones (being able to send the health-supporting signals they are meant to send) are altering and faltering in all of us, from the fetus in the womb to grandparents.

I was a hormone scholar at the Center for Bioenvironmental Research (CBR) at Tulane University, a think tank that put on environmental estrogen conferences for over 30 years. The last several were called e.hormone symposia. At these conferences the heads of environmental science departments at universities and scientists converged to share their concerns about what the environment is doing to our hormones. Especially concerning was the science showing that young girls were going into puberty earlier.

Changing milestones of reproduction is no small thing. It is a "flashing red light" on the dashboard of humanity.

Remember the reports from reproductive toxicologists from Puerto Rico.[20] They report "breast buds" (hormonal maturation of some kind) happening in infants. This is usually a rare condition called premature thelarche (thelarche is the onset of breast development). But not so rare in Puerto Rico.

And it is starting to happen around the world. Cases of six-year-old girls starting to menstruate are being published in the literature.[21] Often these girls are found to have thyroid issues, but the thyroid is the gland most affected by our toxic environment.[22] Barbara Demeneix, PhD, was on *The Dr. Berkson's Best Health Radio Show* and discussed how the thyroid is the gland most vulnerable to our toxic environment and hormone-altering chemicals. When the thyroid is adversely affected, so are the other sex steroid hormones, and mistiming of hormone milestones can occur.

Discussions at the CBR were animated about the lowering age of onset of puberty. Futzing with the timing of Mother Nature has serious negative consequences. Scientists at these conferences got very concerned for the future of humanity, and high emotions reigned as we explored the possible causes, and what to do about them.

Abnormal timing of puberty, menarche, perimenopause, or menopause is associated with a huge host of problems.

What's Going On?

Obesity has something to do with it.[23] Wealthy countries are in the middle of a childhood obesity epidemic. Fat cells manufacture estrogen. More estrogen, more hormonal changes. So that's part of it. Overweight children are at risk of entering puberty at earlier ages.[24]

Stress has some input. Research suggests high levels of psycho-social stress; more demands in school curriculum, after-school activities, and even issues like bullying might influence the onset of puberty.[25,26]

But the biggest finger is pointing at our dirty planet and food, which are flush with endocrine-disrupting chemicals. And it gets a huge start right inside the mother and what is passed on to the unborn child in her womb.

Research at the University of California demonstrated that mothers with high levels of chemcials in their bodies during pregnancy had daughters who began puberty earlier than peers who did not have such high exposures.[27] Many of these chemicals are found in personal care and household products (diethyl phthalate, triclosan, phenols,

➤

➤

and parabens). These *endocrine-disrupting chemicals* are called that because they alter the soldiers of our endocrine system, our hormones. They are also referred to as *hormone-altering* chemicals because they can make our hormones malfunction.

Hormone-disrupting chemicals are ubiquitous. They are found in the home, in food, on the road when you are driving, and in office and school buildings where your kids sit all day long. They are outgassing from modern building materials in walls, paints, and carpets. They are in the bathroom in a broad range of personal care products, such as cosmetics, toothpaste, soaps, shampoos; in the kitchen in non-stick cookware; in flame retardants on clothing and mattresses; and also in the fish that get exposed to these chemicals in ocean waters. They come from food in shrink-wrapped plastic or in cans lined with plastic or in food stored in plastic that's been washed in a dishwasher with harsh detergents.

Today's chemical soup – that mixture of household product chemicals, pesticides, herbicides, heavy metals, and many more – mimic, amplify, block, and alter our own natural hormones.[28]

Pesticides fed to some poultry have been linked to elevating testosterone and blocking progesterone in young female teens and contributing to polycystic ovarian syndrome (PCOS).[29] Placentas are rife with chemicals that send messages to the fetus, including those that can set up their genes to alter their health as the child grows up.[30,31] In other words, placental contamination with endocrine disruptors, such as bisphenol A and phthalates, are altering DNA methylation and causing adverse epigenetic alterations.[32]

All of us are vulnerable.

As we learn more and more that hormones are our body's "physiologic internet system," which sends emails to most of our cells to keep us well, we learn that the plethora of hormone-altering chemicals is potentially damaging our software as well as our hardware.

These chemicals can affect us at any age. But there are "windows of vulnerability" at which they have more potent consequences. This is especially true in the womb.

Hormone-Altering Chemicals in Pregnancy

Kim Harley, PhD, from the University of California at Berkeley, published the first study looking at how prenatal exposure to hormone-altering chemicals influences timing of puberty. Her team followed 179 girls and 159 boys in California who were born to mothers who were pregnant between 1999 and 2000.

The *prenatal period* is the duration of exposure in the womb – the entire time the fetus is developing. The prenatal period is an especially sensitive and critical window of *susceptibility*.

Participants in Dr. Harley's study were enrolled from the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS),[33] a predominantly Latino population. The mothers were interviewed twice during pregnancy and again when their children were nine years old. The levels of the mothers' chemical exposure were measured in urine samples during pregnancy and in the children at age nine.

The children were assessed every nine months between ages nine and 13 years.

By nine years of age, 55% of the children were overweight or obese, and 69% were living below the federal poverty level.

Chemicals exposure was assessed from daily life: perfumes, deodorants, shampoos, cosmetics, and other scented products containing phthalates. Parabens were also tracked, as these are often added to cosmetic and self-care products as a preservative. Phenols in toothpaste, soap, lipstick, and skin lotions were monitored.

Higher chemical exposure meant earlier menstruation. The bottom line was the more chemicals in the mom's body during pregnancy, the more significantly the daughters experienced earlier puberty. Remember, earlier puberty puts a young girl at higher risk of a lot of health problems.

Daughters of women with the highest levels of these chemicals in their urine started their periods an average of four months earlier. You might think that this sounds insignificant. But these four months make a huge difference when you are tweaking Mother Nature. This study showed no evidence of earlier development for boys.

- Higher prenatal mono-ethyl phthalate concentrations were associated with earlier development of pubic hair.
- Higher levels of prenatal triclosan, propyl paraben, and 2,4-dichlorophenol were linked to earlier onset of menarche in the children.
- Methyl paraben and 2,5-dichlorophenol were associated with earlier breast and pubic hair development.

Most of the chemicals tested in "personal care products" promote estrogenic activity, which affects sexual development like the hormone estrogen.[34] I wrote about this association between chemicals and early puberty and altered milestones of reproduction in *Hormone Deception,*[8] one of the first exposé books on hormone-altering chemicals. I also write in-depth in this book about the issue of hormone-altering chemicals in breast milk, baby's first natural beverage. But we won't address that in this article.

Today, a growing number of studies are linking endocrine-disruptor exposure to early onset of puberty.[35-37]

To clarify one more time, girls that go through puberty earlier tend to have more health problems throughout the rest of their lives.

The levels of chemicals found in the bodies of women and children in this study are *typical* of exposure of many US citizens. In the United States, well over 90% of women have been shown to have detectable concentrations of phthalates, phenols, and paraben metabolites in their urine.[38-40] Keep in mind that these are just a few of the thousands of hormone-altering

chemicals that exist in the chemical soup of our daily lives.

How to Reduce Risk

Eating organic food and reducing chemical exposure can greatly reduce your body burden of hormone-altering chemicals. Detox has to move mainstream and help get this stuff out of us, so consider Receptor Detox™.

Consider getting the PowerPoint on "How and Why to Have Green Pregnancies." It's professionally done, and you can share this with your family or patients.

Effective steps include the following:

1. Eat organic, especially fatty foods (meat, dairy, oils, nuts), as hormone-altering chemicals love to store in fat.
2. Don't store foods in plastic.
3. Don't wash plastic in the dishwasher and then reuse to hold food or beverages, even water.
4. Do not microwave food or beverages in plastic.
5. *Hormone Deception* takes you through step-by-step tours of your home, supermarket cart, and office.
6. Avoid the "dirty dozen" foods identified by the Environmental Working Group (EWG).
7. Use the EWG app. The EWG has created a Skin Deep® Cosmetics Database that allows consumers to search for personal care products and determine the hazard level of each product. One study found that only 23.4% of 128 women surveyed had received advice about personal care product use, and only 18.9% of them had received advice about make-up product use, that it might be unhealthy or related to hormonal issues.[41]
8. Use water filters for your shower.
9. Take shoes off at the front door. Wipe your feet outside several times and then inside the house several times as this has been found to most effectively remove most of the potentially dangerous chemicals off the bottom of your shoes.
10. Wipe pet paws, too.
11. Limit exposures to tea tree and lavender oils during pregnancy and infancy. Even though they are natural substances, there are reports that associate exposure to them with early breast development.[42]
12. Use phthalates or paraben-free personal care products. Most perfumes contain phthalates, so try different essential oils, like vanilla.
13. Do daily and more in-depth detoxes on a regular basis as we keep getting exposed, so you want to keep cellular house cleaning going.
14. Detox must move mainstream. And it is. There are many forms.

Take a look at this report on Ground Zero-exposed individuals. In 2005, the Olive Leaf Wholeness Center conducted a demonstration project that provided ➤

➤

health assessment, testing, and treatment to 160 uniformed service personnel and residents of Lower Manhattan who were exposed to the air at Ground Zero following September 11, 2001, for extended periods of time. The program, known as Project Olive ReLeaf, found that most individuals had eight or more serious health complaints, including severe respiratory problems, digestive problems, skin rashes, sleeplessness, anxiety, depression, weight gains, elevated blood pressure, lethargy, and recurrent headaches. Heavy metal toxicity was suspected as a causal factor for many of these symptoms.

Of those tested for heavy metal toxicity, using a challenge urine test, 85% had excessively high levels of lead and mercury. Chelation treatment using dimercaptuosuccinic acid (DMSA), a Food and Drug Administration (FDA)-approved sulfur compound, was the primary treatment prescribed. After three to four months of treatment, the first cohort of 100 individuals reported significant (greater than 60%) improvement in all symptoms. (This demonstration program was developed based on the results of an earlier pilot in 2003 for 25 emergency service officers of the New York City Police Department.) In addition, adjunctive therapies to assist with the detoxification process and build the immune system were offered. A small grant has been received to conduct follow-up tests on a sample of those treated with DMSA.[43]

References

1. Blumberg B. *The Obesogen Effect. Why We Eat Less and Exercise More but Still Struggle to Lose Weight.* Grand Central; March 2018.
2. Worthman CM, Dockray S, Marceau K. Puberty and the Evolution of Developmental Science. *Journal of Research on Adolescence*. 2019; 29 (1): 9.
3. Kaplowitz P. Pubertal development in girls: secular trends. *Curr Opin Obstet Gynecol.* 2006;18(5),487-491.
4. Adams Hilliard PJ. Menstruation in adolescents: what's normal, what's not. *Ann NY Acad Sci.* 2008;1135,29-35.
5. Sáenz de Rodríguez CA, Bongiovanni AM, Conde de Borrego L. An epidemic of precocious development in Puerto Rican children. *J Pediatr*. 1985 Sep;107(3):393-6.
6. Leonardi A, et al. The Effect of Bisphenol A on Puberty: A Critical Review of the Medical Literature. *Int J Environ Res Public Health.* 2017 Sep 10;14(9). pii: E1044.
7. Fisher MM, Eugster EA. What is in our environment that effects puberty? *Reprod Toxicol*. 2013;44:7-14.
8. Berkson DL. *Hormone Deception*. McGraw Hill, 2000; Awakened Medicine Press, 2016.
9. Savonitto S, Ferri LA, Colombo D. Perimenopause vasomotor symptoms, coronary atherosclerosis and risk of myocardial infarction during menopause: the cardiologist's perspective. *Prz Menopauzalny.* 2018 Jun;17(2):53-56.
10. Mosconi L, et al. Perimenopause and emergence of an Alzheimer's bioenergetic phenotype in brain and periphery. *PLoS One.* 2017 Oct 10;12(10):e0185926.
11. Brown S. Endocrine disrupting chemicals associated with earlier menopause. *Post Reprod Health.* 2015 Mar;21(1):5-6.
12. Chow ET, Mahalingaiah S. Cosmetics use and age at menopause: is there a connection? *Fertil Steril.* 2016 Sep 15;106(4):978-90.
13. Smith KW, et al. Urinary paraben concentrations and ovarian aging among women from a fertility center. *Environ Health Perspect*. 2013 Nov-Dec;121(11–12):1299–305.
14. Knox SS, et al. Implications of early menopause in women exposed to perfluorocarbons. *J Clin Endocrinol Metab.* 2011 Jun;96(6):1747-53.
15. Shi J, et al. Age at menarche and age at natural menopause in East Asian women: a genome-wide association study. *Age* (Dordr). 2016 Dec;38(5-6):513-523.
16. Sullivan SD, et al. Age of menopause and fracture risk in postmenopausal women randomized to calcium + vitamin D, hormone therapy, or the combination: results from the Women's Health Initiative Clinical Trials. *Menopause.* 2017 Apr;24(4):371-378.
17. Mauduit C, Siddeek B, Benahmed M. [Developmental and environmental origin of male infertility: role of endocrine disruptors]. *Med Sci* (Paris). 2016 Jan;32(1):45-50.
18. Rattan S, et al. Exposure to endocrine disruptors during adulthood: consequences for female fertility. *J Endocrinol.* 2017 Jun;233(3):R109-R129.
19. Travison TG, et al. A population-level decline in serum testosterone levels in American men. *J Clin Endocrinol Metab.* 2007 Jan;92(1):196-202. Epub 2006 Oct 24.
20. Larriuz-Serrano MC, et al. Natural history and incidence of premature thelarche in Puerto Rican girls aged 6 months to 8 years diagnosed between 1990 and 1995. *P R Health Sci J.* 2001 Mar;20(1):13-8.
21. Banu J, Sultana P, Chowdhury MA. Precocious puberty presenting with menarche at the age of 6 years - a case report. *Mymensingh Med J.* 2014 Jul;23(3):578-80.
22. Demeneix B. *Toxic Cocktail: How Chemical Pollution is Poisoning Our Brains.* Oxford University Press, 2017.
23. Lian Q, et al. Puberty timing associated with obesity and central obesity in Chinese Han girls. *BMC Pediatr.* 2019 Jan 3;19(1):1.
24. Jasik CB, Lustig RH. Adolescent obesity and puberty: the "perfect storm." *Ann N Y Acad Sci*. 2008;1135:265-279.
25. Kelly Y, et al. Early puberty in 11-year-old girls: Millennium Cohort Study findings. *Arch Dis Child*. 2017;102:232-237.
26. Smith SS. The influence of stress at puberty on mood and learning: role of the α4βδ GABAA receptor. *Neuroscience*. 2013;249:192-213.
27. Harley KG, et al. Association of phthalates, parabens and phenols found in personal care products with pubertal timing in girls and boys. *Hum Reprod*. 2019;34:109-117.
28. Diamanti-Kandarakis E, et al. Endocrine-disrupting chemicals: an Endocrine Society scientific statement. *Endocr Rev*. 2009;30:293-342.
29. Ahmad S, et al. Daily consumption of commercial chicken feed and meat lead to alterations in serum cholesterol and steroidal sex hormones in femalerats. *Pak J Pharm Sci.* 2017 Jan;30(1 Suppl):257-261.
30. Caserta D, et al. Maternal exposure to endocrine disruptors and placental transmission: a pilot study. *Gynecol Endocrinol*. 2018 Nov;34(11):1001-1004.
31. Strakovsky RS, Schantz SL. Using Experimental Models to Assess Effects of Bisphenol A (BPA) and Phthalates on the Placenta: Challenges and Perspectives. *Toxicol Sci.* 2018 Dec 1;166(2):250-268.
32. Strakovsky RS, Schantz SL. Impacts of bisphenol A (BPA) and phthalate exposures on epigenetic outcomes in the human placenta. *Environ Epigenet*. 2018 Sep 7;4(3):dvy022.
33. Eskenazi B, et al. CHAMACOS, a longitudinal birth cohort study: lessons from the fields. *J Children's Health*. 2003;1:3-27.
34. Welschons WV, et al. Large effects from small exposures. I. Mechanisms for endocrine-disrupting chemicals with estrogenic activity. *Environ Health Perspect*. 2003;111:994-1006.
35. Ozen S, Darcan S. Effects of environmental endocrine disruptors on pubertal development. *J Clin Res Pediatr Endocrinol*. 2011;3:1-6.
36. Leonardi A, et al. The effect of bisphenol A on puberty: a critical review of the medical literature. *Int J Environ Res Public Health*. 2017;14:1044.
37. Buttke DE, Sircar K, Martin C. Exposures to endocrine-disrupting chemicals and age of menarche in adolescent girls in NHANES (2003-2008). *Environ Health Perspect*. 2012;120:1613-1618.
38. Calafat AM, et al. Concentrations of the sunscreen agent benzophenone-3 in residents of the United States: National Health and Nutrition Examination Survey 2003-2004. *Environ Health Perspect*. 2008;116:893-897.
39. Calafat AM, et al. Urinary concentrations of four parabens in the U.S. population: NHANES 2005-2006. Environ Health Perspect 2010;118:679-685.
40. Zota AR, Calafat AM, Woodruff TJ. Temporal trends in phthalate exposures: findings from the National Health and Nutrition Examination Survey, 2001-2010. *Environ Health Perspect*. 2014;122:235-241.
41. Marie C, et al. Changes in Cosmetics Use during Pregnancy and Risk Perception by Women. *Int J Environ Res Public Health*. 2016; 13(4)
42. Henley DV, Korach KS. Physiological effects and mechanisms of action of endocrine disrupting chemicals that alter estrogen signaling. *Hormones* (Athens). 2010;9:191-205.
43. Kokayi K, et al. Findings of and treatment for high levels of mercury and lead toxicity in ground zero rescue and recovery workers and lower Manhattan residents. *Explore* (NY). 2006 Sep-Oct;2(5):400-7.

◆

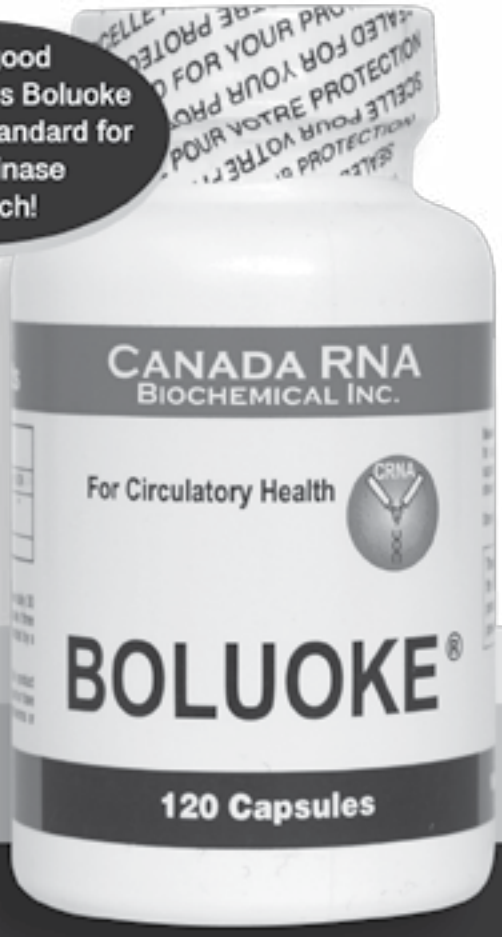
D. Lindsey Berkson, DC, has been a leader in functional medicine, with an emphasis on the gut, hormones, and the environment for several decades. Dr. Berkson has been teaching certification relicensing courses for MDs, pharmacists, NPs, NDs and chiropractors for decades—in the last few years focusing on the gastroenterology module for A4M and hormones and oxytocin for PCCA.

Dr. Berkson formulated Metagenic's first female nutrient line for physicians. Dr. Berkson was a scholar at an estrogen think tank at Tulane University where she worked with the top scientists that discovered "receptor physiology" and growing epidemic of competitive inhibitors found in endocrine disruptors.

Dr. Berkson has authored 21 books; several have been best sellers. She also hosts the Dr. Berkson's Best Health Radio, writes the Berkson Blog (@ DrLindseyBerkson.com), and is a research fellow with Health Sciences Collegium.

HYPERCOAGULATION

It's so good that FDA uses Boluoke as the gold standard for lumbrokinase research!



A central issue in:

- conditions with a poor circulation
- growth and spread of malignant cells
- chronic infections with biofilm
- poor tissue healing due to hypoxia

Boluoke (lumbrokinase), simply the best in:

- Enzymatic strength
- Research data
- Quality, safety, and efficacy

Your Patients. Your Reputation.

TRUST NOTHING LESS!

Boluoke is also available through

Researched Nutritionals
solutions for life

BIORESOURCE

antiaging-systems.com

return 2 health

MP
Mountain States Health Products, Inc.

Pro Health Network

NaturoDoc

Dragon's Medical Bulletin
www.dragonsmedicalbulletin.com
Your Quick Stop for Integrated Clinical Research Updates

CRNA

1-866-287-4986

www.canadaRNA.com

Bile Acids: Beyond Fat Digestion

by Carrie Decker, ND

Although our discovery of the distinct constituents of bile goes back to the mid-19th century,[1] record of their first use therapeutically dates far earlier than this. Bile from many different animals and even human sources at times of battle have a record in traditional Chinese medicine (TCM) beginning in the Zhou dynasty from 1046-256 BCE.[2] In TCM, bile acids have an array of uses, including the treatment of gallstones (still a common use for bile acids, in particular ursodeoxycholic acid[3,4]), infectious skin diseases or burns, vision and eye conditions, respiratory infections, and even coma and epilepsy. Ox bile was one of the first forms of bile to be used in TCM and contains many of the same bile acids found in human bile.[2]

In addition to their well-known role in the digestion of dietary fats, bile acids influence the balance of flora in the gut,[5] gastrointestinal motility,[6] immune system function,[7] and bind with numerous receptors distributed throughout the human body.[8] Lower levels of bile acids in the gut are associated with an overgrowth of *Clostridium difficile* and *Helicobacter pylori,*[9,10] constipation,[11] and increased bacterial translocation.[12] Given their origination in the liver, it may not come as a surprise that bile acids also have a significant impact on metabolism[13] and liver/gallbladder health,[14] reviewed herein.

Bile Acid Metabolism and Receptor Interactions

The human bile salt pool is primarily comprised of cholic acid (CA), chenodeoxycholic acid (CDCA), and deoxycholic acids (DCA), with smaller amounts of lithocholic acid (LCA) and ursodeoxycholic acid (UDCA).[15,16] The primary bile acids CA and CDCA are produced in the hepatocyte from cholesterol by the classic or alternative pathways involving multiple cytochrome P450 (CYP450) enzymes.[17] They are then conjugated with glycine or taurine (increasing their water solubility) prior to being excreted from the hepatocyte across the canalicular membrane via transporters also associated with Phase III detoxification: bile salt export protein (BSEP) and multidrug resistance-associated protein-2 (MRP2).[18]

In the digestive tract, enzymes produced by certain microbes in the gut deconjugate and dehydroxylate these bile acids, forming the secondary bile acids DCA (from CA) and LCA (from CDCA).[19] Deconjugated bile acids are more hydrophobic and have greater detergent action, which increases their ability to facilitate solubilization and absorption of dietary lipids, fat soluble vitamins, and break down bacterial membranes.[20,21] DCA is a particularly strong antimicrobial agent, having 10 times the antimicrobial activity of CA, its precursor.[22]

Bile acids have a multitude of effects throughout the body due to their interactions with the nuclear receptors farnesoid X receptor (FXR),[23] pregnane X receptor (PXR),[24] and the vitamin D receptor, as well as multiple G-protein coupled receptors (GPCRs), which are found on the cell membrane.[7] In the hepatocyte, the majority of the actions of bile acids are mediated by FXR, which also plays a role in the synthesis, transport, and enterohepatic circulation of the bile acids themselves. Interactions of bile acids with FXR in the hepatocyte serves a self-regulatory role, protecting the cell from damage that can take place when an excessive amount of bile exists (such as occurs with cholestasis) by increasing transcription of efflux transporters[25] and reducing bile acid synthesis,[26] which both help lower the intracellular bile acid concentration.

In addition to protecting hepatocytes in the setting of cholestasis,[27] activation of FXR by bile acids induces genes involved in the different phases of detoxification,[28] protecting the cells of the liver from drug and xenobiotic toxicity.[29,30] This is one reason why supplemental bile acids are a life-saving intervention for individuals with bile acid synthesis disorders,[31] as they help protect the liver by increasing bile acid-dependent bile flow and toxin transport out of the hepatocyte. For individuals with bile acid synthesis disorders, CA is the primary bile acid used as a therapy.[32]

FXR is known to be expressed in the liver, pancreas, ileum, kidney, and adrenal glands, and at lower levels in the heart, central nervous system, adipose tissue, and arterial walls.[15] The ability of the different bile acids to activate FXR varies, with CDCA being the strongest activator and CA the weakest. Animal and in vitro studies suggest that activation of FXR by bile acids decreases plasma triglycerides, cholesterol, and hepatic steatosis; reduces gluconeogenesis; and increases insulin sensitivity, glucose transporter type 4 (GLUT4) transcription, and

glycogen synthesis.[33-37] Stimulation of the ileal enterocytes with bile acids also activates FXR and increases secretion of fibroblast growth factor 19 (FGF19), which has insulin-sensitizing and hypolipidemic effects.[38]

Interactions of bile acids with TGR5, a cellular membrane GPCR, is another major route via which their metabolic actions are exerted. TGR5 is *not* expressed in the hepatocyte but is expressed in brown adipose tissue, pancreatic beta cells, intestinal neuroendocrine cells, the biliary tract, as well as Kupffer cells and liver endothelial cells.[39] Interactions of bile acids with TGR5 increases cyclic-AMP synthesis, which impacts energy production and increases insulin secretion by pancreatic beta cells;[40] and increases production of glucagon-like peptide-1 (GLP-1) and peptide YY (PYY),[41] which play important roles in appetite and blood sugar regulation.

Metabolic Disease

The effect of bile acids on blood sugar, cholesterol, appetite, and even weight via their interactions with FXR and TGR5 have been demonstrated in numerous animal and human studies.

In animals, enhanced expression of the primary CYP450 enzyme regulating bile acid synthesis enlarged the bile acid pool and led to increased hepatic cholesterol catabolism and decreased expression of several genes involved in lipogenesis and glucogenesis.[42] Despite being subject to high-fat diet (HFD) feeding, these mice were resistant to HFD-induced obesity, fatty liver changes, and insulin resistance, and had increased whole body energy expenditure.

Supplementation of CA along with HFD feeding was shown to prevent the increases in weight and adipose mass seen in mice fed a HFD alone, also preventing brown adipose tissue (BAT) whitening (which has negative metabolic effects).[43] In mice initially fed a HFD for 120 days, the addition of CA to the diet also returned their body weight to that of the typical chow-fed mice within 30 days. Similar effects of weight normalization, in addition to improved glucose tolerance, were also seen in mice fed CDCA along with HFD feeding.[44] In both of these studies, it was shown that these effects were at least in part due to increased expression of cyclic-AMP-dependent type 2 iodothyronine deiodinase (D2) in the BAT. D2 converts thyroxine (T4) to triiodothyronine (T3) within the cells of the BAT,[45] mediated by TGR5. In the investigation using CA as an intervention,[44] it was noted that serum levels of T3 and T4 in the mice did not change. Both CA and CDCA have also been shown to induce mitochondrial uncoupling protein 1 (UCP1),[46,47] which is known to regulate BAT-mediated thermogenesis.

Several studies suggest that the weight loss and improved glycemic control seen with bariatric surgery, or other weight-loss procedures such as gallbladder bile diversion to the ileum, may be due to altered bile acid availability.[48,49] In patients post-gastric bypass, total bile acid levels, as well as the bile acid subfractions, were significantly higher than overweight controls.[50,51] Total bile acid levels and their subfractions were inversely correlated with 2-hour post-prandial glucose and triglyceride levels as well as thyroid stimulating hormone, and positively correlated with adiponectin and GLP-1 levels.[51]

Multiple studies have also shown altered bile acid homeostasis in individuals with type 2 diabetes (T2D).[52,53] Serum fasting levels of CDCA and FGF19 (a marker commonly used to assess for FXR activation) have been shown to be independently related and significantly lower in individuals with impaired glucose tolerance and T2D.[54,55] Interestingly, serum levels of FGF19 have also been observed to be lower in patients with overt and subclinical hypothyroidism,[56] which may contribute to metabolic changes seen in this setting as well.

As a therapy, there are currently only a few human studies investigating the impact of bile acids on metabolic health and weight. In one study of healthy females, short-term oral supplementation with CDCA at a dose of 15 mg/kg/day was shown to be bioavailable and significantly increase BAT activity as well as whole body energy expenditure without any deleterious effects such as diarrhea.[57] In obese individuals with T2D, rectal administration of taurocholic acid dose-dependently increased secretion of GLP-1, PYY, and insulin, simultaneously decreasing plasma glucose,[58] while in healthy volunteers, in addition to stimulating GLP-1 and PYY, it dose-dependently increased the sensation of fullness.[59] Tauroursodeoxycholic acid (UDCA conjugated with taurine), taken orally at a dose of 1,750 mg/day, was shown to significantly improve hepatic and muscle insulin sensitivity compared to placebo in obese individuals after four weeks of supplementation.[60]

Bile acids have a multitude of metabolic effects on blood sugar, cholesterol, and weight.

One additional item worthy of note in a discussion of bile acids and metabolic disease is the use of probiotic bacteria to modify the balance of bile acids. Known as bile salt hydrolase (BSH)-active bacteria, these bacteria produce the enzyme BSH that deconjugates bile acids, reducing the absorption of cholesterol and increasing FXR activation, as the deconjugated bile acids are strong activators of FXR.[61] Human studies using the BSH-active probiotic strain *Lactobacillus reuteri* NCIMB 30242 have shown that, indeed, such a probiotic is capable of improving not only the balance and levels of cholesterol,[62,63] but also improves symptoms of irritable bowel syndrome,[64] which may be somewhat attributable to the antimicrobial effects of the secondary bile acids in addition to other well-known properties of *Lactobacillus* spp. bacteria.

Fatty Liver Disease

Given that the main uses of bile acids in modern medicine are for the

➤

➤

dissolution of cholesterol gallstones and as a treatment for cholestatic disease,[65-67] it should not come as a surprise that bile acids have other potential applications in the setting of liver and gallbladder disease. Although UDCA is the primary bile acid indicated for uncomplicated cholelithiasis, at one time, CDCA, found in both human and ox bile, was also a common intervention.[68] CDCA was abandoned as a primary intervention with UDCA taking its place due to the reduced occurrence of side effects, such as diarrhea, and lower dose required for resolution of gallstones.[69]

Although the condition of non-alcoholic fatty liver disease (NAFLD), frequently seen in conjunction with obesity and T2D, is primarily attributed to increased triglyceride accumulation in the cells of the liver, it also is associated with dysbiosis, intestinal inflammation, and increased gut permeability.[70,71] In addition to the antimicrobial, insulin-sensitizing, and triglyceride-reducing effects that bile acids have,[72,73] activation of FXR by bile acids also supports intestinal barrier integrity and reduces bacterial translocation, positioning bile acids as a very promising agent for the treatment of this condition, which to date has no recommended pharmaceutical intervention. Activation of FXR by bile acids may reduce hepatic inflammation and injury associated with alcoholic liver disease as well,[74,75] mediated by many of the same mechanisms. Both FXR and TRG5 play a role in protecting the liver from fibrosis,[76] the end stage of both NAFLD and alcoholic liver disease.

In animals fed a HFD, increased bile acid synthesis prevented fatty liver changes, suggesting similar effects also may be seen in humans.[42] Obeticholic acid (OCA) is a synthetic variant of CDCA, produced by the addition of an ethyl group, which increases its binding affinity for FXR approximately 100-fold.[77] It also is a TRG5 activator, much like CDCA.[78] Cellular studies comparing CDCA to OCA have shown that they have similar effects of increasing the transport of bile acids out of the hepatocyte (protecting it in cholestasis)[79] and reducing the production of proinflammatory mediators such as tumor necrosis factor alpha.[80] OCA has been shown in clinical studies to be beneficial at very low doses (typically 5 to 25 mg) for liver disease including non-alcoholic steatohepatitis, the more severe form of NAFLD,[81] also possibly supporting weight loss in this population as well.[82] Occasionally, the side effect of pruritis may occur with this and other FXR agonists. Given their similar mechanism of action, natural forms of the bile acids also may be of benefit in NAFLD.

Clearly, although bile acids have a long history of use medicinally, we are only starting to understand their broad therapeutic application. Unfortunately, we will likely only see such research with regards to their more potent, synthetic derivatives – which neglects the importance that a blend of bile acids, similar in composition to what is naturally produced by our body, may offer as a natural therapy. Often, lower doses of such substances gently stimulate the body rather than pushing a single pathway very strongly, leading to great potential for their systemic healing action.

Dr. Carrie Decker graduated with honors from the National College of Natural Medicine (now the National University of Natural Medicine) in Portland, Oregon. Prior to becoming a naturopathic physician, Dr. Decker was an engineer and obtained graduate degrees in biomedical and mechanical engineering from the University of Wisconsin-Madison and University of Illinois at Urbana-Champaign respectively. Dr. Decker continues to enjoy academic research and writing and uses these skills to support integrative medicine education as a writer and contributor to various resources. Dr. Decker supports Allergy Research Group as a member of their education and product development team.

References

1. Wieland Ho. The chemistry of the bile acids. *Chemistry: 1922-1941*. 1966;2:94.
2. Wang DQ, Carey MC. Therapeutic uses of animal biles in traditional Chinese medicine: an ethnopharmacological, biophysical chemical and medicinal review. *World J Gastroenterol*. 2014 Aug 7;20(29):9952-75.
3. Rubin RA, et al. Ursodiol for hepatobiliary disorders. *Ann Intern Med*. 1994 Aug 1;121(3):207-18.
4. Tsumita R, et al. Long-term evaluation of extracorporeal shock-wave lithotripsy for cholesterol gallstones. *J Gastroenterol Hepatol.* 2001 Jan;16(1):93-9.
5. Ridlon JM, et al. Bile acids and the gut microbiome. *Curr Opin Gastroenterol*. 2014 May;30(3):332-8.
6. Kirwan WO, et al. Bile acids and colonic motility in the rabbit and the human. *Gut*. 1975 Nov;16(11):894-902.
7. Biagioli M, Carino A. Signaling from Intestine to the Host: How Bile Acids Regulate Intestinal and Liver Immunity. *Handb Exp Pharmacol*. 2019 May 22.
8. Zhou H, Hylemon PB. Bile acids are nutrient signaling hormones. *Steroids*. 2014 Aug;86:62-8.
9. Buffie CG, et al. Precision microbiome reconstitution restores bile acid mediated resistance to Clostridium difficile. *Nature*. 2015 Jan 8;517(7533):205-8.
10. Hänninen ML. Sensitivity of Helicobacter pylori to different bile salts. *Eur J Clin Microbiol Infect Dis*. 1991 Jun;10(6):515-8.
11. Vijayvargiya P, et al. Bile Acid Deficiency in a Subgroup of Patients With Irritable Bowel Syndrome With Constipation Based on Biomarkers in Serum and Fecal Samples. *Clin Gastroenterol Hepatol.* 2018 Apr;16(4):522-527.
12. Slocum MM, et al. Absence of intestinal bile promotes bacterial translocation. *Am Surg*. 1992 May;58(5):305-10.
13. Vítek L, Haluzík M. The role of bile acids in metabolic regulation. *J Endocrinol*. 2016 Mar;228(3):R85-96.
14. Chiang JYL. Bile acid metabolism and signaling in liver disease and therapy. *Liver Res*. 2017 Jun;1(1):3-9.
15. de Aguiar Vallim TQ, et al. Pleiotropic roles of bile acids in metabolism. *Cell Metab*. 2013 May 7;17(5):657-69.
16. Baars A, et al. The Gut Microbiota as a Therapeutic Target in IBD and Metabolic Disease: A Role for the Bile Acid Receptors FXR and TGR5. *Microorganisms*. 2015 Oct 10;3(4):641-66.
17. de Aguiar Vallim TQ, et al. Pleiotropic roles of bile acids in metabolism. *Cell Metab.* 2013 May 7;17(5):657-69.
18. Trauner M, Boyer JL. Bile salt transporters: molecular characterization, function, and regulation. *Physiol Rev*. 2003;83:633–671.
19. Ridlon JM, et al. Bile salt biotransformations by human intestinal bacteria. *J Lipid Res.* 2006 Feb;47(2):241-59.
20. Begley M, et al. The interaction between bacteria and bile. *FEMS Microbiol Rev*. 2005 Sep;29(4):625-51.
21. Islam KB, et al. Bile acid is a host factor that regulates the composition of the cecal microbiota in rats. *Gastroenterology*. 2011 Nov;141(5):1773-81.
22. Kurdi P, et al. Mechanism of growth inhibition by free bile acids in lactobacilli and bifidobacteria. *J Bacteriol*. 2006 Mar;188(5):1979-86.
23. Rizzo G, Renga B, Mencarelli A, et al. Role of FXR in regulating bile acid homeostasis and relevance for human diseases. *Curr Drug Targets Immune Endocr Metabol Disord*. 2005 Sep;5(3):289-303.
24. Xie W, Radominska-Pandya A, Shi Y, et al. An essential role for nuclear receptors SXR/PXR in detoxification of cholestatic bile acids. *Proc Natl Acad Sci U S A*. 2001 Mar 13;98(6):3375-80.
25. Boyer JL. New perspectives for the treatment of cholestasis: lessons from basic science applied clinically. *J Hepatol.* 2007 Mar;46(3):365-71.
26. Holt JA, et al. Definition of a novel growth factor-dependent signal cascade for the suppression of bile acid biosynthesis. *Genes Dev*. 2003 Jul 1;17(13):1581-91.
27. Liu Y, et al. Hepatoprotection by the farnesoid X receptor agonist GW4064 in rat models of intra- and extrahepatic cholestasis. *J Clin Invest*. 2003 Dec;112(11):1678-87.
28. Noh K, et al. Farnesoid X receptor activation by chenodeoxycholic acid induces detoxifying enzymes through AMP-activated protein kinase and extracellular

signal-regulated kinase 1/2-mediated phosphorylation of CCAAT/enhancer binding protein β. *Drug Metab Dispos*. 2011 Aug;39(8):1451-9.
29. Lee FY, et al. Activation of the farnesoid X receptor provides protection against acetaminophen-induced hepatic toxicity. *Mol Endocrinol.* 2010 Aug;24(8):1626-36.
30. Modica S, et al. Master regulation of bile acid and xenobiotic metabolism via the FXR, PXR and CAR trio. *Front Biosci (Landmark Ed)*. 2009 Jan 1;14:4719-45.
31. Heubi JE, et al. Oral Cholic Acid Is Efficacious and Well Tolerated in Patients With Bile Acid Synthesis and Zellweger Spectrum Disorders. *J Pediatr Gastroenterol Nutr*. 2017 Sep;65(3):321-326.
32. Setchell KD, Heubi JE. Defects in bile acid biosynthesis--diagnosis and treatment. *J Pediatr Gastroenterol Nutr*. 2006 Jul;43 Suppl 1:S17-22.
33. Cariou B, et al. The farnesoid X receptor modulates adiposity and peripheral insulin sensitivity in mice. *J Biol Chem.* 2006 Apr 21;281(16):11039-49.
34. Zhang Y, et al. Activation of the nuclear receptor FXR improves hyperglycemia and hyperlipidemia in diabetic mice. *Proc Natl Acad Sci U S A*. 2006 Jan 24;103(4):1006-11.
35. Chen J, et al. Interaction of gut microbiota with dysregulation of bile acids in the pathogenesis of nonalcoholic fatty liver disease and potential therapeutic implications of probiotics. *J Cell Biochem*. 2019 Mar;120(3):2713-2720.
36. Ma K, et al. Farnesoid X receptor is essential for normal glucose homeostasis. *J Clin Invest.* 2006 Apr;116(4):1102-9.
37. Shen H, et al. Farnesoid X receptor induces GLUT4 expression through FXR response element in the GLUT4 promoter. *Cell Physiol Biochem*. 2008;22(1-4):1-14.
38. Rysz J, et al. Fibroblast growth factor 19-targeted therapies for the treatment of metabolic disease. *Expert Opin Investig Drugs.* 2015 May;24(5):603-10.
39. Duboc H, et al. The bile acid TGR5 membrane receptor: from basic research to clinical application. *Dig Liver Dis.* 2014 Apr;46(4):302-12.
40. Kumar DP, et al. Activation of transmembrane bile acid receptor TGR5 stimulates insulin secretion in pancreatic β cells. *Biochem Biophys Res Commun*. 2012 Oct 26;427(3):600-5.
41. Kuhre RE, et al. Bile acids are important direct and indirect regulators of the secretion of appetite- and metabolism-regulating hormones from the gut and pancreas. *Mol Metab.* 2018 May;11:84-95.
42. Li T, et al. Transgenic expression of cholesterol 7alpha-hydroxylase in the liver prevents high-fat diet-induced obesity and insulin resistance in mice. *Hepatology*. 2010 Aug;52(2):678-90.
43. Watanabe M, et al. Bile acids induce energy expenditure by promoting intracellular thyroid hormone activation. *Nature*. 2006 Jan 26;439(7075):484-9.
44. Chen X, et al. Chenodeoxycholic acid attenuates high-fat diet-induced obesity and hyperglycemia via the G protein-coupled bile acid receptor 1 and proliferator-activated receptor γ pathway. *Exp Ther Med.* 2017 Dec;14(6):5305-5312.
45. Bianco AC, McAninch EA. The role of thyroid hormone and brown adipose tissue in energy homoeostasis. *Lancet Diabetes Endocrinol*. 2013 Nov;1(3):250-8.
46. Teodoro JS, et al. Enhancement of brown fat thermogenesis using chenodeoxycholic acid in mice. *Int J Obes (Lond).* 2014 Aug;38(8):1027-34.
47. Zietak M, Kozak LP. Bile acids induce uncoupling protein 1-dependent thermogenesis and stimulate energy expenditure at thermoneutrality in mice. *Am J Physiol Endocrinol Metab*. 2016 Mar 1;310(5):E346-54.
48. Albaugh VL, et al. Role of Bile Acids and GLP-1 in Mediating the Metabolic Improvements of Bariatric Surgery. *Gastroenterology*. 2019 Mar;156(4):1041-1051.
49. Flynn CR, et al. Metabolic Effects of Bile Acids: Potential Role in Bariatric Surgery. *Cell Mol Gastroenterol Hepatol*. 2019;8(2):235-246.
50. Patti ME, et al. Serum bile acids are higher in humans with prior gastric bypass: potential contribution to improved glucose and lipid metabolism. *Obesity (Silver Spring).* 2009 Sep;17(9):1671-7.
51. De Giorgi S, et al. Long-term effects of Roux-en-Y gastric bypass on postprandial plasma lipid and bile acids kinetics in female non diabetic subjects: A cross-sectional pilot study. *Clin Nutr.* 2015 Oct;34(5):911-7.
52. Suhre K, et al. Metabolic footprint of diabetes: a multiplatform metabolomics study in an epidemiological setting. *PLoS One.* 2010 Nov 11;5(11):e13953.
53. Prawitt J, et al. Bile acid metabolism and the pathogenesis of type 2 diabetes. *Curr Diab Rep*. 2011 Jun;11(3):160-6.
54. Fang Q, et al. Serum fibroblast growth factor 19 levels are decreased in Chinese subjects with impaired fasting glucose and inversely associated with fasting plasma glucose levels. *Diabetes Care*. 2013 Sep;36(9):2810-4.
55. Zhang J, et al. Lowered fasting chenodeoxycholic acid correlated with the decrease of fibroblast growth factor 19 in Chinese subjects with impaired fasting glucose. *Sci Rep*. 2017 Jul 20;7(1):6042.
56. Lai Y, et al. Serum fibroblast growth factor 19 is decreased in patients with overt hypothyroidism and subclinical hypothyroidism. *Medicine (Baltimore).* 2016 Sep;95(39):e5001.
57. Broeders EP, et al. The Bile Acid Chenodeoxycholic Acid Increases Human Brown Adipose Tissue Activity. *Cell Metab.* 2015 Sep 1;22(3):418-26.
58. Adrian TE, et al. Rectal taurocholate increases L cell and insulin secretion, and decreases blood glucose and food intake in obese type 2 diabetic volunteers. *Diabetologia*. 2012 Sep;55(9):2343-7.
59. Wu T, et al. Effects of rectal administration of taurocholic acid on glucagon-like peptide-1 and peptide YY secretion in healthy humans. *Diabetes Obes Metab*. 2013 May;15(5):474-7.
60. Kars M, et al. Tauroursodeoxycholic Acid may improve liver and muscle but not adipose tissue insulin sensitivity in obese men and women. *Diabetes*. 2010 Aug;59(8):1899-905.
61. Jones ML, et al. Cholesterol lowering with bile salt hydrolase-active probiotic bacteria, mechanism of action, clinical evidence, and future direction for heart health applications. *Expert Opin Biol Ther*. 2013 May;13(5):631-42.
62. Jones ML, et al. Cholesterol-lowering efficacy of a microencapsulated bile salt hydrolase-active Lactobacillus reuteri NCIMB 30242 yoghurt formulation in hypercholesterolaemic adults. *Br J Nutr*. 2012 May;107(10):1505-13.
63. Jones ML, et al. Cholesterol lowering and inhibition of sterol absorption by Lactobacillus reuteri NCIMB 30242: a randomized controlled trial. *Eur J Clin Nutr*. 2012 Nov;66(11):1234-41.
64. Jones ML, et al. Improvement of gastrointestinal health status in subjects consuming Lactobacillus reuteri NCIMB 30242 capsules: a post-hoc analysis of a randomized controlled trial. *Expert Opin Biol Ther*. 2013 Dec;13(12):1643-51.
65. Gattini D, et al. Bile acids for cholelithiasis. *Cochrane Database Syst Rev*. 2018 Jun;2018(6).
66. Gossard AA, Lindor KD. Current and promising therapy for primary biliary cholangitis. *Expert Opin Pharmacother*. 2019 Jun;20(9):1161-1167.
67. Paumgartner G, Beuers U. Ursodeoxycholic acid in cholestatic liver disease: mechanisms of action and therapeutic use revisited. *Hepatology*. 2002 Sep;36(3):525-31.
68. Iser JH, Sali A. Chenodeoxycholic acid: a review of its pharmacological properties and therapeutic use. *Drugs*. 1981 Feb;21(2):90-119.
69. Meredith TJ, et al. Retrospective comparison of 'Cheno' and 'Urso' in the medical treatment of gallstones. *Gut*. 1982 May;23(5):382-9.
70. Belei O, et al. The relationship between non-alcoholic fatty liver disease and small intestinal bacterial overgrowth among overweight and obese children and adolescents. *J Pediatr Endocrinol Metab*. 2017 Oct 26;30(11):1161-1168.
71. Jiang W, et al. Dysbiosis gut microbiota associated with inflammation and impaired mucosal immune function in intestine of humans with non-alcoholic fatty liver disease. *Sci Rep.* 2015 Feb 3;5:8096.
72. Watanabe M, et al. Bile acids lower triglyceride levels via a pathway involving FXR, SHP, and SREBP-1c. *J Clin Invest*. 2004 May;113(10):1408-18.
73. Inagaki T, et al. Regulation of antibacterial defense in the small intestine by the nuclear bile acid receptor. *Proc Natl Acad Sci U S A*. 2006 Mar 7;103(10):3920-5.
74. Wu W, et al. Activation of farnesoid X receptor attenuates hepatic injury in a murine model of alcoholic liver disease. *Biochem Biophys Res Commun*. 2014 Jan 3;443(1):68-73.
75. Manley S, Ding W. Role of farnesoid X receptor and bile acids in alcoholic liver disease. *Acta Pharm Sin B*. 2015 Mar;5(2):158-67.
76. Ferrell JM, et al. Deficiency of Both Farnesoid X Receptor and Takeda G Protein-Coupled Receptor 5 Exacerbated Liver Fibrosis in Mice. *Hepatology*. 2019 Sep;70(3):955-970.
77. Pellicciari R, et al. Bile acid derivatives as ligands of the farnesoid X receptor. Synthesis, evaluation, and structure-activity relationship of a series of body and side chain modified analogues of chenodeoxycholic acid. *J Med Chem.* 2004 Aug 26;47(18):4559-69.
78. Fiorucci S, et al. Obeticholic Acid: An Update of Its Pharmacological Activities in Liver Disorders. *Handb Exp Pharmacol.* 2019;256:283-295.
79. Guo C, et al. Farnesoid X Receptor Agonists Obeticholic Acid and Chenodeoxycholic Acid Increase Bile Acid Efflux in Sandwich-Cultured Human Hepatocytes: Functional Evidence and Mechanisms. *J Pharmacol Exp Ther*. 2018 May;365(2):413-421.
80. Gadaleta RM, et al. Farnesoid X receptor activation inhibits inflammation and preserves the intestinal barrier in inflammatory bowel disease. *Gut*. 2011 Apr;60(4):463-72.
81. Neuschwander-Tetri BA, et al. Farnesoid X nuclear receptor ligand obeticholic acid for non-cirrhotic, non-alcoholic steatohepatitis (FLINT): a multicentre, randomised, placebo-controlled trial. *Lancet*. 2015 Mar 14;385(9972):956-65.
82. Hameed B, et al. Clinical and metabolic effects associated with weight changes and obeticholic acid in non-alcoholic steatohepatitis. *Aliment Pharmacol Ther*. 2018 Mar;47(5):645-656.

◆

Sample Women's Health Treatment Plans

by Tori Hudson, ND

This article is intended to offer a few of my best sample treatment plans for some select women's health issues. It is assumed that we treat the individual patient; but with diagnosed medical conditions, we have the advantage of using long-standing historical therapies, reliable empirical medicine, and modern evidence-based therapies for condition specific issues with some expectation of reproducible results. We can then individualize our overall treatment approach based on the multitude of considerations for each patient. I offer these core sample treatment plans that can be considered an optimistic option for all of these selected conditions. Individuals with multiple health care problems and important individual subjective and objective findings can then be addressed with the insight and experience of each practitioner.

Acute Primary Dysmenorrhea

Key concepts

- Primary dysmenorrhea should be distinguished from secondary dysmenorrhea.
- Typical menstrual cramps are due to primary dysmenorrhea.
- Secondary causes of dysmenorrhea and pelvic cramping include endometriosis, adenomyosis, pelvic inflammatory disease, adhesions, ovarian cysts, celiac disease, thyroid conditions, congenital malformations, narrowing of the cervical opening, polyps, or uterine fibroids.
- Provide adequate acute pain relief in addition to trying to correct the underlying mechanism that is causing the problem.

Featured Supplement: Ginger

A long history of historical use, mechanisms of action, and two published studies provide the backbone of rationale for the use of ginger as a single agent for the relief of acute primary dysmenorrhea. One study compared mefenamic acid vs ibuprofen vs ginger (250 mg qid).[1] The severity of dysmenorrhea decreased in all groups, and no differences were found between the groups in pain severity, pain relief, or patient satisfaction. More women in the ginger group became completely pain free vs the mefenamic acid and ibuprofen groups. The rate of satisfaction from the treatments was 20/50 women in the mefenamic acid group, 22/50 women in the ibuprofen group, and 21/50 women in the ginger group.

The second study compared two different doses of ginger vs placebo.[2] Ginger capsules were given in one of two methods: 1) 500 mg ginger capsules or placebo 3x/daily starting two days before the beginning of menses and continued through day 3 of menses. 2) 500 mg ginger capsules or placebo 3x/daily on days 1, 2, and 3 of menses. The severity of pain was significantly reduced in the ginger group compared to the placebo group for both dosing methods with better results in the first dosing method. The second ginger dosing regimen was not significantly different than placebo in duration of pain.

Sample Acute Plan

- Ginger root powder, 250 mg qid starting two days before the beginning of menses and continued through day 3 of menses.
- Consider combination products containing niacin, borage, vitamin E, calcium, crampbark, valerian, black cohosh and more (3 caps every 3 hours during acute pain).

Conventional Acute Options (one of the following)

- Ibuprofen, 600 mg every 6-8 hours
- Naproxen, 500 mg every 12 hours
- Mefenamic acid, 250 mg tablets; two tablets at onset of pain followed by one tablet every 8 hours
- Naproxen sodium (Aleve), two tablets every 6 hours

Sample Treatment Plan- Prophylaxis

The cause of primary dysmenorrhea may be attributed to one of several factors, including behavioral and psychological ones, lack of blood flow and therefore oxygen to the uterus (ischemia), and increased production and release of uterine prostaglandins. Increased prostaglandins, specifically called PGF2alpha and PGE2, cause uterine contractions that lead to ischemia and pain. The levels of both PGF2alpha and PGE2 are low during the first half of the cycle and early part of the second half, but then they rise sharply and reach their highest levels shortly before and during the onset of menses. This increase in prostaglandin production may be related to the decline in progesterone levels towards the end of the cycle just before the onset of menses. These mechanisms are then the basis for many of the therapies used, both natural and conventional.

An alternative approach to menstrual cramps needs to provide effective pain relief while at the same time correcting the underlying dysfunction that is creating the cyclic menstrual pain. Because we are dealing with a functional problem and not a disease state that is causing the pain, we can truly focus on a holistic approach by looking for aggravating factors in the diet, lifestyle, and emotional environment.

- Diet changes: reduce saturated fats and trans fats; decrease sugar/white flour products.
- Regular exercise.
- Omega 3 oils: approximately 1080 mg/day of EPA with approximately 720 mg DHA daily.
- Ginger capsules, 250-500 mg daily.

Consider (one of the following): cyclic progesterone (100 mg-200 mg h.s. days 15-26); birth control pills; Progestin IUD.

Premenstrual Syndrome/Premenstrual Dysphoric Disorder

Premenstrual syndrome (PMS) refers to the cyclic constellation of troublesome symptoms that appear during the luteal phase of the menstrual cycle – more so in the late luteal phase – disappear by the end of the full flow of menses, and do not appear during the follicular phase. Premenstrual dysphoric disorder (PMDD) is a severe form of PMS that interferes with life activity. Although some 150 symptoms have been listed as premenstrual, the most common symptoms include irritability, anger, food cravings, depression, anxiety, mastalgia, headaches, tension, fatigue bloating, and water retention.

Key Concepts

- Understanding the days of the month symptoms occur is key in diagnosing PMS/PMDD accurately.
- Investigate not only the severity of symptoms, but the duration, as well as which symptoms are dominant and significantly affect quality of life.
- Normal ovarian function, and not a true hormonal imbalance, triggers the central nervous system and predisposes a woman to hormone-induced instability, and thus the PMS/PMDD symptoms. We do not currently know why the extent of sensitivity to the ovarian steroid-induced neurotransmitter changes varies in different women. Of the neurotransmitters studied, serotonin is the principal one implicated in the pathogenesis of PMS and PMDD. Whether PMS and PMDD are related to absolute levels or reduced blood levels of serotonin or to serotonin transport remains unclear. Other neurotransmitter systems may also be involved in PMS and PMDD. They include the adrenergic, opioid, and gamma-aminobutyric acid (GABA) systems.
- Testing saliva, serum, or urinary hormone levels are not diagnostic of PMS nor indicative in providing treatment directions.

Select Diet, Supplement/Botanical Research

Declining levels of serotonin, and also of dopamine, have been implicated in the etiology of PMS. *Vitamin B6* (pyridoxine) is thought to be unique in its ability to increase the cerebral synthesis of several neurotransmitters, including serotonin and dopamine, and more than a dozen studies have been done using vitamin B6 for PMS. These studies used vitamin B6 at a dose of 50 to 500 mg/day. Some of them found no effect, but others reported a substantial and broad effect. An overview of these studies has been published in the *British Journal of Obstetrics and Gynaecology*.[3]

A prospective, open, uncontrolled, observational pilot study using *St. John's wort* standardized extract, 300 mg three times daily, was investigated in order to establish a hypothesis and to test methods for a future randomized controlled trial.[4] Nineteen women with PMS underwent a preliminary screening interview and completed a daily symptom rating for one cycle. After taking the St. John's wort for two complete menstrual cycles, daily symptoms were rated using the Hospital Anxiety and Depression scale and a modified Social Adjustment Scale. The degree of improvement in overall premenstrual syndrome scores between baseline and the end of the trial was 51% with over two-thirds of the population demonstrating at least a 50% decrease in symptom severity. The mood subscale showed the most improvement (57%) and the symptoms with the greatest reductions in scores were crying (92%), depression (85%), confusion (75%), feeling out of control (72%), nervous tension (71%), anxiety (69%) and insomnia (69%).

An alternative approach to menstrual cramps needs to provide effective pain relief while at the same time correcting the underlying dysfunction that is creating the cyclic menstrual pain.

Chaste tree berry, aka Vitex agnus-castus, is well published in terms of cyclic menstrual related symptoms. In a systematic review and meta-analysis, ten databases were searched and updated as of January 2016.[5] Included studies were randomized controlled trials that used a preparation of chaste tree although not all studies used the same dose or preparation; and the herbal group was compared to either a placebo or pharmacological or other natural agent for a minimum of two menstrual cycles. No studies of homeopathic preparations of chaste tree were included. In the final search and analysis, seventeen randomized controlled trials were included in the qualitative analysis and 14 of those were also included in the quantitative analysis; there was insufficient data for the other three. Ten studies were placebo controlled and nine were other agent controlled, including SSRI, fluoxetine, an oral contraceptive, vitamin B6, magnesium, St. John's wort, or vitamin E. Two of the trials compared chaste tree to both an oral contraceptive and a placebo.

In 10 of the studies that used a placebo control, chaste tree was found to be superior in nine of them. These nine used an extract and the one negative study used ground berries. Chaste tree was superior for relieving PMS symptoms in all the studies comparing it to any of the other natural agents. Chaste tree was comparable to oral contraceptives in the studies where this was compared. Chaste tree was comparable to fluoxetine in one study; but in another, some components of the Hamilton depression rating scale scored higher for fluoxetine. Fewer side effects occurred in the women on chaste tree vs fluoxetine or the oral contraceptives.

Sample Treatment Plan

- Diet changes: low in sugar, starchy carbs
- Aerobic exercise (walking or other, a minimum of 30 minutes, 5 times weekly)

➤

Sample Treatment Plans

➤

- Combination product that includes all or most of the following: B6, calcium, chromium, kelp, chaste tree, St. John's wort, ginkgo, borage seed oil extract, vitamin E, magnesium, passion flower, or chamomile, dong quai, wild yam, dandelion leaf (2 capsules twice daily throughout whole cycle).
- If not a combination product, then consider B6 (50-100 mg/day), calcium (1,000 mg/day), St John's wort (300 mg three times daily), Vitex extract (1 capsule per day - especially if cyclic mastalgia is part of the picture).
- If PMDD, add on chamomile for irritability; SAMe 200-400 mg/day for depression.

Acute Bacterial Vaginosis

Bacterial vaginosis (BV) consists of a significant polymicrobial overgrowth in which the bacteria act synergistically to cause an odor and discharge and may lead to potential complications in the uterus and fallopian tubes. It is best to consider BV to be the result of alterations in the vaginal ecosystem, rather than an infection caused by any single microorganism. In BV, the environment of the vagina shifts from a predominance of lactobacilli to a predominance of anaerobes (mainly *Prevotella*, *Peptostreptococcus* species, *Eubacterium* species, and *Mobiluncus*) and facultative bacteria (*Mycoplasma* species, *Staphylococcus epidermidis, Streptococcus* species and *Gardnerella vaginalis*). This overgrowth results in the degradation of the mucus membrane and shedding of the vaginal epithelium, resulting in a discharge. The destruction of these mucins exposes the epithelium to other organisms, with the subsequent appearance of clue cells.

Key Concepts

The best treatment for BV is one that will lead to resolution of symptoms and offers the most likelihood for restoring the lactobacilli ecosystem.

The goal of treatment is to restore the vaginal pH to <4.5 and to re-establish normal ecology by having dominance of *Lactobacillus* species.

- Remove/limit obstacles to cure
- Improve vaginal immunity
- Support systemic immunity
- Restore pH
- Restore vaginal microenvironment
- Restore gut ecology
- Provide symptom relief
- Correct co-medical conditions

Tori Hudson, ND, graduated from the National College of Naturopathic Medicine (NCNM), now National University of Natural Medicine (NUNM), in 1984 and has served the college in several capacities. She is currently a clinical professor at NUNM, Southwest College of Naturopathic Medicine, and Bastyr University. Dr Hudson has been in practice for more than 34 years, is the medical director of her clinic, A Woman's Time (Portland, Oregon), is co-owner and director of product research and education for VITANICA, and is the program director for the Institute of Women's Health and Integrative Medicine. She is also the founder and co-director of NERC (Naturopathic Education and Research Consortium), a non-profit organization for accredited naturopathic residencies.

Dr. Hudson has received numerous awards, including the 1990 President's Award from the American Association of Naturopathic Physicians, the 1999 prestigious Naturopathic Physician of the Year Award, the 2009 Natural Products Association NW Pioneer Award, and in 2012 was inducted into the NUNM Hall of Fame.

She is a nationally recognized author, speaker, educator, researcher, and clinician. Dr. Hudson serves on several editorial boards, advisory panels and as a consultant to the natural products industry.
www.drtorihudson.com
www.instituteofwomenshealth.com

Featured Ingredient: Lactobacillus rhamnosus/reuteri

A randomized double-blind placebo-controlled trial of 100 women (mean age 34 years) with BV were treated with 2% vaginal clindamycin cream for 7 days and then randomized to receive vaginal capsules for 10 days containing either a placebo or a combination of *L. gasseri* and *L. rhamnosus* (10 bn CFU/capsule) for three menstrual cycles.[6] Probiotics did not improve efficacy of BV treatment during the first month of treatment. However, women initially "cured" were followed for six menstrual cycles or until relapse within that time. At the end of six months, 64.9% of the probiotic-treated group were still BV-free and compared to 46.2% in the placebo group.

Sample Acute BV Treatment Plan

- Vaginal vitamin C tablet (250 mg) for six days, then
- Boric acid (600 mg suppository 1/day for 10 days, then once weekly for 6 weeks to prevent relapse/recurrence).
- *Lactobacillus rhamnosus/rheuteri* in suppository (or capsule inserted in vagina); once weekly for 6 weeks, during the same weeks as the boric acid.
- *Lactobacillus* species (eg, *Lactobacillus rhamnosus* with *Lactobacillus rheuteri*) combinations, 1-10 billion per day for four months.

Sample Chronic or Chronic Recurring BV Treatment Plan

- Low glycemic index diet
- Vitamin D (4,000 i.u. daily)
- Avoid vaginal exposure to semen (to facilitate vaginal pH becoming acidic) and optimal to avoid oral sex for six months (to avoid mixing oral flora with vulvo-vaginal flora).
- Insert vaginal specific vitamin C suppository nightly for six nights
- Then follow with boric acid (600 mg compounded suppositories or capsules nightly for 1 week then 2x/weekly for 3-6 months).
- Oral *L. rhamnosis/L. rheuteri* (1-10 billion daily for 4-6 months)
- Vaginal *L. rhamnosus/L. rheuteri* capsules once weekly for 3-6 months

Consider vaginal metronidazole once weekly for 4 months. Add vaginal estrogen in peri or postmenopausal woman twice weekly. Also, consider biofilm disruptors.

Conventional Acute Treatment Options

- Metronidazole 250 mg 3x/day orally for 7 days or
- Metronidazole 2 g as a single oral dose or
- Metronidazole gel 0.75% (MetroGel-Vaginal, 3M) intravaginally once a day for 5 days or
- Clindamycin 2% intravaginally once a day for 7 days; or clindamycin ovules insert once daily for 3 days.

References

1. Ozgoli G, Goll M, Moattar F. Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrhea. *J Alternative and Complementary Med.* 2009;15(2):129-132.
2. Rahnama P, et al. Effect of *Zingiber officinale* R. rhizomes (ginger) on pain relief in primary dysmenorrhea: a placebo randomized trial. *BMC Complement Altern Med.* July 10, 2012;12(1):92.
3. Kleijnen J, ter Riet G, Knipschild P. Vitamin B6 in the treatment of the premenstrual syndrome – review. *Br J Obstet Gynaec.* 1990;97:847-852.
4. Stevinson C, Ernst E. A pilot study of Hypericum perforatum for the treatment of premenstrual syndrome. *British J Obstetrics and Gynaecology*. 2000;107: 870-876.
5. Verkaik S, et al. The treatment of premenstrual syndrome with preparations of Vitex agnus-castus: a systematic review and meta-analysis. *Am J Obstet Gynecol*. August 2017;217(2):150-166.
6. Larsson P-G, et al. Human lactobacilli as supplementation of clindamycin to patients with bacterial vaginosis reduce the recurrence rate; a 6-month, double-blind, randomized, placebo-controlled study. *BMC Women's Health.* 2008;8:3.

◆

Still the Best

A Must Have for Kidney Function Support!

CORDIMMUNE ™

The only cordyceps product that is standardized for and declares its cordycepin content

- Supports mitochondrial function and ATP production
- Modulates immune system
- Enhances athletic performance safely
- An excellent adaptogen and adrenal support
- Supports hematopoiesis
- 0.2% Cordycepin (worth over $100 per bottle)
- 0.3% Adenosine • 22% Polysaccharides

Immune Support Beyond Just Polysaccharides!

CORIO PSP ™

The most clinically researched mushroom in Japan and China

- Unmatched 38% polysaccharides
- Lessens the side effects of toxic treatments
- Raises the quality of life
- Raises the activities of NK cells and macrophages
- Increases thymus weight

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

CRNA

CANADA RNA BIOCHEMICAL INC.
Tel: (604) 273-2233 • **www.canadaRNA.com**

1-866-287-4986

Depression, Amino Acids, and Rubidium

by Jonathan Wright, MD

Originally published in *Green Medicine Newsletter*, November 2016

For over 40 years, my observation has been that low levels of essential amino acids are one major cause of depression. Among very many other things, our bodies use amino acids to make the large majority of "neurotransmitters," molecules which help nerve cells to communicate. If essential amino acids are low, then neurotransmitters are very likely to be low also, and depression is a frequent result. Patent medicine companies know this too; but since amino acids aren't patentable, they've looked for artificial, patentable molecules to raise levels of neurotransmitters. Many patent "antidepressants" do exactly that.

Mrs. Jones (of course not her real name) came to see me at Tahoma Clinic sometime in the 1990s with several problems. The main one was chronic depression; it was "successfully" being treated with one of the common patented antidepressants that raise neurotransmitter levels. As is more usual than not, the patented antidepressant was also causing "side effects."

Mrs. Jones asked if her depression could be treated by more natural means. I told her that was very likely; if the neurotransmitter-raising patented antidepressant helped her depression, it was also very probable that neurotransmitter-raising amino acids would do the same thing, as it had for literally dozens of others. Along with other lab tests, she had a blood test done for essential amino acids.

When the test returned, it was quite typical for many depressed individuals. Mrs. Jones was low on five of the nine essential amino acids, and low-normal on two more. She asked which one or ones of these lower than normal essential amino acids might be responsible for her depression. Although at least one or two were very probably involved, there was no way to know for sure, since the function in our brains of all of the essential amino acids and their derivatives wasn't (and still isn't) completely known.

She looked simultaneously puzzled and disappointed and asked how to know which ones she should take. We didn't need to know exactly which ones because she could just take *all* of the essential amino acids, blended together in proportions individualized for her personally, according to the results of her test. Her brain would do the rest, choosing exactly what it needed to raise its own levels of neurotransmitters towards normal levels. Even though science doesn't yet know everything about normal human biochemistry, our bodies "know," and – if we're born intact – will function normally if given all the raw materials needed to do so.

After a moment, she agreed that this approach made sense; but she wanted to know how her levels of essential amino acids got so low since she ate enough protein. There were several possibilities, but inadequate protein digestion due to low stomach acid (hypochlorhydria or achlorhydria) and poor amino acid absorption because of "hidden" gluten sensitivity were (and still are) at the top of the list. A stomach test ("gastric analysis by radiotelemetry") showed that Mrs. Jones stomach was secreting hydrochloric acid in much less than optimal amounts; fortunately, a stool test (in my opinion, the most sensitive test for "hidden" gluten sensitivity) showed that she did not have that problem, so absorption of any supplemental amino acids she took should be good.

She took her individualized amino acid blend, hydrochloric acid with pepsin capsules with every meal to replace her "missing" stomach acid and learned to give herself vitamin B12 injections with folate (recommended for everyone with low stomach acid). At the beginning, she was given amino acids and minerals intravenously, since this enables much quicker symptom relief for hypochlorhydric individuals. In just a few weeks she felt much better; the intravenous nutrients were discontinued. She continued with all her oral supplementation and was able to taper and stop her patented antidepressant.

After nearly a year, she returned. Even though she had continued everything recommended, depression was starting to become noticeable again. She was disappointed, and so was I. My experience to that point had been that once depression has cleared up with individualized amino acids, it usually stays away, as long as protein digestion is improved and other supplementation is continued.

Her records had a clue. She'd had a screening test for minerals (hair mineral analysis), and her rubidium levels were so low that the laboratory couldn't find any of it at all. Italian researchers were the first to report that rubidium used alone was helpful against some cases of depression in the 1970s. Rubidium is a mineral, part of the lithium-sodium-potassium "family" of minerals.

Unfortunately, at that time there were no rubidium supplements available in natural food stores or the Tahoma Clinic Dispensary. However, we did have very low dose rubidium available for IV use, so I got a bottle and asked Mrs. Jones to just take the top off and swallow the equivalent of approximately fifty milligrams daily.

Initially, adding rubidium seemed to help, but in a few weeks her depression came back, more rapidly this time, and Mrs. Jones returned to her patented antidepressant. Since rubidium had helped her initially, it appeared more rubidium study was needed! Checking research publications thoroughly (took a while), it became apparent that – used at higher doses than she had used – rubidium alone is at least as effective, if not more so, than patented "antidepressants"! And used properly (See Sidebar), it's safe!

Here are summaries of some of the published research:

- In 1973, depressed patients who had not responded to any other form of treatment took rubidium chloride. 70% of those who took rubidium chloride for a minimum of four weeks had a "good to excellent" response.[1]
- In 1975, researchers found that the response rate of chronically depressed individuals who took rubidium chloride was 65%. Rubidium chloride was found to work as well as imipramine, a "major" patented antidepressant.[2]
- In 1980, a double-blind study compared the effects of rubidium chloride, 540 milligrams daily, with a widely sold (at that time), patented antidepressant, chlorimipramine, 100 milligrams daily. The researchers found that rubidium chloride's antidepressant results were *superior* to the chlorimipramine.[3]
- In 1988, thirty-one women hospitalized with depression took rubidium chloride, 180 to 720 milligrams daily. By the second week, 2/3 had significantly improved.[4]
- In 1993, 20 individuals with "major depression" were treated with 360 to 720 milligrams of rubidium chloride. The researchers wrote: "rubidium chloride showed a marked and rapid anti-depressive action…."[5]
- In 1996, researchers reported that fifteen individuals hospitalized with depression were treated with rubidium chloride 540 milligrams daily. They wrote: "Speedy therapeutic efficacy has been shown, with lack of side effects."[6]

With all this study (and additional rubidium research now easily available through the National Library of Medicine's online service) why isn't rubidium treatment of major depression well-known? You know the answer: as a naturally occurring mineral, rubidium isn't PATENTable. No one can make megabucks selling rubidium.

My only excuse for not finding these research reports much sooner was that patients suffering from depression usually did very well with other natural treatments, particularly individualized amino acids and (at appropriate ages) bio-identical hormones.

How Does Rubidium Improve Depression?

Most *Green Medicine* readers know about the hormone adrenalin, secreted into the blood by the adrenal glands, and its cousin noradrenalin, mostly secreted by nerves to communicate with other nerves. Noradrenalin, adrenalin, dopamine, and closely related molecules are termed "catecholamines" and are well-known nervous system stimulants. Increasing levels of noradrenalin and adrenalin is well-known to have a significant antidepressant effect. ("Amphetamine" ➤

Using Rubidium Safely

Rubidium is a member of the same mineral family as lithium, sodium, and potassium. Reviewers have pointed out that rubidium and potassium behave in many of the same ways, as do lithium and sodium. Potassium and rubidium are mostly found inside of body cells ("intracellular"); sodium and lithium are mostly found outside of body cells ("extracellular"). Potassium given in excess or too rapidly intravenously can be dangerous, even causing deaths; rubidium can do the same. So except in very small doses, rubidium should always be taken orally.

In reasonable doses, oral rubidium is safe. According to a major English-language review of rubidium and rubidium therapy: "Rubidium chloride appears to be a safe therapeutic agent when administered orally….Some minor side effects that have been noted are constipation, diarrhea, agitation, insomnia, and a transient decrease in heart and pulse rate."[7] Other investigators have noted transient skin rashes and frequent urination.[5]

Rubidium should not be used by individuals with bipolar ("manic-depressive") illness, as it appears to increase the length of any manic phase of the illness even though it decreases the extremes of mood.

Most importantly, *if you're taking rubidium supplementation, it's important to take an equal or greater amount of potassium.* As there's clearly more potassium than rubidium naturally present in our bodies, we don't want to allow too much "replacement" of potassium with rubidium over any length of time. One individual who ignored advice to take as much rubidium as potassium developed very sore muscles which very fortunately became entirely better after he took relatively large (but safe) quantities of potassium.

All of the rubidium vs. depression studies cited in this article used between 180 and 720 milligrams daily. The largest review suggests 180 milligrams three times daily. Mrs. Jones took 500 milligrams total daily, with food.

Because of the rubidium-potassium interaction, it's best to consult with a physician skilled and knowledgeable in natural medicine before taking rubidium supplementation. Rubidium is available through some compounding pharmacies and – combined with an equal amount of potassium for greater safety – at the Tahoma Clinic Dispensary.

➤

and "methamphetamine" or "meth" are previously patented, and much more powerful synthetic versions of catecholamines. Both of these "uppers" are powerful and dangerous stimulants/antidepressants.)

Our nerve cells and other cells use specialized enzymes to transform the essential amino acid phenylalanine and its derivative tyrosine into noradrenalin, adrenalin, dopamine, and other naturally occurring stimulatory catecholamines (pronounced "cat-e-kol-ah-means"). Without enough phenylalanine and/or tyrosine, our bodies can't make nearly as much of these catecholamines, and many of us become depressed. (Some patented antidepressants are thought to artificially raise levels of catecholamines in the brain.)

Rubidium (along with other vitamin and mineral "co-factors) stimulates the enzymes that use phenylalanine and tyrosine to produce catecholamines. In addition to stimulating catecholamine build-up, rubidium also slows its breakdown and (in a parallel to many patented antidepressants) slows the "re-uptake" of catecholamine neurotransmitters into the nerve cells that secrete them, thus keeping them working for longer.[7]

Rubidium appears to affect other neurotransmitter systems as well. In research volunteers, rubidium administration increased blood and urine levels of alpha-ketoglutarate, which (among other things) promotes the formation of gamma-amino butytric acid (GABA) and glutamate, non-catecholamine neurotransmitters.[7]

Before you consider rubidium for depression, make sure to have your fasting essential plasma amino acids checked. Although not every clinically depressed individual has low essential amino acids, the majority do; so, testing and treatment for these essential nutrients should never be omitted. In case your essential amino acids are all normal, but you're suffering from depression, rubidium can still be tried anyway; it is more likely to work with sufficient essential amino acids already available.

"Fasting plasma essential amino acids" is a blood test. What's in the blood is what the body has available for use; amino acids in urine are of course no longer available to the body. Except in unusual circumstances, it's not necessary to check dozens of amino acids as our bodies will transform the essential amino acids into the much more abundant "non-essential amino acids" according to the body's needs.

For years Meridian Valley Lab (www.meridianvalleylab.com, 206-209-4200, where I am Medical Director) and Metametrix Laboratory (purchased by another laboratory) did the best job on this test for the best price. Meridian Valley Labs continues to do so. After Metametrix was purchased, the "normal values" on the test were changed (I find the original "normals" still used by Meridian to be the most useful in practice), and then the test itself was changed. That test report and recommendations became less useful. Whichever lab you choose, if your essential amino acids are low, make sure to use a blend of all the essential amino acids (including tryptophan) *individualized for you.*

Just as importantly, look for the cause, which is quite likely to be gastric hypochlorhydria (low stomach acid) and/or "hidden" gluten sensitivity and occasionally both. If low stomach acid is a problem case, "replacement" hydrochloric acid with pepsin should be taken with meals, along with injections of vitamin B12 with folate. Individualized amino acid combinations alone along with these injections can frequently help your depression clear up over a few weeks to few months' time.

If this isn't effective enough or if you want to "go faster," then rubidium could be helpful. As you can tell, all of this may be a little complicated, so it's best to work with a physician skilled and knowledgeable in nutritional and natural medicine to help you co-ordinate it all. That physician can also suggest other nutrient "co-factors" that work with rubidium to make those antidepressant "catecholamines." With those "co-factors," the over-all dose of rubidium can be less while still being effective.

While using rubidium "by itself" without any of these other nutrients can be effective (the research reports cited show significant effectiveness with rubidium alone in 65-70% of depressed individuals), you might well be overlooking deficiencies in essential amino acids (as well as other co-factor nutrients) that rubidium alone cannot replace. Your depression would go away while other body functions unnecessarily decline. You also might have symptoms of rubidium-induced intracellular potassium deficiency. Make sure to work with a knowledgeable physician to avoid this possibility!

A Harvard University and University of Michigan graduate, Dr. Jonathan V. Wright, MD (Hon. ND), was also awarded an honorary ND by Bastyr University (1993). He continues to be a forerunner in research and application of natural treatments for healthy aging and illness. He has taught natural biochemical medical treatments since 1983 to thousands of physicians in the USA, Europe, and Japan. He was the first to develop and introduce the use of comprehensive patterns of bio-identical hormones (including estrogens, progesterone, DHEA and testosterone) in 1982 and directed the development of tests to ensure their safe use. Other accomplishments include originating successful natural treatment for elimination of childhood asthma, developing natural treatment to stop vision loss and/or improve vision in the majority of individuals with "dry" macular degeneration, pioneering the use of aldosterone to reverse age-related hearing loss, discovering the effects of iodine on estrogen metabolism and cobalt on steroid detoxification, and popularizing the use of the natural sugar D-mannose for elimination of 85-90% of urinary tract infections. He also originated effective natural treatment for seborrheic dermatitis, allergic and viral conjunctivitis, Osgood-Schlatter's disease, and treatment that improves bone density in the large majority of those with osteoporosis. Dr. Wright serves as medical director of Tahoma Clinic in Tukwila, Washington (www.TahomaClinic.com).

References

1. Fieve RR, et al. Rubidium: Biochemical, behavioral, and metabolic studies in humans. *Am J Psychiatry*. 1973;130:55-61.
2. Carolei A, et al. Azionefarmacologicadelcluorodirubidio – effetoantidepressivo: confronts con l'imipramina. *ClinTer*. 1975;75:469-478.
3. Calandra C, Nicolisi M. Confronts fra due farmaciadazioneantidepressiva: rubidiocluoro a chlorimipramina. Proc 34th Congress Italian Society of Psychiatry, Catania, Italy, 1980.
4. Placidi G, et al. Exploration of the clinical profile of rubidium chloride in depression: a systemic open trial. *J Clin Psychopharmacol*. 1988;8(3):184-188.
5. Torta R, et al. *[*Rubidium chloride in the treatment of major depression*]. Minerva Psichiatr*. 1993;34(2):101-110.
6. Brundisino AO, Cairoli S. *[*The pharmacological action of rubidium chloride in depression*] Minerva Psichiatr*. 1996;37(1):45-49.
7. Williams RH, Maturen A, Sky-Peck HH. Pharmacologic role of rubidium in psychiatric research. *Comprehensive Therapy*. 1987;13(9):46-54.

◆

Homeopathy Lives!

by Richard Moskowitz, MD

I've been practicing general and family medicine for the past 50 years, with homeopathy my principal method of treatment since 1974. I have no doubt that pharmaceutical drugs have value; I often refer patients I haven't been able to help to my allopathic colleagues and am more than grateful for what they do. But I prefer homeopathy, first, because it makes sense to begin with gentler and safer methods whenever possible; and second, because homeopathic remedies are tailored to the individuality of the patient, and thus capable of a deeper and more comprehensive level of healing than is attainable with drugs that seek only to counteract a specific symptom or correct a particular abnormality by applying superior chemical force at that strategic point.

I can readily understand and sympathize with the common belief that homeopathic remedies are nothing but placebos, which was already current in Hahnemann's time, became famous when Oliver Wendell Holmes, Sr. devoted some elegant prose to ridiculing it more than 150 years ago,[1] and has since been incorporated into the conventional wisdom. When I was in medical school, the term "homeopathic dose" was used almost affectionately to signify an amount of medicine far too small to have any noticeable effect whatsoever; and even today, as various modalities of alternative and complementary medicine enter the mainstream and many American physicians seek to broaden their outlook in order to accommodate them, most would probably still agree, at least in private, that homeopathy defies common sense, ordinary logic, and some basic laws of chemistry.

Indeed, even I feel a little uneasy when my patients eagerly gulp down the whole idea of homeopathy with no doubt or hesitation, blissfully untroubled by the profound mysteries at the very heart of it. Hahnemann's Law of Similars, "Let likes be cured by likes," the basic principle of homeopathy, is still far from intuitively obvious, even to those of us who use it every day, and remains essentially a *postulate,* not yet amenable to conclusive proof or disproof as a scientific hypothesis must be. Still less satisfactorily has anyone ever explained how medicines diluted beyond the level of Avogadro's number could possibly have *any* effect on a patient, let alone a curative one.

For myself and my colleagues, homeopathy has stood the test of time as both a method of healing the sick and a *philosophy* of health and disease.

But the fact that homeopathy is based on a phenomenon as yet unexplained by the science we now have is far from proving that the phenomenon doesn't exist, or that the method of treatment based on it is simply a fake. It almost embarrasses me to have to point out that the entire argument of those who make a point of ridiculing it still boils down to the same defective syllogism that even the eminent Dr. Holmes couldn't improve upon: Homeopathy *can't possibly* work; therefore, it *doesn't* work!

Once that flagrant *non sequitur* is permitted, to be sure, all sorts of dire consequences can be made to follow from it. Two recent examples are a law enacted by the House of Commons that removes homeopathic medicines from the list of treatments approved and paid for by the British National Health Service,[2] and a proclamation by the Spanish Ministry of Health that homeopathy is a "pseudoscience," thereby excluding it from their health care system, abolishing all training programs based on it, and warning doctors not to practice it or face disciplinary action, in spite if not precisely because of its growing popularity there.[3] In the United States, the Homeopathic Pharmacopoeia was officially recognized in the founding document of the FDA, but the agency has never stopped trying to curtail its influence on similar grounds.

To these familiar indictments an Australian philosopher has proposed the novel addendum that homeopathy is not only ineffective, but also *immoral*, according to the utilitarian standard of doing the greatest good for the greatest number, mainly to the extent that it dissuades people from deploying the kind of heavy artillery that really *does* work.[4]

With strong financial and political support from the pharmaceutical industry, a growing movement to discredit homeopathy, resorting to the same fallacious argument, has recently embraced a militant, debunking *scientism,* exemplified by professional 'quackbusters' like Wallace Sampson[5] and Stephen Barrett,[6] who regard homeopathy on a par with magic and the paranormal and have adopted discrediting such illusions as their life's work.

➤

➤

In the end, however, all their impressive and learned reasoning goes for naught, because the twin premises it is based on – the implausibility of the Law of Similars, and the improbability that substances diluted past the threshold of molecular structure could be capable of biological activity – both turn out to be simply and demonstrably false. The basic "law" of homeopathy, for example, based on the phenomenon that medicines can go both ways, that those with the power to relieve certain symptoms can elicit or provoke them as well, is widely familiar even in allopathic circles where "paradoxical" effects such as antihypertensives raising blood pressure, antidepressants making depression worse to the point of suicide, and so forth, are commonplace and well-documented in standard reference texts like the *Physicians' Desk Reference*,[7] just not yet proclaimed as a general rule.

As for our notorious "infinitesimal" doses, scientific experiments have repeatedly shown that these highly diluted remedies are capable of both stimulating and inhibiting colony growth in bacterial cultures,[8] *in vitro* enzymatic activity in tissue culture and cell-free extracts,[9] seed germination and growth in various plant species,[10] and various global properties of higher animals.[11] While equally unambiguous results are perforce more difficult to attain with human subjects in clinical situations, it is nevertheless abundantly clear that even ultradilute homeopathic preparations are capable of significant biological activity.

No matter what the correct explanation of those results may be, it is also undeniable that qualified and dedicated physicians have continued to follow the same principles and to practice medicine in accordance with them for more than two hundred years and now do so on every continent and in most countries of the world. In the face of determined opposition, general ridicule, and the sacrifice of more prominent and lucrative careers for their sake, the mere fact that homeopathic medicine has survived intact for so long and even continued to grow and develop under such adverse conditions is already more than sufficient answer to the militant conviction of the quackbusters that it is a delusion and nothing more, and indeed suggests precisely the opposite conclusion. For no matter what mode of treatment we prefer to use, every practicing physician knows and must live by the obvious truth that our reputations and livelihoods depend on the extent to which our patients are benefited by our efforts on their behalf.

I will give a few examples from the early years of my practice. The first was an eight-pound baby girl, born covered with thick meconium, who took one gasp and then breathed no more. After brisk suctioning produced only more of the same, the child lay limp, white, and motionless, with a heartbeat of 40 per minute, responding feebly to mouth-to-mouth resuscitation but incapable of breathing on her own. I put a few tiny granules of *Arsenicum album* 200C[12] on her tongue, and almost instantaneously she awoke with a jolt, crying and flailing, her heart pounding at 140 per minute, her skin glowing pink with the flame of new life. The whole evolution took no more than a few seconds. After a night in the hospital to be on the safe side, mother and baby went home in the morning with no outward sign that anything untoward had happened. Experiences like these are inscribed for life in every practitioner's mind.[13]

Of course, since the child was full-term, well-formed, and appeared normal in every other respect, she might just as well have recovered spontaneously on her own, without any remedies at all. In any case, she was just one patient, a mere "anecdote," utterly without statistical significance. But all of us who were present, including my nurse, the baby's mother and father, and I daresay the child herself, by now fully-grown and undoubtedly steeped in the legend of her birth, know as surely as we can know anything that the conjunction of the infinitesimal dose and her abrupt awakening was no mere coincidence.

Another patient was a 34-year-old registered nurse who had been plagued with severe endometriosis ever since her teens. After four surgeries to remove large blood-filled cysts from her bladder and pelvic organs, and several courses of male hormones to suppress the condition, her periods had become dark-brown, scanty, and essentially "dead," as she described them; she came seeking only to restore a healthy menstrual flow, having long since abandoned any hopes of childbearing.

After a few remedies, her periods became fuller and richer, and within six months she was pregnant. By the next time I saw her, for a different ailment nearly eight years later, she had given birth to two healthy children after uncomplicated pregnancies and normal vaginal births and had remained in good health ever since.[13] While no one can attribute such an outcome to a homeopathic remedy or indeed any other agency in precise, linear fashion, my patient has never stopped thanking me for it, which is reason enough to be grateful for a process that is inherently catalytic and persuasive, rather than forcible or compulsory.

Still less can these happy endings be imputed to any unusual skill of mine since they are entirely comparable to what every competent prescriber has seen or could easily duplicate; and I might just as well have cited other patients whose conditions were far from hopeless, who believed in the remedies and in me, but whom I was nevertheless unable to help.

Homeopathic remedies are safe, economical, simple to use, and gentle in their action, with vanishingly few serious or prolonged ill effects. What our critics don't say and almost certainly don't know is that they are also capable of acting thoroughly, deeply, and for a very long time, requiring only infrequent repetition of the dose and posing minimal risks of chronic dependence. Patients, friends, and loved ones alike often notice a general improvement in vitality and a sense of well-being, such that recurrences seem less frightening and indeed less likely.

On the other hand, at least in my experienced but far from expert hands, it is by no means a panacea for all ills. Homeopathy is a difficult and exacting

art, and even after years of study and practice a skilled prescriber may need to try several remedies before obvious benefit is obtained; while in some cases, despite the most devoted efforts, there is little or no benefit at all. But if such ultradilute remedies have worked well enough and often enough to sustain me in a general practice for more than 40 years, as they have so many others, that too is more than enough evidence to refute the conventional wisdom that they are no treatment at all.

To put it the other way, if it's really true that our remedies are blanks, then we must be healing our patients by means of magic or shamanic spells that we're casting over them unawares, which would be high praise indeed. But I prefer to believe what my experience has taught me, that the "placebo effect," the starved and tattered remnant of the innate self-healing capacity, is an indispensable component of all healing, even with drugs, but by no means the whole of it.

For medicinal substances, our reigning standard of efficacy is the random controlled trial, or RCT, in which subjects are randomized into two groups, one receiving the drug, the other only a placebo or inert imitation, with both patients and doctors kept in the dark as to who gets which. In these experiments, the causal power of any drug against a particular symptom or abnormality equals the extent to which patients actually taking it outperform their placebo controls. Rather than an optimal *qualitative* fit with the signs and symptoms of each patient as a whole, such as homeopaths aspire to, the best drugs and the ones most diligently sought after are simply the most *potent* ones, those with the most chemical power to compel the organism to function in whatever minutely targeted ways the profession decrees that it should.

Thus modern physicians are duly equipped with the latest chemical weapons to attack a vast array of diseases and abnormalities as if they were enemies on a battlefield: *anti*biotics to kill bacteria, *anti*hypertensives to lower the blood pressure, *anti*convulsants to control seizure activity, *anti*metabolites to destroy cancer cells, *anti*histamines to suppress the allergic response, and so forth, all developed to act as selectively as possible, but with little or no regard for the individuality of the patient. In advanced cases, such drugs may indeed save life, give miraculous relief, buy valuable time, or do the best that can be done under adverse or extreme circumstances.

Leaving aside for the moment the bottom-line question, whether most patients taking such drugs will actually feel better, live longer, and suffer fewer complications as a result of taking them, I am prepared to stipulate what is not always true in practice, that many of the drugs in common use do indeed have the power to accomplish at least some of what we ask and expect of them, in the hope that those more subjective and personal goals will eventually follow. But the high and often exorbitant price that we must pay for such seemingly precise and overriding causal power comprises at least three enormous and largely hidden cost and risk centers that usually go unrecognized or are talked about only after the fact, if at all.

First, when a drug really works to suppress or counteract the target symptom or abnormality, the condition is likely to reappear with equal or greater intensity as soon as the drug wears off. Using potent chemicals in this way, to force the issue, rather than simply to assist whatever self-healing processes are already under way, cannot fail to impose the threat of needing to *continue* using them for long periods of time, if not indefinitely, and thus of transforming what often began as an idiomatic *episode* in the patient's life into an ongoing if not permanent *chronic* illness with the power to propagate itself through time.

Second, narrowly targeting drug treatment to specific chemical abnormalities and abstract pathological "entities" without rebalancing the energy dysfunction of the patient as an integrated whole naturally and inevitably leads to *polypharmacy,* the need for still other drugs to correct, counteract, or control whatever additional diseases and abnormalities we manage to identify in the future, with the further risk of synergistic or antagonistic interactions between them.

And third, drugs powerful enough to do what we hope and expect them to do are capable of acting coercively on various other physiological functions as well, although these usually undesirable "side effects" tend to vary more or less infinitely, according to the unique tendencies and predispositions of each individual patient, and will therefore be much more difficult to attribute unequivocally to the action of the drug.

In any case, the ubiquity and relative invisibility of such adverse reactions make it a lot easier to understand why homeopathy has become so popular with patients caught in the tentacles of the medical system, on the one hand, yet so easily dismissed by those who administer that system as ineffective, impossible, or unworthy of serious study on the other. In pointed contrast to allopathic drugs, which are developed solely for their power to force the organism to do what it has no natural inclination to do, homeopathy seeks rather to assist and enhance the innate self-healing capacity that is synonymous with life, continually at work in every patient, and encompasses precisely those same individualizing tendencies, sensitivities, and predispositions that physicians are trained and expected to ignore in our diagnoses, outperform in our research, and override in our treatment.

➤

Homeopathy Lives!

➤

That is also the reason why, even when homeopathic remedies act curatively, the results are simply written off as isolated cases, perhaps "miraculous" at times, but in any case mere "anecdotal evidence" without scientific import and therefore always located on the placebo side of the ledger – because medical science as presently constituted restricts the term "cause" to those interventions that *force* things to happen and measures that power against the idiomatic and somewhat unpredictable tendency of every individual patient to recover without their help.

Even in the case of well-designed RCT's that demonstrate statistically significant benefits from homeopathic treatment, the result still "feels" unscientific and unpersuasive to most clinicians, simply because no such chemical force had to be exerted and no such resistance overcome, while to trained scientists its looser interpretation of causality and its emphasis on subjective and individual variables both disqualify it from serious consideration as a force potent, measurable, and consistent enough to count as "hard science."

For all of these reasons, the standard argument that homeopathic remedies are merely placebos actually cuts both ways. In the first place, it's simply *wrong*. Over and above the evidence I've already presented, I can attest from my own experience that homeopathy has an impressive track record in the treatment of animals, newborn babies, like the one I mentioned, and comatose or unconscious patients, in all of whom the possibility of suggestion is negligible.

Second, if giving placebo, natural remedies, or nothing at all can achieve clinical results comparable to those obtainable with suppressive drugs or crippling surgery, it is difficult to understand why anyone of sound mind would not prefer the cheaper, gentler, and safer alternative, at least to begin with.

Third, and best of all, when homeopathic remedies do act curatively, our patients rightly feel that they have healed themselves and may therefore even wonder if they might have done so on their own, without our help. To my mind at least, that "delicious quandary" is hardly cause for complaint, let alone ridicule. I'm hard put to imagine a better result from a medicine than one more or less indistinguishable from a gentle, spontaneous, and long-lasting cure requiring no further treatment.

Indeed, I submit that the irony lies wholly on the other side, that this optimal response is relegated to the placebo half of the equation, while pharmaceutical drugs are valued and considered effective only to the extent that they can overpower the physiology of as many patients and for as long a time as possible. To me it is absurd and contemptible to boast of standards that prize this kind of brute force over elegance of fit, and subordinate our timeless mission of healing the sick to the modern temptation of manipulating life functions artificially in the name of science, ambition, mastery over nature, or some equally abstract, hypothetical goal that we must accept on faith.

That is why, for the present at least, I am thankful that our cures tend to remain snugly ensconced on the placebo side of things; because until we develop a kinder, more accurate, and inclusive model of causality, and a workable notion of the unified life energy of the patient as a whole, that is precisely where they belong. What the nuclear physicist J. R. Oppenheimer once told a group of psychologists thus seems even more apposite for the medical community as a whole:

> We inherited at the beginning of the Twentieth Century a notion of the physical world as a causal one, in which every event could be accounted for if we were ingenious, a world characterized by *number,* where everything interesting could be measured, and anything that went on could be broken down and analyzed. This extremely rigid picture left out a great deal of common sense which we can now understand with a complete lack of ambiguity and phenomenal technical success. One [such idea] is that the world is not completely determinate. There are technical predictions you can make about it, but they are purely statistical. Every event has in it the nature of a surprise, a *miracle,* or something you could not figure out. Every pair of observations taking the form "we know this and can predict that" is global and cannot be broken down. Every atomic event is individual: it is not in its essentials reproducible.[14]

For all of these reasons, instead of competing with the placebo effect in order to *defeat* it, I have come to believe that the highest goal of medicinal treatment, whether homeopathic or otherwise, is rather to assist and enhance it by doing everything possible to promote healing in its most global sense, not just correcting abnormalities, and by cultivating a deeper and more thorough knowledge of our patients rather than ignoring, circumventing, or overriding what they have to teach us. To that end, while admiring the ingenuity and dedication of my colleagues who design and conduct RCT's to demonstrate the effectiveness

Richard Moskowitz, MD, has practiced as a family medicine physician since 1967. Patient education and advocacy, holistic medicine, and classical homeopathy are integral to his practice. He has written numerous articles and several books, including *Homeopathic Medicine for Pregnancy and Childbirth*, *Plain Doctoring: Selected Writings, 1983-2013,* and *Vaccines: A Reappraisal.* He lives and practices in the Boston, Massachusetts, area.

of homeopathic treatment in the usual way, I offer an alternative model for clinical research, based on the bottom line of self-healing, which is equally relevant for allopathic medicine as well:

1. *Nobody is blinded:* all subjects know whether they are receiving homeopathic or allopathic treatment, having chosen it beforehand, precisely because of their interest, belief, or faith in it.

2. *Nobody gets placebo:* everyone gets the treatment they select, while the doctors giving it out are matched to them by *their* beliefs, and encouraged to use prayer, suggestion, exhortation, shamanic incantation, or whatever they or their subjects believe will most effectively assist them on their healing path. In other words, *each group will serve as the control of the other.*

3. *Using the totality of signs and symptoms over time,* including both subjective and objective criteria, and reports of family, friends, teachers, employers, etc., *both homeopathic and allopathic subjects will be followed for a period of months or years,* depending on the condition, and extending beyond the acute phase to include the chronic dimension. Both groups will then be evaluated as to how well or badly they are measuring up in their own lives, by their own standards and those of their community, and also with respect to appropriate clinical and pathological criteria.

4. *Qualified judges not exclusively or doctrinally committed to either point of view* will then ascertain which form of treatment proves more beneficial in which respects, and will publish the results in a friendly, fair, and unbiased journal of good repute, to be selected and agreed upon in advance.[15]

For myself and my colleagues, homeopathy has stood the test of time as both a method of healing the sick and a *philosophy* of health and disease, a coherent, logical system of thought, derived from the self-evident unity of the life force, a simple truism, and the "Law of Similars," a bold postulate; neither of which follows logically from anything else or is as yet subject to experimental proof or disproof, like ordinary scientific hypotheses, as in Bertrand Russell's whimsical definition: ". . . the point of philosophy is to start with something so obvious as not to seem worth stating, and to end with something so paradoxical that no one will believe it."[16]

I freely admit, as I think most would agree, that homeopathy fits this description admirably. But the authenticity of the homeopathic phenomenon, the enduring relevance of the point of view it offers, and the obvious effectiveness of its minute doses when competently used, together imply the existence of a bioenergetic science that is still in its infancy, one that will undoubtedly add to the natural laws that we already know a whole set of new rules, laws, hypotheses, and predictions as it develops in the future. In that sense, homeopathy also looks beyond itself, to a more open and inclusive conceptual scheme that can accommodate and indeed reconcile both points of view, as well as perhaps others as yet unknown to us. Helping to envision, identify, and elaborate this new synthesis thus becomes our highest mission, which we share with like-minded physicians and healers of all persuasions and in every part of the world.

References

1. Holmes OW. Homeopathy and Its Kindred Delusions. 1847; included in *Medical Essays,* Houghton Mifflin, Boston, 1895, pp. 1-102, *passim*.
2. British Parliamentary Debate, March 29, 2017, UK Citizens Online Democracy, mysociety.org.
3. "No More Homeopathy on the Spanish National Health Service," Reporting the News, Spain, August 3, 2017, rtnnewspaper.com; "The Paradoxical Struggle of Homeopathy in Spain," Association for Natural Medicine in Europe (ANME), November 14, 2016, www.anme-ngo.eu; and "And so it came to pass…," Institute for Homeopathic Medicine, January 2, 2017, instituteforhomeopathic medicine.wordpress.com/spain.
4. Smith K. Against Homeopathy: a Utilitarian Perspective. *Bioethics.* February 2011;14:1-12.
5. Cf. Sampson W. *The Braid of Alternative Medicine.* Prometheus, New York, pp. 21-31; and Homeopathy Does Not Work. *Alternative Therapies in Health and Medicine.* 1995;1:48-52. Cf. also the Health Care Reality Check website, www.hcrc.org: "Dr. Sampson is Emeritus Professor of Medicine at Stanford, Editor-in-Chief of *Scientific Review of Alternative Medicine,* and teaches about unscientific and aberrant medical claims. He sits on the Board of Directors of the National Council Against Health Fraud, and is affiliated with other organizations that protect consumers from bogus healthcare claims and products."
6. Cf. Barrett S. "Homeopathy's Law of Similars" and "Homeopathy's Law of Infinitesimals," Homeowatch Home Page, www.homeowatch.org, posted March 20, 2002; and "Homeopathy: the Ultimate Fake," *Quackwatch* Home Page, www.quackwatch.org, revised August 23, 2009.
7. *Physicians Desk Reference,* 63rd Edition, 2009, Montvale, NJ. Cf., e.g., "Catapres, Overdosage," p. 842: "Hypertension may develop early…"; and "Prozac, Warnings: Clinical Worsening and Suicide Risk," p. 1854: "Patients with major depressive disorder may experience worsening of their depression and/or the emergence of suicidal ideation and behavior…"; *et passim.*
8. Cf., for example, Noiret P. Activity of several dilutions of copper sulfate in different microbial species. Proceedings of the 31st Congress, International League of Homeopathic Physicians, Athens, 1976, pp. 137-147; and Brack A, et al. Effect of ultra-high dilutions of 3,5-dichlorophenol on luminescence of the bacterium *Vibrio fischeri." Biochimica et Biophysica Acta.* 1621:253-260.
9. Cf., for example, Davenas E., et al. Effect on mouse peritoneal macrophages of orally-administered, very high dilutions of *Silica. European Journal of Pharmacology.* 135:313-319; Petit C. Effect of homeopathic dilutions on subcellular enzymatic activity. *Human Toxicology.* 8:125-129; and Shabir S, et al. "Effect of homeopathic drugs on *in vitro* activity of alpha-amylase from human saliva." *Indian Journal of Homeopathic Medicine*. 31:93-98.
10. Cf., for example, Betti L, et al. Effect of high dilutions of *Arsenicum album* on wheat seedlings from seeds poisoned with the same substance. *British Homeopathic Journal.* 1997;86:86-89; and Binder M, et al. Effects of *Arsenicum alb.* 45X on wheat seedling growth. *Forschende Komplementär medizin und Klassische Naturheilkunde.* 12:284-291.
11. Cf., for example, Banerjee P. Comparative efficacy of two dilutions of *Arsenicum album* to ameliorate toxicity by repeated sublethal injections of arsenious trioxide in mice. *Pathobiology.* 2008;75:156; Fisher P. The influence of the homeopathic remedy *Plumbum metallicum* on the excretion kinetics of lead in the rat. *Human Toxicology.* 1987;6:321; Doutremepuich C, et al. Aspirin at ultra-low dosage in healthy volunteers: effects on bleeding time, platelet aggregation, and coagulation. *Hemostasis.* 20:99-105.
12. "200C," or the 200th centesimal dilution, means a dilution on a scale of 1:100, carried out 200 times, for a concentration on the order of 10^{-400}!
13. Cited in Moskowitz R. *Resonance: the Homeopathic Point of View.* Philadelphia: Xlibris; 2001:pp. 14-15.
14. Oppenheimer J R. Analogy in Science. *The American Psychologist*. 2:134, March 1956.
15. Moskowitz, op. cit., p. 342.
16. Russell B. The Philosophy of Logical Atomism. *Logic and Knowledge: Essays, 1901-1950.* London: Allen & Unwin: 1968; p. 193. ◆

Homeopathy Lives!

The Potential Influence of Nutrition on Lupus

by Bill Misner, PhD

Lupus is a chronic inflammatory disease driven and exacerbated by autoimmunity. Patients with lupus have blood antibodies targeted against their body, damaging the skin, blood vessels, heart, lungs, kidneys, joints, brain, and nervous system. Women are more at risk than men; however, lupus is two times more common in Hispanic, Asian, Native American, and African American women than Caucasians.

A whole foods, plant-based diet lessens the inflammation and pain of lupus.

Lupus provokes onset of symptoms that may differ from person to person. The intensity of these symptoms is called a "flare" that may range from mild to severe. Typical symptoms are chest pain upon taking a deep breath, upper respiratory infections, fatigue, fever, hair loss, mouth sores, muscle pain, painful swelling in joints, pale or purple fingers/toes, a red rash on the face (called a butterfly rash), sun sensitivity, swelling in legs, ankles, eyes, and swollen glands. I know these symptoms from having observed their recurring phenomena in my wife for the past 37 years.

Unfortunately, there is no known cure for lupus, only a few medicines or lifestyle changes that may help those who have this disease to tolerate lupus. Patients with lupus must see not only their primary care physician but also other specialists to treat a plethora of specific symptoms such as inflammation, high cholesterol, high blood pressure, heart disease, diabetes, balancing hormones, and recurring infections.

Reducing Inflammatory Substances

Because lupus is a long-term autoimmune disease that induces the body's immune system to become hyperactive in attacking normal healthy tissue, the resultant pro-inflammatory cycle that increases pain throughout the body, which raises individual discomfort and malaise, may be reduced. There are a number of substances that cause inflammation and should be avoided.

- Any common food ingredients that have less than 1-gram fiber to 5-grams carbohydrate ratio (<1:5} including processed sugar (sucrose), processed high-fructose corn syrup (HFCS), processed carbohydrates found in white bread, white pasta, gluten, snack foods, chips, and crackers.[1-6]
- Trans fats, vegetable oils, seed oils, alcohol, and processed meat increase systemic internal inflammation. The high bacteria load in raw or cooked animal foods and fermented foods trigger an endotoxemic surge of inflammation, which is exacerbated by the presence of saturated animal fat. The primary reason increased inflammation results after people consume animal foods is related to dead bacteria releasing their endotoxins absorbed by our digestive system. "Endotoxemic inflammation" is directly associated with eating meat, egg, chicken, and dairy, but does not occur when eating most plant foods. Exposure to a high-fat meal elevates circulating endotoxins irrespective of metabolic state, as early as one hour after a meal.[7-9] Dr. Michael Greger stated: "Though the bacteria can be dead; they can be cooked; but their endotoxins are still there. You can boil meat for two hours straight; dip it in an acid bath (like our stomach); and expose it to digestive enzymes. Bacterial endotoxins have been found to survive both cooking and our bodies' best attempts at acid and enzyme digestion."[10]
- Alfalfa sprouts contain an amino acid called L-canavanine that may increase inflammation in people with lupus by stimulating an overactive immune system.

Increasing Anti-Inflammatory Substances

What anti-inflammatory foods should you eat if you have lupus? In general, you should try to eat a nutritious whole plant food diet that contains fresh fruits, vegetables, rice, beans, nuts, and organic corn. While antioxidant supplements are available, it is rather

the combination of nutrient-rich whole foods high in antioxidants from a diet high in fruits and vegetables that may have the greatest effect rather than through supplements. Examples include nuts, apples, ground flax seeds, prunes, raisins, blueberries, blackberries, beets, red bell peppers, broccoli, Brussels sprouts, kale, asparagus, mushrooms, spinach, and with an emphasis on green leafy vegetables.

Is Remission from Lupus Plausible?

There is an interesting case report of a young lady, who at age 16, was diagnosed with systemic lupus (lupus nephritis). She was in stage 4 kidney failure and was told she had six months to live. Her doctor told her that the best-case scenario with standard treatments was dialysis versus the worst case scenario that she would die. She suffered severe arthritis and debilitating migraines and a typical butterfly rash that went from one cheek to another. She consistently tested positive for lupus. She had chemotherapy for two years straight, once a month. Her lupus went into remission for the first four years while she attended undergraduate school and the first three years in medical school, though she always tested positive for lupus. She was careful and got frequent blood tests, did not go in the sun, was very careful about her sleep and self-care, and was on a low dose medication prescription to ease modest joint pain.

It is generally recommended that people with autoimmune disorders do not go to medical school because of the impact stress and sleep deprivation have on their health. During her third year of medical school, she worked stressful 100-hour weeks; and then during her fourth year, she suffered a severe relapse. She had double vision and collapsed in the clinic one day, then woke up and drove home disoriented and confused. Tests revealed she had new antibodies that were causing blood clots that passed into her brain, causing double vision and a transient ischemic attack, a mini-stroke. Her physicians told her she would be at serious risk for a major stroke for the rest of her life and that she probably wouldn't live to age 50. They also warned her that having children would kill her and that she would have to inject herself with a blood thinner for the rest of her life.

Shortly after her husband put her on an exercise program and a whole plant food diet, she began to have no joint pain, no migraines, felt incredible, was full of energy, even working 30-hour overnight shifts at the hospital multiple times a week. Her lupus blood tests only four months after changing her diet came back negative, while blood clotting tests were on the high side of normal. Her doctors assumed there had been a mistake at the lab. No one ever knew what had happened – it was unheard of, such a dramatic remission. In all documented cases, lupus may be in long-term remission, but the blood tests typically reflect the autoimmune condition, lupus. After more testing every month, she discontinued all meds after one year in 2006. Since then, she has continued completely off meds with healthy blood work that has actually improved over the years. After these events, she decided to have children. Her physicians once again warned her that having a baby would bring the lupus back and kill her. She became pregnant and gave birth to two healthy children in five years.

Who is this lady? She is Brooke Goldner, MD, who is a board-certified physician known worldwide for developing a nutrition-based treatment for her own autoimmune disease, lupus. She is a graduate of the Temple University School of Medicine, was chief resident at UCLA-Harbor's residency program in psychiatry, and holds a certificate in plant-based nutrition from Cornell University. She is the creator of the hyper-nourishing healing protocol for lupus recovery and the bestselling author of *Goodbye Lupus*.[11]

References

1. Grooms KN, et al. Dietary fiber intake and cardiometabolic risks among US adults, NHANES 1999-2010. *Am J Med*. 2013 Dec;126(12):1059-67. e1-4.
2. Schmier JK, et al. Cost savings of reduced constipation rates attributed to increased dietary fiber intakes: a decision-analytic model. *BMC Public Health*. 2014 Apr 17;14:374.
3. Threapleton DE, et al. Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis. *BMJ*. 2013 Dec 19;347:f6879.
4. Baron RB. Eat more fibre. *BMJ*. 2013; 347. A Satija, F B Hu. Cardiovascular benefits of dietary fiber. Curr Atheroscler Rep. 2012 Dec;14(6):505-14.
5. Landberg R. Dietary fiber and mortality: convincing observations that call for mechanistic investigations. *Am J Clin Nutr*. 2012 Jul;96(1):3-4.
6. North CJ, Venter CS, Jerling JC. The effects of dietary fibre on C-reactive protein, an inflammation marker predicting cardiovascular disease. *Eur J Clin Nutr.* 2009 Aug;63(8):921-33.
7. Harte AL, et al. High fat intake leads to acute postprandial exposure to circulating endotoxin in type 2 diabetic subjects. *Diabetes Care*. 2012 Feb; 35(2):375-82.
8. Erridge C. The capacity of foodstuffs to induce innate immune activation of human monocytes in vitro is dependent on food content of stimulants of Toll-like receptors 2 and 4. *Br J Nutr*. 2011 Jan; 105(1):15-23.
9. Deopurkar R, et al. Differential Effects of Cream, Glucose, and Orange Juice on Inflammation, Endotoxin, and the Expression of Toll-Like Receptor-4 and Suppressor of Cytokine Signaling-3. *Diabetes Care*. 2010 May; 33(5):991-7.
10. Greger M. Dead Meat Bacteria Endotoxemia. 2012. https://nutritionfacts.org/video/dead-meat-bacteria-endotoxemia/
11. Goldner B. *Goodbye Lupus*: How a Medical Doctor Healed Herself Naturally with Supermarket Foods. Austin, Texas; Express Results: 2015.

Bill Misner graduated from Indiana University, and later completed both his MS and PhD at the American Holistic College of Nutrition. He is an AAMA board-certified alternative medicine practitioner. He published papers in the American College for Advancement in Medicine (ACAM) journal, *Journal of the International Society of Sports Nutrition* (JISSN), and seven original research papers in past issues of the *Townsend Letter*. Misner wrote *Endurance Nutrition – Finding Another Gear,* Editions I and II of *What Should I Eat? A Food Endowed Prescription for Well Being*, and *Phytonutrition: Finding Fitness for Life!* Misner, age 78, continues to run races from one mile up to 13.1 miles to demonstrate "Practice (what he preaches) really works!"

CALENDAR

Please visit TownsendLetter.com for the complete calendar

JANUARY 31-FEBRUARY 2: 10th INTERNATIONAL ISLA CONFERENCE FOR MEDICAL LASER APPLICATIONS AND REGENERATIVE MEDICINE in San Diego, California. CONTACT: https://www.islalaser-us.com/

FEBRUARY 1-2: CHELATION WORKSHOP in Kuala Lampur. Malaysia. CONTACT: drmaung@hotmail.com

FEBRUARY 3-17: INTENSIVE CLINICAL TRAINING in India. 160+ live cases demonstrated in 2 weeks to show action of homeopathy in gross pathologies. CONTACT: https://homoeopathy-course.com/courses/india

FEBRUARY 7-9: LABORATORY, ENDOCRINE, & NEUROTRANSMITTER SYMPOSIUM in Las Vegas, Nevada. Practical and applicable advanced neuroendocrine training for your integrative practice. Earn up to 14.5 CMEs. CONTACT: www.fx-ed.com

FEBRUARY 7-9: GREAT PLAINS LABORATORY PRACTITIONER WORKSHOPS – Organic Acids Testing and Environmental Toxin Testing in Fort Lauderdale, Florida. Also, **JULY** in Portland, Oregon. CMEs available. CONTACT: 913-341-8949; http://www.gplworkshops.com/

FEBRUARY 12: LDN 2020 CONFERENCES in Nassau, the Bahamas. Also, **MAY 20** in Cape Town, South Africa. CONTACT: https://www.ldnrtevents.com/

FEBRUARY 19-23: FREQUENCY SPECIFIC MICROCURRENT SEMINAR (CORE) in Phoenix, Arizona. Also, **JUNE 15-19** in Tuscany, Italy; **OCTOBER 22-26** in Taiwan. CONTACT: 360-695-7500; https://frequencyspecific.com/

FEBRUARY 25-26: FREQUENCY SPECIFIC MICROCURRENT SEMINAR-SPORTS COURSE in Phoenix, Arizona. Also, **DECEMBER 9-10** in San Francisco, California. CONTACT: 360-695-7500; https://frequencyspecific.com/

FEBRUARY 28-MARCH 1: CNDA 2020 CONFERENCE – New Frontiers in Naturopathic Medicine in Palm Springs, California. CEs available. CONTACT: https://www.calnd.org/newfrontiers

FEBRUARY 29-MARCH 1: FREQUENCY SPECIFIC MICROCURRENT ADVANCED SEMINAR in Phoenix, Arizona. Also, **JUNE 20-21** in Tuscany, Italy; **SEPTEMBER 9-11 (Master Class)** in London, United Kingdom; **OCTOBER 30-NOVEMBER 1 (Master Class)** in Taiwan; . CONTACT: 360-695-7500; https://frequencyspecific.com/

MARCH 5-7: AMERICAN ACADEMY OF ENVIRONMENTAL MEDICINE SPRING MEETING – The Roots of Toxicity in Dallas, Texas. In collaboration with ICIM, IABDM, and IAOMT. AMA Category 1 credits available. CONTACT: http://aaemconference.com/

MARCH 7: CLINICAL TOOLS FOR MENTAL HEALTH in Vancouver, British Columbia, Canada. Online & in person registration options. Earn up to 7 CE Credits. CONTACT: info@collaborativeeducation.ca http://www.collaborativeeducation.ca/vancouver-naturopathic-conference/

MARCH 7-8: ICIM STAFF TRAINING FOR IV THERAPY AND IV DISODIUM EDETATE CHELATION THERAPY in Dallas, Texas. CONTACT: https://icimed.com/

MARCH 9-13: APPLYING FUNCTIONAL MEDICINE IN CLINICAL PRACTICE in Charleston, South Carolina. Up to 34.5 CMEs. CONTACT: 800-228-0622; info@ifm.org; www.ifm.org/afmcp-charleston

MARCH 26-28: THE FORUM FOR INTEGRATIVE MEDICINE – "Solutions for Complex Illness: Putting the Pieces Together" in Seattle, Washington. CONTACT: https://forumforintegrativemedicine.org/

MARCH 27-29: SOUTHWEST CONFERENCE ON BOTANICAL MEDICINE in Tempe, Arizona. Up to 17.5 CE hours for acupuncturists and naturopathic physicians. CONTACT: 541-482-3016; https://www.botanicalmedicine.org/.

MARCH 27-29: FLORIDA HOMEOPATHIC SOCIETY ANNUAL CONFERENCE – The Microbiome and Homeopathic Bowel Nosodes with Hilery Dorrian, LicAc, LCH in Orlando, Florida. CONTACT: https://www.floridahomeopathicsociety.org/

APRIL 2-4: FREQUENCY SPECIFIC MICROCURRENT CORE MODULE 1 – PAIN/INJURY MODULE in Portland, Oregon. Also, **APRIL 24-26** in Denver, Colorado; **MAY 15-17** in Raleigh-Durham, North Carolina; **SEPTEMBER 18-20** in Chicago, Illinois; **OCTOBER 16-18** in Anaheim, California; **DECEMBER 6-8** in San Francisco, California. CONTACT: 360-695-7500; https://frequencyspecific.com/

APRIL 2-4: 17th INTEGRATIVE MEDICAL CONFERENCE FOR CANCER AND CHRONIC DISEASE in Grapevine (Dallas), Texas. Pre-conference training. CONTACT: https://bestanswerforcancer.org/

APRIL 2-5: ENVIRONMENTAL HEALTH SYMPOSIUM 2020 – Immunotoxicity: The Intersection Between Toxic Exposure, Infectious Disease, and Autoimmunity in Scottsdale, Arizona. CMEs available. CONTACT: 855-347-4477; https://environmentalhealthsymposium.com/

APRIL 3-5: SIBOCON2020 – Clinical Applications in San Diego, California. CONTACT: https://www.synergycmegroup.com/sibocon2020

APRIL 5-7: FREQUENCY SPECIFIC MICROCURRENT CORE MODULE 2 – NEURO & VISCERAL in Portland, Oregon. Also, **APRIL 27-29** in Denver, Colorado; **JULY 10-12** in Philadelphia, Pennsylvania; **NOVEMBER 6-8** in Chicago, Illinois; **DECEMBER 3-5**

in San Francisco, California. CONTACT: 360-695-7500; https://frequencyspecific.com/

APRIL 17-18: THE GREAT PLAINS LABORATORY, INC. presents GPL ACADEMY PRACTIONER WORKSHOP in San Diego, California. Organic acids testing, toxic chemical testing, and mycotoxin testing, and more. CMEs available. CONTACT: http://www.gplworkshops.com/san-diego-2020

APRIL 23-26: ACUPUNCTURE MERIDIAN ASSESSMENT (AMA) TRAINING For Doctors, Dentists & Health Professionals: Detecting Parasites, Dental & Fungal in St. Louis, Missouri. Simon Yu, MD, CONTACT: www.preventionandhealing.com**.** 314-432-7802.

APRIL 28-MAY 1: INTEGRATIVE CONGRESS ON INTEGRATIVE MEDICINE AND HEALTH in Cleveland, Ohio. CONTACT: http://www.icimh.org/#home

MAY 2-3: PRIMARY CARE UPDATE FOR NATUROPATHIC DOCTORS in Toronto, Ontario, Canada. Online & in person registration options. Earn up to 11 CEs. CONTACT: info@collaborativeeducation.ca ; http://www.collaborativeeducation.ca/toronto-naturopathic-conference/

MAY 14-16: 28th ANNUAL A4M/MMI SPRING CONFERENCE in Orlando, Florida. CONTACT: 561-997-0112; https://www.a4m.com/

MAY 15-17: 15th ANNUAL JOINT AMERICAN HOMEOPATHIC CONFERENCE – Homeopathy in Pain Management in Orlando, Florida. CONTACT: https://www.homeopathycenter.org/2020-joint-american-homeopathic-conference

MAY 20-24: 12th INTERNATIONAL CONGRESS ON AUTOIMMUNITY in Athens, Greece. Special session on diet and autoimmunity, chaired by Dr. Aristo Vojdani. CONTACT: https://autoimmunity.kenes.com/

MAY 20-24: AUTISM-ONE CONFERENCE – Where Science, Hope, and Recovery Meet in Chicago, Illinois. CONTACT: https://autismoneconference.com/

MAY 28-30: INSTITUTE FOR FUNCTIONAL MEDICINE 2020 CONFERENCE – Advancements in Clinical Research and Innovative Practices in Functional Medicine in Phoenix, Arizona. CONTACT: 800-228-0622; info@ifm.org; www.ifm.org/aic

MAY 29-31: ADVANCED APPLICATIONS IN MEDICAL PRACTICES (AAMP) SPRING EVENT – Chronic Digestive Disorders in Scottsdale, Arizona. CMEs available. CONTACT: https://aampscottsdale.com/

MAY 29-JUNE 1: MEDICINES FROM THE EARTH HERB SYMPOSIUM in Black Mountain, North Carolina. CE credits for nurses, acupuncturists and naturopathic physicians. CONTACT: 541-482-3016; https://www.botanicalmedicine.org/.

JUNE 12-14: INTERNATIONAL CONGRESS OF REGENERATIVE MEDICINE on Captiva Island, Florida. CONTACT: https://www.icrmconference.com/

JUNE 12-14: THE GREAT PLAINS LABORATORY, INC. presents GPL ACADEMY MASTER PRACTIONER WORKSHOP in Kansas City, Missouri. CONTACT: http://www.gplworkshops.com/kansas-city

JUNE 20-27: CLINICAL AND COMPARATIVE MATERIA MEDICA @ Allen College of Homeopathy in the United Kingdom. On-site or interactive online course. CONTACT: https://homoeopathy-course.com/courses/england/7-day-summer-school

AUGUST 27-30: ACUPUNCTURE MERIDIAN ASSESSMENT (AMA) TRAINING For Doctors, Dentists & Health Professionals: Detecting Parasites, Dental & Fungal in St. Louis, Missouri. Simon Yu, MD, CONTACT: www.preventionandhealing.com. 314-432-7802**.**

SEPTEMBER 11-13: FREQUENCY SPECIFIC MICROCURRENT MASTER CLASS in London, United Kingdom. CONTACT: 360-695-7500; https://frequencyspecific.com/

OCTOBER 9-11: ADVANCED APPLICATIONS IN MEDICAL PRACTICE (AAMP) FALL EVENT – Immunology in Seattle, Washington. CMEs available. CONTACT: https://aampseattle.com/

OCTOBER 31-NOVEMBER 1: ARIZONA NATUROPATHIC MEDICAL ASSOCIATION CONFERENCE – Neurological and Musculoskeletal Issues in Scottsdale, Arizona. CONTACT: https://www.aznma.org/

◆

Notices

Correction Notice

In Dr. Alan Gaby's November 2019 "Literature Review and Commentary," reference 1 on page 26 at the end of the column is incorrect. The correct reference is

Wickens K, et al. A differential effect of 2 probiotics in the prevention of eczema and atopy: a double-blind, randomized, placebo-controlled trial. *J Allergy Clin Immunol*. 2008;122:788-794.

◆

Notice of Plagiarism

Editor's note: Dr. Alan Gaby notified us that a large portion of a letter to the editor, "Vitamin C and Kidney Stones: A Comment" by Michael J. Gonzalez et al (December 2019) was taken verbatim, without attribution, from chapter 22 of his textbook, *Nutritional Medicine*. The authors of this letter to the editor acknowledge that this was the case, and they regret their error.

◆

Book Excerpt | Book Excerpt | Book Excerpt

Is Health Care Fixable?

by Travis Christofferson

The following excerpt is from Travis Christofferson's book *Curable: How an Unlikely Group of Radical Innovators Is Trying to Transform Our Health Care System* (Chelsea Green Publishing, October 2019) and is reprinted with permission from the publisher.

I became part of the health care system in the summer of 2017. Three years earlier I had published a book titled *Tripping over the Truth: How the Metabolic Theory of Cancer Is Overturning One of Medicine's Most Entrenched Paradigms*. The book illuminates the emerging work of a small group of scientists who are offering an alternative explanation for the origin of cancer and, critically, a new treatment paradigm centered on targeting cancer though metabolism rather than genetics. The book's modest success led me to all sorts of interesting people and interesting opportunities. One such opportunity occurred while I was giving a talk for a small charity event in London. The charity had organized a one-day event focused on the promise of metabolically active cancer treatments. One of the other speakers was Ndaba Mazibuko, a practicing medical doctor at a start-up called Care Oncology Clinic located in London. He began his talk by explaining that the clinic had been conceived to address a well-characterized problem in oncology. That is, that there are numerous off-patent, generic medications with regulatory approval for the treatment of other diseases that could be "repurposed" to treat cancer.

There was no good reason why this had not yet been done, other than lack of financial incentive. The research to support using these drugs for cancer was vast, yet because the medications had aged off their patents the health care system provided no incentive either for physicians to prescribe them or for pharmaceutical companies to usher them through the necessary trials to win formal approval for their use in cancer. To address this problem, Care Oncology made the bold decision to open a clinic and offer a combination of four carefully selected, metabolically acting, generic medications to patients with cancer. The medications, Mazibuko explained, had to meet several criteria. Because cancer patients are going through so much already, they had to have very minimal side effects; minimal interaction with standard-of-care therapies (they don't get in the way, in other words), and abundant evidence to suggest they could help improve outcomes when added to the standard therapeutics the patients would also be receiving. From a patient's perspective, especially those with a dire prognosis, it made lots of sense – very little risk and a potentially large benefit.

The doctors at Care prescribed the medications in their Care Oncology Clinic protocol (COC Protocol) "off-label," meaning the drugs were being prescribed for a disease other than that for which they had received formal regulatory approval. Importantly, the four-drug protocol was administered only as an *adjunctive* therapy, meaning the treatment was to be taken alongside the standard of care, never competing with or replacing it. And the mechanistic data unequivocally backed this strategy: By targeting critical metabolic pathways exclusive to cancer cells, the drugs weakened the cells in a way that made standard therapies more effective. In addition to treating patients, Care Oncology would also conduct a formal "real-world" clinical trial to measure the outcomes of their patients, adding to the existing body of evidence supporting the treatment.[1] Additionally, and this is critical, in using off-label drugs in their trial, Care could take advantage of the generic price of the medications. A sort of clinical trial in reverse. If it worked, eventually enough data could be

accumulated to win US Food and Drug Administration (FDA) approval for a treatment comprised of a handful of generic drugs. This had never been done. A generic drug had never won FDA approval for a new disease indication without a pharmaceutical company first tinkering with it in a way that garnered them a new patent (varying the arrangement of a few atoms in the drug or switching the delivery method, for example). By cutting pharmaceutical companies out of the loop, the savings would all pass directly to the patients.

I loved this model.

In the end, we struck up a collaboration. I would help bring Care Oncology to the United States. I had already started a research foundation in 2012 to support the "financially stranded" therapies I had highlighted in my first book: the ketogenic diet, exogenous ketones, fasting before the administration of chemotherapy or radiation, repurposing off-patent drugs, and hyperbaric oxygen, to name a few. All these therapies hold tremendous promise yet linger in a financial purgatory – again, mostly because it is difficult to patent them. My foundation supported research for the *future* use of these therapies. But here, with Care, there was an opportunity to do something tangible and immediate, to offer patients one of these promising treatments *right now*. I was all in. But I didn't realize how difficult it would be.

A year later a close friend and I opened the first US clinic in my hometown of Rapid City, South Dakota. Rapid City is a small, conservative community, but I had hoped the oncologists at the local cancer center would embrace this new treatment option for some of their patients, especially those with an almost always terminal diagnosis such as glioblastoma, the viciously aggressive form of brain cancer that took the life of John McCain. The director of the cancer center was receptive. He set up a time for me to present to the oncologists and other staff. In a small room packed with nurses, the head pharmacist, the medical director, and numerous medical and radiation oncologists, I went through a twenty-minute slide presentation detailing the logic and data supporting the use of the drugs in the COC Protocol. Immediately after I finished, one of the radiation oncologists sitting to my right launched into a rant that had nothing to do with the presentation. "We have all gone through medical school, we understand clinical trials, and, frankly, I'm offended you don't think we do," he said. I had no idea how I had offended him. I had simply presented the rationale behind Care's treatment and the data that supported it. The director, who seemed slightly taken aback, intervened to diffuse the tension. Even so, the oncologist flung another accusation. "I see what you're doing here. You're taking advantage of desperate people." I was befuddled by his reaction and didn't know what to say. The fee Care charged was minimal, the four drugs combined cost patients $60 per month. The mission of the company was to "capture" the generic price of the meds through their off-label use. From a cost perspective, operating within the current "patent-centric" health care system, Care's model seemed to be a revelation. And we had just gone through slide after slide of massive blocks of data, including internal data from Care's ongoing trial in the UK that suggested that the four drugs could improve outcomes with very little risk and few side effects.

The tension was palpable. After a flurry of questions from the other attendees, the radiation oncologist, still apparently smoldering, spoke up again about one of the medications in the COC Protocol, a drug approved for type 2 diabetes called metformin. "And why would you use a drug for type 2 diabetes in cancer?" he asked. Before I could answer, a medical oncologist, standing in the far corner, said, "I sometimes prescribe it to help prevent recurrence."

This disturbing encounter sparked my motivation for writing my latest book *Curable*. Who was on the right side? Was Care Oncology doing the right thing? Were we solving a problem that was truly in patients' best interest? Oncology – and medicine as a whole – is only about measuring the effectiveness of a treatment and weighing it against the risk. Yet, as easy as this sounds, it is anything but. How often is this delicate equation subverted by human irrationality? And, in this modern medical era that we like to believe we live in, how could such a massive chasm in knowledge exist between two oncologists – in the same room, from the same hospital? One baffled by why a type 2 diabetes drug would ever be prescribed for cancer and another sufficiently confident in the data supporting its off-label use in the prevention of recurrence.

As I lay out in *Curable*, the answers to these questions can be uncomfortable. In medicine, an antiquated culture that has always protected a physician's autonomy, intuition, and self-reliance above all else, the fallibility of the human mind often goes unchecked. The truth is we have an extraordinarily complex health care system that often relies on a physician's intuition in making critical decisions – an intuition, which psychological research shows, can at times be terribly flawed.

No one is questioning the ability of our nation's doctors, and my book does not aim to demonize doctors for making the "wrong" decisions. This country's physicians are incredibly well-trained, smart, and well-intended people. They are our nation's best. But we are at a turning point in the history of medicine at which the complexity of medicine is challenging the capability of the human mind. As we move into the future, medicine will require evidence-based systems to answer these increasingly difficult questions. My hope is that *Curable* will help, even in a small way to clarify the path forward.

Travis Christofferson, MS is a science journalist and health care advocate. He is the author of *Curable* (Chelsea Green Publishing, October 2019) and *Tripping over the Truth,* which is now available in paperback. He lives in South Dakota.

References

1. Health Clinics Limited. Study of the Safety, Tolerability and Efficacy of Metabolic Combination Treatments on Cancer (METRICS). https://clinical trials.gov/ct2/show/NCT02201381?term=metformin+mebendazole&cond =cancer&rank=1.

◆

Harmal: The Genus Peganum

review by Jacob Schor, ND, FABNO

Harmal: The Genus Peganum by Ephraim Lansky, Shifra Lansky, and Helena Paavilainen
CRC Press, New York, London, Boca Raton
2017; 241 pp; hardback ($155); eBook ($77.50)

Ephraim Lansky sent me his new book in the mail from Israel, but it's taken me months to read it. Lansky is the medical doctor from the US who immigrated to Israel and first popularized pomegranate for breast cancer. His wife Shifra has probably still not forgiven me. She took offense at the way I described her husband in a 2006 issue of *Naturopathy Digest*:

> At NCNM, every class had what I used to refer to as their "hippy": the brilliant and perhaps eccentric student who, while the rest of us tried to look like doctors and adjusted to wearing ties and white coats, somehow got away with dreadlocks and a tie-dyed wardrobe. Every so often, you meet an intelligent mind more creative than you would ever hope to be, who sees the world in a way you never will. I bet Einstein fell into this category when he was a student. Whether we say the fellow "marched to the beat of a different drummer" or the guy took the "road less traveled," Ephraim Lansky was probably not your typical medical student. I don't know what Lansky looked like when he graduated from the University of Pennsylvania's Medical School in 1982, but he certainly looks a bit fringe now.[1]

I countered her complaints by sending an old photo of him I downloaded online from a website that advocated the medical use of psychedelic drugs. I didn't hear further from her, but Lansky and I have stayed in touch. He has gone on to earn both a PhD in pharmacognosy and an MBA. He has co-authored several scholarly books on medicinal herbs that include volumes on capers, figs and, of course, pomegranates.

The new book titled *Harmal: The Genus Peganum* is also rather scholarly, the sort of book that makes excellent bedtime reading if you are plagued by insomnia. It is volume 20, part of a series called *Traditional Herbal Medicines for Modern Times* that is being published by CRC Press. The back cover suggests that the book will be an invaluable addition to the personal libraries of professional pharmacognosists, botanists, physicians, psychologists and all persons interested in the interrelationship of consciousness, medicine, and coevolution.

It's something of a boring book, targeting mostly PhD sorts who might take pleasure in obsessing about the minutiae of plant classification. That sentence may have put me back on Shifra's blacklist. Particularly as she is listed as a co-author on the book cover along with Helena Paavilainen. Apparently the beautiful watercolor painting reproduced on the cover of someone riding a flying carpet was painted by their daughter Zipora Lansky.

Boring, yes, but keep in mind I tend to read murder mysteries that are plot driven. This book feels important to me in something of a serendipitous way. Serendipity is a word Lansky likes to use by the way.[2]

Three things happened in close chronological proximity that made me sit up and take notice. I had recently proofread a paper by Benton Bramwell, ND, that has subsequently been published in the *Natural Medicine Journal* (NMJ) on the herb *Arum palaestinum*.[3] I had also written about vanillin both as a December 2018 blog in *NMJ*[4] and as a full-length article for the *Townsend Letter*.[5]

Shortly after my vanillin blog was published in *NMJ,* I heard from a fellow named Preston Douglas, a PhD pharmacist who told me that the company he worked for, Hyatt Science, had developed an herbal product that I would find interesting because it contained vanillin. However, it contained more than vanillin; there were two other ingredients, *Harmal peganum* and *Arum palaestinum.* That felt like more than coincidence.

I was already primed to pay attention to Palestinian herbs as my daughter Sophie Schor had acted as my personal tour guide of Israel and the West Bank a few months prior. We had toured the Natural History Museum of Palestine in Bethlehem and been guided through the desert by a man whose family had lived in a desert cave for generations. He had pointed out these and many other unfamiliar herbs to us.

Jacob Schor, ND, (left) and his desert guide

I was thus not too surprised when I attended the annual conference of the Oncology Association of Naturopathic Physicians (ONCANP) mere weeks later where Paul Saunders, ND, who, by the way, also has an PhD in botany, focused his annual lecture on this very herbal combination. Dr. Saunders quoted a 2013 thesis written by a student in Nablus on these two herbs that suggested they were non-toxic but would trigger apoptosis in several cancer cell lines. A 2015 study reported that a combination of *Arum palaestinium*, vanillin, linoleic acid and beta-

sitosterols eradicated prostate cancer cells while the individual ingredients had no effect.[6] Other studies suggested that an extract of Arum acted against breast cancer, lymphoblastic leukemia, and prostate cancer.[7,8]

I came home for the ONCANP conference and picked Lansky's book back up. Harmal is the tricky herb in this mix. Harmal is a hallucinogen and has been used for this action in traditional Persian medicine. It's the warp drive that gets flying carpets to lift off the ground.

In their 1989 book, *Haoma and Harmaline*, the linguistic scholars, David Flattery and Martin Schwartz, put forth a rather fascinating theory, that *Harmal peganum* is the same herb as Avestan haoma that is mentioned in the ancient Persian Zoroastrian texts and that "haoma" in turn is likely the "soma plant" mentioned in ancient Vedic texts; both plants are famously special plants employed in religious ceremonies, plants whose exact identities have been lost over time.[9]

There is one word in Lansky's book that makes the entire book worth reading. The word is entheogenesis and we should note right now that harmal's chief action is entheogenic.

The term entheogenic was invented in 1979 by a group of ethnobotanists and scholars of mythology as a way to describe the action of psychedelic drugs and differentiate certain uses that were not recreational. *Entheos* is a Greek term for 'the God within' and is the root for the term enthusiasm. *Genesthe* means to create as in generate or genesis. Thus, an entheogen is a substance that generates the experience of God, or divinity within oneself. Humankind has been using various plants to trigger entheogenic experiences long before there was such a thing as organized religion. Some have theorized that inebriation with entheogenic plants is what eventually gave rise to religion.

The seeming value of entheogenesis, of generating this internal experience, is that it may trigger some shift in perception and allow a physiologic shift that allows healing. At its least, the entheogenic experience may give the individual a perspective on their life journey imbuing it with meaning.

Lansky notes that a now popular entheogenic brew called ayahuasca, which is made from *Baniteriopsis caapi,* contains harmala alkaloids, similar to those found in *Harmal peganum*. In Zoroastrian rituals, haoma (which Lansky and others argue is *Harmal*) is often blended with several companion plants: in particular, Ephedra*, Punica granatum* (pomegranates) and *Ruta graveolens*.

I have either a sneaking suspicion, or better, a deep intuition that we are going to hear a lot more about these plants, in particular, *Harmal peganum* soon. This little book may become a classic you wish you had on your shelf.

References

1. Schor J. Pomegranate People: The Alchemist and the Capitalist. *Naturopathy Digest.* April 2006. http://www.naturopathydigest.com/archives/2006/apr/schor.php
2. Goodman S. Israel's Mr. Pomegranate. *Israel 21c.* September 18, 2005.
3. Bramwell B. Arum palaestinum as a Food-Medicine. *Natural Medicine Journal.* February 2019.
4. Schor J. Vanillin Found in Jars in Ancient Tomb Leads to Questions on Its Use on Inflammation. December 31, 2018.
5. Schor J. Vanilla: the next curcumin? *Townsend Letter.* June 2019.
6. Cole C, et al. Arum Palaestinum with isovanillin, linolenic acid and β-sitosterol inhibits prostate cancer spheroids and reduces the growth rate of prostate tumors in mice. *BMC Comp Alt Med.* 2015;15:264.
7. Husein AI, et al. *In vitro* antioxidant and antitumor activities of six selected plants used in the Traditional Arabic Palestinian herbal medicine. *Pharm Biol.* 2014;27:1-7.
8. Vishwakarma V, et al. Potent Antitumor of a Combination of Three Nutraceutical Compounds. *Scientific Reports.* November 2018;8(1).
9. Flattery DS, Schwarz M. *Haoma and Harmaline: The Botanical Identity of the Indo-Iranian Sacred Hallucinogen "Soma" and Its Legacy in Religion, Language, and Middle Eastern Folklore.* University of California Publications Near Eastern Studies. Berkeley: University of California Press. https://archive.org/details/HaomaHarmaline/page/n3

◆

Townsend Letter

ISSN 1940-5434

Subscriptions • Editorial • Advertising

360/385-6021

24 Hr. Fax – 360/385-0699

911 Tyler Street

Pt. Townsend, Washington 98368-6541 USA

http://www.townsendletter.com | info@townsendletter.com

Editor-in-Chief	Jonathan Collin, MD
Publisher	Jonathan Collin, MD
Editor	Jule Klotter
Contributing Medical Editor	Alan Gaby, MD
Managing Editor	Barbara Smith
Circulation Manager	Joy Reuther-Costa
Managing Assistants	Julie Reuther; Jill Tomasi
Advertising Projects & Accounts	Barbara Smith Joy Reuther-Costa Jonathan Collin

Columnists & Writers
Majid Ali, MD
Eleonore Blaurock-Busch, PhD
Jim Cross, ND, LAc
Nancy Faass, MSW, MPH
Peter A. Fields, MD, DC
Alan R. Gaby, MD
Michael Gerber, MD, HMD
Robert Goldman, MD, PhD, DO, FAASP
Ira Goodman, MD
Tori Hudson, ND
Ronald Klatz, MD, DO
Ingrid Kohlstadt, MD, MPH, FACN
Sarah A. LoBisco, ND
Marianne Marchese, ND
Alan B. McDaniel, MD
Ralph W. Moss, PhD
Judyth Reichenberg-Ullman, ND
Jacob Schor, ND, FABNO
Pamela Smith, MD
Jacob Teitelbaum, MD
Jade Teta, ND
Keoni Teta, ND
John Trowbridge, MD
Robert Ullman, ND
Rose Marie Williams, MA
Elaine Zablocki

Contributing Writers
Katherine Duff
Bob Frost
Gary Null, PhD

Layout & Design
Barbara Smith/Sign Me Up! Inc.

Design Team
Jonathan Collin
Joy Reuther-Costa
Barbara Smith

Cover Photo Credit
Chris De Lorenzo

Printing
Dartmouth Printing Company

Website Design & Maintenance
Joy Reuther-Costa

Published by
Townsend Letter for Doctors & Patients, Inc.
Jonathan Collin, President
Deborah Nissen-Collin, Vice-President

Disclosure: The *Townsend Letter* publishes information about alternative medicine written by researchers, health practitioners, and patients. As a forum for the entire alternative medicine community, we present information discussing a wide variety of alternative and integrative medicine practices. In addition to publishing original research and literature abstracts and reviews, we encourage case studies and anecdotal reports. Detailed anecdotal reports are not viewed as proof but as possibilities that need further investigation. All authors are requested to submit their reports to other professionals for review.

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

Latest FDA Draft Guidance on Homeopathy

On October 24, 2019, the US Food and Drug Administration (FDA) announced that it was withdrawing the Compliance Policy Guide 400.400, "Conditions Under Which Homeopathic Drugs May Be Marketed," which had been in effect since May 1988.[1] The agency also revealed a revision of a 2017 draft guidance for FDA staff and industry: "The draft guidance details a risk-based enforcement policy prioritizing certain categories of homeopathic products that could pose a higher risk to public health, including products with particular ingredients and routes of administration, products for vulnerable populations, and products with significant quality issues." Vulnerable populations include infants and children, pregnant women, immunocompromised people, and the elderly.

FDA is pursuing its new "risk-based" approach in response to the rapid growth of the homeopathic industry. The October press release points out that homeopathic products are made from a variety of substances, including poisonous or toxic substances, that can be harmful if poorly manufactured. When manufacturing practices are poor or inexact, these substances can be detected in the product; they are not homeopathic. FDA sent Newton Laboratories a warning letter this year for mislabeling and for failing to have manufacturing controls in place that ensure the potency and identity of ingredients used in homeopathic products designed for children. These products included potentially toxic ingredients such as belladonna, nux vomica (source of strychnine), *Aconitum napellus*, and *Gelsemium sempervirents*. (I don't know if the letter was simply precautionary or stemmed from a report of an actual adverse event.)

Homeopathic products that are not used topically or orally – such as eye drops – are also seen as a risk. This year, FDA sent warnings to four companies that jointly produced a homeopathic eye drop product (Puriton Eye Relief Drops) that was manufactured in non-sterile conditions.

FDA also has labeling concerns. Some "homeopathic" products are not true homeopathics; they do not follow traditional homeopathic dilution principles. Other homeopathic products are being marketed as alternative treatments for serious or life-threatening conditions.

The American Institute of Homeopathy, North American Society of Homeopaths, National Center for Homeopathy, and Americans for Homeopathy have been keeping a close eye on the FDA's policy change. In their initial response to the October 2019 revised draft, the groups expressed their support for FDA's role in enforcing good manufacturing practices and for ensuring that labels are accurate.[2]

After further review of the revised draft, Americans for Homeopathy Choice began to campaign for a 180-day extension to FDA's comment period (scheduled to end in January 2020): "The new Draft Guidance, if adopted, will allow the FDA to withdraw even properly manufactured and labeled homeopathic medicine from the marketplace."[3] In particular, *Belldonna, Nux vomica,* and other commonly used homeopathics derived from toxic substances that, in a diluted, homeopathic dosage, address a multitude of common symptoms could be withdrawn. FDA wants to treat homeopathic medicines like new drugs that go through the same testing for effectiveness and safety as pharmaceuticals. Since homeopathic medicines are unpatentable (being derived from natural sources), withdrawal would become a permanent ban in the US.

Accurate labelling and good manufacturing processes are laudable and necessary. Homeopathic medicines, like supplements, nutraceuticals, and pharmaceuticals, should adhere to both. But treating traditional homeopathic products, products that have been on the commercial market for over a hundred years (in the case of Hyland's homeopathics), like a major risk to the public is deceitful and goes against the US Food, Drug, and Cosmetic Act of 1938, which recognized the Homeopathic Pharmacopoeia of the United States (HPUS) as the authority on safe and effective homeopathic medicines. Homeopathic products, including long-used homeopathic dilutions of toxic substances, have a far better safety record than commonly used over-the-counter drugs such as acetaminophen.

It is difficult not to view the proposed draft guidance as a way to stem the rising popularity of homeopathy and protect the pharmaceutical industry from competition.

Jule Klotter

References

1. Sharpless NE, Woodcock J. Statement on the agency's efforts to protect patients from potentially harmful drugs sold as homeopathic products. October 24, 2019.
2. Joint Statement: Statement Regarding the FDA's Notice of Withdrawing Compliance Policy Guide Sec. 400.400 for Homeopathy. October 26, 2019.
3. Americans for Homeopathy Choice. Update on Latest FDA Draft Guidance on Homeopathy. December 2, 2019.

◆

Pediatric Pearls

by Michelle Perro, MD

Depression in a Teenaged Girl: Not Just Skin Deep

As integrative physicians, many of us have "pet peeve practices" that are residuals from our conventional medical training. The longer I practice, the longer my list; but there are certainly a few standouts in the crowd.

Kylie came to my practice as a 15-year-old girl, accompanied by her mom, with the chief complaint of "depression." This diagnosis is certainly not uncommon in our pediatric practices with mental health complaints hovering around 46% of teens aged 13-18 years old. As we began to uncover her medical history and medication list, two glaring positives emerged: a history of moderate acne and its concomitant traditional pharmacologic treatment approach and chronic constipation. (One-third of visits to pediatric GI docs is for constipation!)

Acne can be a debilitating disease, appearing around puberty, just as teens try to fit it and not be outliers with scarred faces. Even mild acne can seem like a volcanic eruption to a young teen, so patients with acne should be treated with CSI thoroughness. Kylie had a cystic component of her acne, but it was mostly comprised of whiteheads and blackheads. She tried topical therapy, including benzoyl peroxide and clindamycin, which helped somewhat; but the positive effect diminished upon stopping therapy.

Here's where the great divide comes into play between conventional and functional care. The patient was prescribed oral birth control pills (OCPs), a standard Western practice, especially when birth control is being considered in addition to the acne treatment. Kylie was started on OCPs when she was 13, one year after the onset of her menstruation (additionally, she was not sexually active). What is called into question is the cavalier usage of OCPs in young women with a disorder that can be approached via its root cause, particularly in a teen that is not sexually active.

There are three types of OCPs presently prescribed containing estrogen/progesterone combinations, and she received a low dose estrogen/synthetic progestin (drospirenone) and combination hormone therapy, which is what's recommended in conventional medicine.

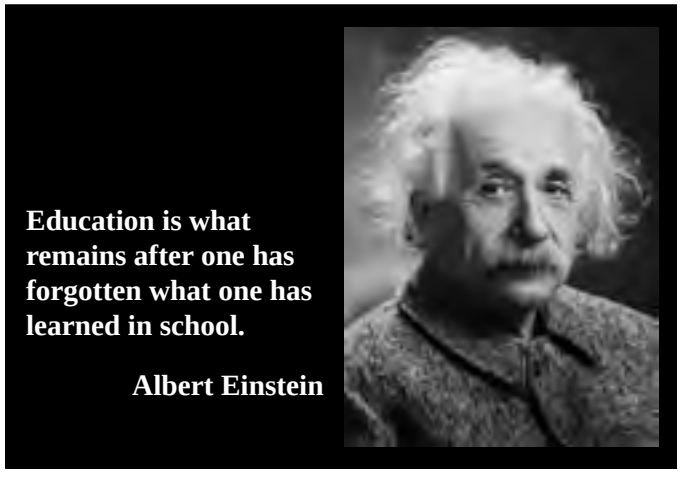
After the first few months of treatment, her acne improved; and she had a quiet skin period. However, after six months of treatment, the patient developed acute onset of depression and fatigue (which was thought to be secondary to her depression). She was then prescribed a SSRI, gained weight, and got further depressed.

Time to get off the pharmacologic merry-go-round….

As our colleague Dr. Ross Pelton reminds us (*Townsend Letter*, November 2019), OCPs are associated with significant nutrient depletion. After six months of oral contraceptives, there can be a decrease in vitamin B6 with depleted tryptophan and, hence, lower serotonin, which can certainly lead to depression. A SSRI is likely the worst treatment for this young girl with further brain serotonin depletion. Not to mention, OCPs can also cause a decrease in folic acid, vitamin B12, magnesium, selenium, and CoQ10; all are required for energy production, which could certainly account for her fatigue.

Deep in the rabbit hole….

During my time on the front line, I have seen mainly kids with gut issues that do not have skin problems. However, show me a skin disorder and there is gut pathology; so once again we ➤



Pediatric Pearls

➤

start with the gut. What has really caught my eye was the gut-brain-skin axis, written about initially in 1930![1] In the past decade, there is recognition that acne vulgaris is frequently associated with depression as well as anxiety; these relationships are making their appearance in the relatively new field of psychodermatology. Additionally, acne patients have a higher association with constipation and reflux, noted in a study of over 13,000 teens. And as one can predict, the role of the microbiome, first noted in 1910,[2] and microbes such as Lactobacillus strains, which "improved depressive symptoms in adults with melancholia," are prominent.

From the literature, there have been links reported between constipation and acne. Patients with constipation have been shown to have lower levels of *Lactobacillus* and *Bifidobacterium*.[3] Research also reveals that alterations in the microbiota can cause changes in microglial gene function and expression. Gut microbes are metabolically very active, and their by-products may be classified as metabolic response modifiers. These metabolites have been shown to affect behaviors, such as autism-like conditions, in mice. As we begin to unravel the complexities of the gut-brain axis, modulation of the microbiome and its metabolites could become a cornerstone therapy in the treatment of disorders such as depression, acne, and constipation.

Data is just beginning to emerge indicating changes in the gut microflora directly from OCPs as well; however, the mechanism is not fully understood. We do note from a concerning study reported in 2012 in the *BMJ*[4] that OCPs were associated with Crohn's disease and with ulcerative colitis in women that had smoked.

Back to our gal….

A lot of work evolved in Kylie's care undoing the damage already done. After having mom leave the room, discussions of her sexual activity ensued and whether she could come off OCPs without worrying about an unwanted pregnancy. (Fifteen is the average age of sexual activity in the US.) After a contract was drawn between us and a donation of a significant number of condoms in her backpack, Kylie reported not to be sexually active. We stopped the OCPs as a first line of business.

I also started a topical *Streptococcus thermophilus* probiotic (which can increase ceramides and trap moisture in the skin) as well as an oral probiotic focusing on *Lactobacillus paracaseii* and *Bacillus coagulans*, microbes shown to be beneficial in the treatment of acne. We began her on a multivitamin and mineral supplement as well as CoQ10. After several months, her skin showed improvement and her constipation was marginally better. We did a trial of a gluten- and dairy-free diet as well as working on her water consumption, and those modifications improved her constipation.

Lastly, we did an SSRI taper over several months while increasing the aromatic amino acids in her organic diet and brought in a homeopathic combination remedy for depression (Elevate, DesBio) and Bach Flower remedies for stress since by this time Kylie was a junior in high school and under a lot of academic pressure.

After six months of treatment, her mood and constipation were markedly improved; and her acne was 80% better. The homeopathic remedy *Calcarea sulfuricum* 30c cleared the rest of her skin. Kylie is now in her first year of college with a beautiful smile, clear skin, and happy gut.

References

1. Stokes JH, Pillsbury DH: The effect on the skin of emotional and nervous states: theoretical and practical consideration of a gastrointestinal mechanism. *Arch Dermatol Syphilol*. 1930; 22: 962-93.
2. Dinan T, Cudmore S. Probiotics for Mental Health and Wellbeing. https://pdfs.semanticscholar.org/18d7/a7ac2dd09f5a241072896262e978169392e2.pdf.
3. Khalif IL, et al. Alterations in the colonic flora and intestinal permeability and evidence of immune activation in chronic constipation. *Dig Liver Dis*. 2005, 7: 838-49.
4. Khalili H, et al. Oral contraceptives, reproductive factors and risk of inflammatory bowel disease. *Gut*. 2013;62:1153-1159.

◆

Ask Dr. J

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

Intermittent Eating/Fasting?

Convincing patients to buy into our unique functional/restorative paradigm of medicine is a precarious business. It is also totally necessary for optimal clinical results and may be the real art of our medicine. If patients are uncomfortable with my recommendations, they will most definitely not follow them**.** Unfortunate fact: even if they are comfortable with my treatment suggestions, they still may choose to either do nothing (which is actually doing something) or to haphazardly follow them, which usually results in lackluster results. I basically feel that I need to be an effective promoter like P.T. Barnum to achieve excellent patient compliance.

I have incorporated an interesting paradigm into my daily health regimen: intermittent fasting. For me, I feel that this technique allows my body to manifest many positive outcomes: lower insulin levels, maximum burning of fat for cellular energy, and decreased fat deposition in key bodily areas to name just a few. I also am attempting to convince most of my patients to follow some modified version of this food regimen. The problem: Americans do not like to feel deprived of one of the two most pleasurable pastimes available to them. Fasting implies not eating. Not eating means lower amounts of dopamine, which leads to depression, which translates into poor patient compliance or BUMMER.

I was cooking dinner and indulging in a stimulating conversation with a friend of mine, Monte Gores, DAOM, in October. We were conversing on a number of health-related topics pertaining to our patients. Fortunately, we moved into intermittent fasting. We looked at one another and realized that fasting is a term of deprivation. We needed a new phrase that made people feel positive about what we want them to incorporate into their lifestyle. Hence, Intermittent Eating/IE sprang into being.

Now I recommend to my patients that they intermittently eat. I explain this concept in two ways. One I want them to eat only two meals/day in a six-to-eight-hour window with no snacking. The other is I want them to not eat in a 14 -18-hour window between the second meal and the first meal. For me, I attempt to eat my first meal around 11 AM and my second meal around 7 PM. This gives me a 16-hour window of no solid food with ample amounts of liquid, usually water and green tea.

What results am I seeing with patients whose conditions were previously recalcitrant despite multiple other therapeutic interventions?

- A 48-year-old woman has finally started to lose approximately one pound/week plus she feels less tired overall.
- A 56-year-old woman diagnosed with Type II diabetes was able to slowly lower the dose of her metformin, blood pressure drugs, and sleep aids so as to be drug free after six months.
- A 33-year-old man with multiple complaints (chronic fatigue, sleep apnea, horrendous bowel gas, tremendous abdominal bloating) felt all the above improved by 50% in the first month and were 90% improved after three months.
- A 16-year-old female had football-sized bloating of her stomach after nearly every meal plus severe GERD. After one week, the bloating was 50% improved. After one month, the GERD was 50% improved and the bloating negligible.

I would be remiss if I suggested that everybody is curing whatever malady ails them with IE. Some of my patients have attempted to incorporate IE into their daily routine and felt absolutely no difference. Most people have some degree of positive improvement. Three primary areas of difficulty that decrease overall compliance are other people's attitudes and opinions, learning to not eat every hour or two, and overcoming their mother's influence.

Unfortunately, like certain anatomical appendages that everyone possesses, all people have opinions, which they share to a greater or lesser degree. For those deep sharers,

➤

➤

hearing that their friend/relative/acquaintance has begun to IE will send them into a twitter storm reminiscent of a certain modern politician. They will berate my patient until many times they cry "uncle" and just give up IE. To paraphrase Paul Simon's song lyrics, a person hears what they want to hear and disregards the rest. These deep sharers have firmly entrenched opinions that couldn't be budged by a limited nuclear strike. Unfortunately, many times they hold so much sway over what people will do that they can force them to give up what is a perfectly reasonable solution to their health-related issues.

Next up, modifying your eating patterns. People who want to use IE probably shouldn't watch network television. It will drive them to not only drinking but also not IE. Our society wants people to consume many items, but food is way up there at the top of the heap. Unfortunately, what they are attempting to advertise as food shouldn't be used as cat or dog food; but that is a bone to pick for another day. Everywhere an IE person looks, there will be someone or something attempting to drive them to eat.

I want everyone who reads this to stop, close your eyes, take a deep breath, and ask themselves when have they gone longer than two-to-three hours without eating and would they even realistically be able to accomplish this herculean task? We have been conditioned by society and our families to EAT. It is ingrained into our psyches. To practice IE a person needs to possess incredible will power. Note to self: Building up self-confidence and will power in my patients needs to become a central part of my IE strategy!

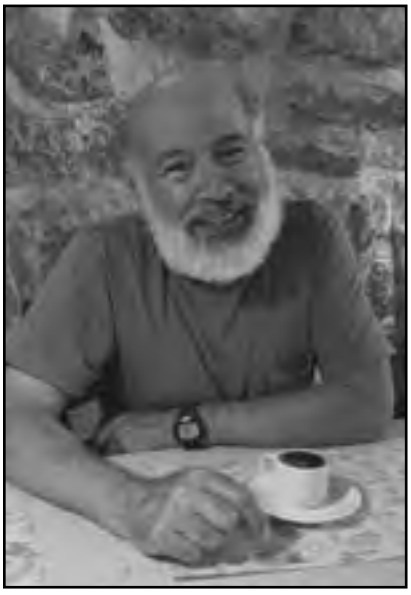
Finally, maybe the strongest influence of gustatory behavior is Mom. Who doesn't remember their mother giving them a cookie when they fell down, or a piece of cake to stop making so much noise, or a candy bar to stop making such a fuss in the store? Another note to self: Make sure patients do not tell their mothers that they are IE!

We are talking severe emotional roadblocks to facilitating the successful incorporation of IE in most patients' lives due to the influence of their mothers. Luckily for me, my mom actually taught me positive attitudes about eating, including fasting when I was sick. Once I had succumbed to whatever virus may or not have been lurking outside my body (or inside since I didn't have darkfield microscopy to verify that in the 50s and 60s), I was given a 16 oz glass with ice and ginger ale and told to drink (My mother must have known about the recuperative powers of ginger as she grew up on a dairy farm). When I appeared to have recovered, I was given a piece of dry white toast to see if I regressed. If I did, back to the ginger ale. If not, on to real food!

To conclude, here is a maxim that I give to all my patients: your body is smarter than you. Try not to get in its way. For me, this is what intermittent eating accomplishes: It allows your body to have a larger than typical block of time to R & R: repair and regenerate. Digesting food is an amazingly large energetic drain on our bodies. Due to the large amount of physical and emotional pollution in our daily worlds, we need our bodies to have a sufficiently large amount of time for the various systems of the body to successfully accomplish R & R. We definitely do not want to have Dr. Bob Naviaux's cell danger response become sufficiently activated until it doesn't turn off and, then, lead our bodies down the road of chronic disease.

So, eat, drink, and be merry, just intermittently!

◆



Curmudgeon's Corner

by Jacob Schor, ND, FABNO
drjacobschor1@msn.com

Purim, Hamantashen, and the Stories We Invent

The Jewish holiday of Purim falls on the 14th day of the month of Adar. In 2020 this will correspond to the evening of Monday, March 9, and end the evening of Tuesday, March 10. In the Jewish calendar, days start at sunset.

The festival of Purim commemorates the salvation of the Jewish people in ancient Persia from Haman's plot "to destroy, kill and annihilate all the Jews, young and old, infants and women, in a single day." as recorded in the Megillah (the Book of Esther).

The short version of the story is that in the fourth century BC the Jews were Persian subjects. During this time, the King of Persia, Ahasuerus, found himself a widower after having had his wife executed for not performing a task he asked of her with adequate alacrity and due diligence. In order to find a new wife, he held a beauty pageant. A Jewish girl named Esther proved to be the most attractive contestant, winning herself the crown, rather literally. Persia's prime minister, a man who bore immense animosity toward the Jewish people, managed to take insult from Mordechai, the leader of the Jews and a close relation to beautiful Esther. Hanan, the prime minister, convinced King Ahasuerus to issue a decree calling for the annihilation of all the Jews in Persia on Adar the 13th, a date apparently chosen by lottery. When the king realized that Esther was Jewish, plans were altered in the nick of time and Haman was hung instead.

Thus, Purim is a holiday celebrating a close call, a reason for an uncharacteristically wild and drunken party. Children and a fair percentage of grownups dress in costumes and a goodly portion of the people, especially the more religious, get drunk. The Babylonian Talmud offers specific instructions: "One is obligated to drink on Purim until one doesn't know the difference between 'cursed be Haman' and 'blessed be Mordechai.'" Many observant, normally very sober people, strive mightily to meet this challenge.

There are specific foods for the holiday, in particular triangle-shaped pastries called hamantashen. In our family we fill these with a paste made from ground poppy seeds and raisins and sometimes with prunes. We annually order half a kilo of poppy seeds from Western Herbs in order to make this filling from scratch in our kitchen.

I was taught as a child that the triangle shape of the hamantashen represents Haman's triangle-shaped hat. You will be hard pressed to find a Jew anywhere on this continent who did not learn this same explanation. This is the story we all grew up with.[1,2]

An Israeli friend of ours, a graduate student attending the Korbel School of International Studies here in Denver, laughed when she heard us tell her about Haman's three-cornered hat. As an undergraduate in Israel, she had studied Biblical history. She explained what historians have long known about Purim. The reason that Purim seems so different from other Jewish holidays is that it originated during the Babylonian exile and was a toned-down version of the Persian New Year festival that "… consisted of a ten-day carnival, during which the people drank, feasted, staged processions, and had sex with people other than their spouses."[3] Ishtar became Esther in this cultural celebratory appropriation. Our Jewish version of this carnival-like drunken party seems out of character because it truly is. In fact, it is a toned-down version of the far wilder pagan holiday it was copied from. The Hebrew priests did all they could to rein in the orgy; they shortened the length of the party from 10 days to 2 days, kept the drunkenness and costumes but eliminated the spouse swapping. The triangle that was symbolic of this sexually focused Ishtar celebration was however preserved. Think of the hamantashen triangle as representing the anatomy covered by the lower triangle of a bikini bathing suit. If the modern Woman's March gave us pussy hats than we must remember where hamantashen originated in a Babylonian orgy. Haman's hat, my foot!

Watching how my brain has processed this information since I first heard the story has been fascinating. I could not

➤

➤

immediately accept this idea; a lifetime of looking at (and eating) hamantashen and seeing them as funny hats does not instantly convert to an image of genitalia.

Still this new view has been an intellectually stimulating experience, the process of substituting a new belief for an accepted belief.

Learning to adapt to and adopt new information may be one of the most important skills we acquire as physicians. Medicine is no longer a system of facts that we must learn but a skill that we acquire that allows us to be forever flexible in the way we understand biology, health, and the practice of medicine.

In a recent meta-analysis of more than 3,000 studies that were published from 2003 through 2017 in *JAMA* and the *Lancet*, and from 2011 through 2017 in the *New England Journal of Medicine*, Vinay Prasad of Oregon Health and Science University and colleagues concluded that more than one in 10 of the studies amounted to a "medical reversal"; the conclusions of the study reversed conventional wisdom. What we view as a pathway of stepping stones made of facts is more like a lily pond in which nothing will support your weight.[4]

Prasad is quoted in the *NY Times*: "You come away with a sense of humility, Very smart and well-intentioned people came to practice these things for many, many years. But they were wrong,"[5]

What do we call things we once thought were true that are disproven? Do they become myths? How long does it take? What percentage of people, or doctors, or scientists have to believe the new version before it becomes real? Asking questions like this in this day and age could lead us down a black hole rather quickly.

Some of these 'decommissioned ideas' are relevant to naturopathic practice. I clearly recall thinking these were true. It's what we learned at school:

1. Peanut allergies occur whether or not a child is exposed to peanuts before age 3. Keeping babies away from peanuts until they are three makes no difference in reducing allergies.[6]
2. Fish oil does not reduce the risk of heart disease.[7]
3. A lifelike doll carried around by teenage girls will not deter pregnancies.[8]
4. Ginkgo biloba does not protect against memory loss and dementia.[9]
5. Aspirin and ibuprofen work as well as opioids to relieve pain in the ER (not to mention safer).[10]
6. Testosterone treatment does not help older men retain their memory.[11]
7. Keeping your house free of dust mites, mice and cockroaches will not reduce asthma attacks.[12]
8. Step counters and calorie trackers do not help people lose weight.[13]
9. Vitamin A supplementation in infant populations does not reduce mortality. [14]

I wrote one in ten, but it actually boiled down to a 13% of the research on vitamins, supplements, and food reversed previously held understandings. Most of the trials looked at in this paper had to do with surgical procedures and not therapies we work with. It's not that scientists are singling out naturopathic therapies to disprove. The authors concluded that this ongoing process was valuable primarily because "the de-adoption of these and other low-value medical practices will lead to cost savings…."

A curmudgeonly mind might suggest that this information should remind us not to be so sure of ourselves, that things we think are true, are only true on a temporary basis, and that a fair proportion of things we take for granted may not be true next week.

Prasad's study of decommissioned ideas reminds me of the many treatments once suggested for menopause hot flashes; they helped reduce symptoms but in the end the placebos worked just as well. Magnesium helped,[15] but then Haeseong Park ran a larger study and proved it didn't.[16] Park, as I recall, had a record of proving hot flash treatments were ineffective, including vitamin E in 1998,[17] soy in 2000,[18] black cohosh in 2006,[19] acupuncture in 2007,[20] flax seed lignins in 2012,[21] and paced breathing in 2013.[22]

We have yet to adopt what the results of Zhang's 2017 paper, "Dietary isoflavone intake and all-cause mortality in breast cancer survivors: The Breast Cancer Family Registry" mean. Recall their results that the greatest benefit of soy consumption was seen in estrogen negative breast cancers. Obviously, our belief that soy blocks estrogen receptors and so hinders breast cancer needs some rethinking.[23] Our old explanation that soy's benefit was similar to tamoxifen and that it blocks estrogen receptors no longer holds true.

Medical knowledge is not nearly as static as it once was and the sooner we accept this and learn how to live with it constantly changing, the better we will be at caring for patients.

I had lunch a few years back with a retired MD and somehow in our conversation the idea of using honey as a vulnerary came up in conversation. His response was something to the effect of, "If I did not learn this in medical school, it can't be true." I wanted to point out that when he went to medical school, the honey as a topical treatment was an old wife's tale, but as we sat eating our salads there were a 150 citations on PubMed supporting its wound healing action [as I write this in 2019, there are 544 citations]. What we learned in school is out of date on the day we graduate. That's a given.

How do we learn to see knowledge as in constant flux? I'm not sure but probably our first rule is to distrust ourselves or anyone else when we sound too certain of something. Especially distrust someone who used the verb believe. In part, this is why I bother authors and speakers for citations. Where does an idea come from and in what time frame? We need to be constantly asking if there is newer information that contradicts our original understanding. The evidence may have changed in the interval since we learned something. Science is a process for discerning the truth, a rather messy method it seems, but it still beats the alternatives.

You can try my line: "We once believed that this is true; I wonder if it still is? Let me take a moment to check."

References

1. https://www.chabad.org/holidays/purim/default_cdo/aid/109190/jewish/Purim.htm. Accessed January 28, 2018.
2. https://en.wikipedia.org/wiki/Hamantash
3. http://ebisupublications.com/esther-ishtar-pagan-origins-purim/
4. Herrera-Perez D, et al. Meta-Research: A comprehensive review of randomized clinical trials in three medical journals reveals 396 medical reversals. *eLife*. 2019;8:e45183.
5. https://www.nytimes.com/2019/07/01/health/medical-myths-doctors.html?smid=nytcore-ios-share.
6. Du Toit G, et al. Effect of Avoidance on Peanut Allergy after Early Peanut Consumption. *N Engl J Med*. 2016 Apr 14;374(15):1435-43.
7. Risk and Prevention Study Collaborative Group, Roncaglioni MC, et al. n-3 fatty acids in patients with multiple cardiovascular risk factors. *N Engl J Med*. 2013 May 9;368(19):1800-8.
8. Brinkman SA, et al. Efficacy of infant simulator programmes to prevent teenage pregnancy: a school-based cluster randomised controlled trial in Western Australia. *Lancet*. 2016 Nov 5;388(10057):2264-2271.
9. DeKosky ST, et al. Ginkgo biloba for prevention of dementia: a randomized controlled trial. *JAMA*. 2008 Nov 19;300(19):2253-62.
10. Chang AK, et al. Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department: A Randomized Clinical Trial. *JAMA*. 2017 Nov 7;318(17):1661-1667.
11. Resnick SM, et al. Testosterone Treatment and Cognitive Function in Older Men With Low Testosterone and Age-Associated Memory Impairment. *JAMA*. 2017 Feb 21;317(7):717-727.
12. Matsui EC, et al. Effect of an Integrated Pest Management Intervention on Asthma Symptoms Among Mouse-Sensitized Children and Adolescents With Asthma: A Randomized Clinical Trial. *JAMA*. 2017 Mar 14;317(10):1027-1036.
13. Jakicic JM, et al. Effect of Wearable Technology Combined With a Lifestyle Intervention on Long-term Weight Loss: The IDEA Randomized Clinical Trial. *JAMA*. 2016 Sep 20;316(11):1161-1171.
14. Imdad A, Ahmed Z, Bhutta ZA. Vitamin A supplementation for the prevention of morbidity and mortality in infants one to six months of age. (2016) Cochrane Database of Systematic Reviews 28:CD007480.
15. Park H, et al. A pilot phase II trial of magnesium supplements to reduce menopausal hot flashes in breast cancer patients. *Supportive Care in Cancer*. 2011;19(6):859–863
16. Park H, et al. North Central Cancer Treatment Group N10C2 (Alliance): a double-blind placebo-controlled study of magnesium supplements to reduce menopausal hot flashes. *Menopause*. 2015 Jun;22(6):627-32.
17. Barton DL, et al. Prospective evaluation of vitamin E for hot flashes in breast cancer survivors. *J Clin Oncol*. 1998 Feb;16(2):495-500.
18. Quella SK, et al. Evaluation of soy phytoestrogens for the treatment of hot flashes in breast cancer survivors: A North Central Cancer Treatment Group Trial. *J Clin Oncol*. 2000 Mar;18(5):1068-74.
19. Pockaj BA, et al. Phase III double-blind, randomized, placebo-controlled crossover trial of black cohosh in the management of hot flashes: NCCTG Trial N01CC1. *J Clin Oncol.* 2006 Jun 20;24(18):2836-41.
20. Vincent A, et al. Acupuncture for hot flashes: a randomized, sham-controlled clinical study. *Menopause*. 2007 Jan-Feb;14(1):45-52.
21. Pruthi S, et al. A phase III, randomized, placebo-controlled, double-blind trial of flaxseed for the treatment of hot flashes: North Central Cancer Treatment Group N08C7. *Menopause*. 2012 Jan;19(1):48-53.
22. Sood R, et al. Paced breathing compared with usual breathing for hot flashes. *Menopause*. 2013 Feb;20(2):179-84.
23. Zhang FF, et al. Dietary isoflavone intake and all-cause mortality in breast cancer survivors: The Breast Cancer Family Registry. *Cancer*. 2017;123(11):2070-2079.

◆

Study Suggests Delta-Tocotrienol in Combination with Standard Therapy Increased Survival in Refractory Ovarian Cancer Patients

A recent study conducted at Denmark's Vejle Hospital, published in *Pharmacological Research*, provides evidence of delta-tocotrienol's benefits for cancer patients. Results of the open-label trial suggest that American River Nutrition-manufactured delta-tocotrienol in combination with bevacizumab had additive effects in chemotherapy refractory ovarian cancer, possibly conferred by the anti-angiogenic activity of both compounds. This is the first-ever clinical trial using tocotrienols in ovarian cancer patients.

In the study of 23 advanced-stage ovarian cancer patients, tocotrienol was administered at a dosage of 300 mg three times a day, with bevacizumab given to patients at 10 mg/kg intravenously every three weeks. Patient disease stabilization was high at 70% with increased survival, which approximately doubled.

Study Details

Ovarian cancer is the fifth most common cause of cancer death in women in the US. According to the American Cancer Society, approximately 22,240 women in the US received a new ovarian cancer diagnosis, while approximately 14,070 people died of the disease in 2018. Since ovarian cancer is usually not diagnosed until it is more advanced, the five-year survival rate is only 47%. Patients with advanced-stage ovarian cancer often have a recurrence of the disease after primary treatment, and despite second- and third-line treatments, these patients eventually become chemotherapy-resistant with few therapeutic options. The goal at this stage is to improve the quality and duration of life with as few side effects as possible.

In 2018, the FDA approved bevacizumab (Avastin®), an anti-angiogenic agent, for frontline treatment of ovarian cancer after surgery, based on its ability to reduce disease progression by 38% in a double-blind, placebo-controlled, multicenter study. In Europe, the drug has been used for first-line and recurrent ovarian cancer treatment for much longer, since 2011, and shows similar promising results.

Similar to bevacizumab, tocotrienols, isomers of the vitamin E family, have anti-angiogenic properties that are thought to contribute to the anti-neoplastic effect. Previous *in vitro* and *in vivo* studies, including a clinical trial in patients with pancreatic cancer, showed that delta-tocotrienol was especially active against malignancies, compared to other vitamin E isoforms.

The Danish study, led by Dr. Anders Jakobsen at Vejle Hospital, aimed to identify the potential additive effects of bevacizumab and delta-tocotrienol by observing the stabilization and control of disease, progression-free survival (PFS), and overall survival (OS). Although the target level of 75% disease control at six months was not reached, the observed disease control of 50% at six months was high compared to only 25% of disease control when using bevacizumab as a single agent in another study conducted by the same researchers. Even more compelling is the result of a high overall disease control of 70% with a combination of bevacizumab and delta-tocotrienol.

Compared to a typically reported median PFS of 2-4 months and median OS of 5-7 months, combined treatment of bevacizumab and delta-tocotrienol nearly doubled survival, allowing patients to reach a median PFS of 6.9 months and a median OS of 10.9 months. Notably, 25% of the patients were alive after 24 months.

The study treatment was shown to have low toxicity, with only three patients discontinuing their medications due to well-known side effects of bevacizumab therapy. Further, quality of life was stable.

The authors noted that "the present study indicates that the combination of bevacizumab and delta-tocotrienol is effective in multiresistant ovarian cancer." They also mention that, "bevacizumab is used in a spectrum of different tumors and an additional effect by an atoxic drug holds high priority."

Commenting on the research, Dr. Barrie Tan, President of American River Nutrition said that "as one of the most deadly cancers in women, ovarian cancer needs further attention, and I applaud Dr. Jakobsen and his group for their novel approach in finding alternative treatment options for these patients." Tan continued, "The fact that a simple vitamin such as tocotrienol in combination with standard therapy could prolong a woman's life and improve its quality under these severe circumstances is nothing short of astonishing."

About Delta-Tocotrienol

Delta-tocotrienol is part of the vitamin E family, which consists of eight separate but related molecules: four tocopherols (alpha, beta, gamma, delta) and four tocotrienols (alpha, beta, gamma, delta). Tocotrienols are derived from three major sources, including rice, palm and annatto. Annatto is the preferred source of high-purity delta-tocotrienol.

Source: Thomsen CB, Andersen RF, Steffensen KD, et al. Delta tocotrienol in recurrent ovarian cancer. A phase II trial. *Pharmacological Research.* March 2019; 141: 392-396.

About American River Nutrition

American River Nutrition, founded in 1998, is the producer of DeltaGold® tocotrienols, the most beneficial form of vitamin E for cardiovascular health, as well as other health benefits. The company is led by Dr. Barrie Tan, a pioneering scientist and researcher credited with identifying the primary sources of plant-based tocotrienols, including rice, palm & the virtually 100% tocotrienol-producing annatto plant. American River products are manufactured in the US using a proprietary process leading to the purest form of natural tocotrienols available. http://americanrivernutrition.com/ ◆

Mushroom Wisdom's Industry Leading Lion's Mane Product, Amyloban 3399, Changes Its Name

With the growing recognition that consumers are becoming more and more aware of the diverse and many health-supporting benefits of mushrooms, Mushroom Wisdom is changing the name of its flag-ship proprietary lion's mane mushroom product. Previously referred to as AMYLOBAN 3399®, the "3399" being part of the patent number, this product made from a standardized extract will now be labelled as "Lion's Mane Amyloban." This comes as the company recognized the need to more closely identify this product with the lion's mane mushroom from which it is derived.

Growing Awareness of the Benefits of Mushrooms

While mushrooms have been utilized as traditional remedies for hundreds, if not thousands of years, the focus has primarily been on their benefits for supporting healthy immune function. As mushrooms have become more widely accepted as health supplements here in the West, knowledge of their use and benefits has expanded beyond just their immune activities. A great example of this is found in the lion's mane mushroom, which, like its mushroom cousins, has been found to benefit immune function, with recent researchers uncovering a number of supporting activities for healthy brain and nerve function.*

Mushroom Wisdom found that, even though Amyloban 3399 was a more highly concentrated and unique, standardized extract of the lion's mane mushroom, consumers and retailers were not identifying it as having been extracted from this promising mushroom. This name change to Lion's Mane Amyloban now should alleviate this issue while making it possible for current users to identify the product. ONLY the name has changed, the trusted product and formula all remains the same.

About Mushroom Wisdom

Mushroom Wisdom has been specializing in only mushroom-based products for close to 30 years with the goal of honoring their traditional uses while at the same time supporting and expanding the science and research. MW goes to great lengths to grow their mushrooms in a "mirroring of nature" process, then extracting them to increase their bioavailability and strength while undergoing several quality-control tests.

Contact: To find out more about Lion's Mane Amyloban, please call 1-800-747-7418 or visit wvvw.MushroomWisdom.com where you can also sign up for our newsletter & updates.

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

◆

Women's Health Update

by Tori Hudson, ND
womanstime@aol.com

Research Highlights 2019

Every year for the past few years, I try to cull what studies in women's health have made an impression on me that influenced my clinical practice. I've written about some of these in past *Townsend Letter* women's health update columns, and others I've read and submit for this annual issue. Whether it is a gynecological issue, a women's only problem, or a primary care issue that has great importance in women's health, I offer these studies below that hopefully will influence your clinical practice or personal health, as well.

Green Tea and Reduction of Breast Cancer Risk and Recurrence

This meta-analysis is a good update on the topic of the role of green tea in breast cancer risk and recurrence. The purpose of this systematic review and meta-analysis was to evaluate green tea consumption and breast cancer risk, recurrence, and risk in relationship to menopause status.

A literature search was done following current systematic review and meta-analysis guidelines, and using three search systems (PubMed, Scopus, and the Web of Science). Observational studies that evaluated breast cancer risk in adult women were included and selected studies evaluated green tea consumption using a questionnaire or interview. A total of 194 studies were detected; but of those, 39 were duplicate studies and 115 did not meet the inclusion criteria. Another 25 studies were excluded because there was insufficient differentiation between the kind of teas that were consumed, and two studies were excluded due to data insufficiencies. That left 13 studies that were included in this meta-analysis. Seven were conducted in Japan, five in China and one in the US.

Seven of these studies analyzed breast cancer recurrence in women with a previous history, and six studies followed healthy women to determine breast cancer risk. Three of the seven studies on breast cancer recurrence showed a possible protective effect of consuming green tea. The remaining four did not find a statistically significant correlation. Of the other six studies analyzing the risk of breast cancer, none of them showed a statistically significant effect. The potential benefit was seen in those studies that reported five cups of green tea per day.

In addition to these findings, an analysis was also done comparing the risk of breast cancer in women before and after menopause and the influence of green tea. A statistically significant protective effect of green tea was seen in pre-menopausal women while no protective effect was seen in postmenopausal women. The protective effect in the overall meta-analysis was a 15% reduction in breast cancer risk. There was also a significant reduction in breast cancer recurrence in the majority of the cohort studies but not in the case-control studies. Green tea was not associated with the risk of a new breast cancer diagnosis in those case-control studies; but conversely, green tea consumption significantly reduced breast cancer recurrence by 19%.

Commentary: One of the limitations of this meta-analysis was that the amount of green tea consumption varied with some studies reporting in grams and others in cups, and the serving size ranged from 100 mL to 350 mL. In addition, diet, other lifestyle factors and cultural differences were not considered. There is also insufficient information about breast cancer staging and what stage and receptor markers might be more influenced by green tea and breast cancer recurrence. None the less, green tea, for risk reduction, at least in pre-menopausal women, and breast cancer recurrence reduction, in at least stage I-II breast cancer patients, is still good advice. For both these effects, I would encourage approximately 3-5 cups per day which is often equal to 1-2 capsules per day of a green tea extract containing 330 mg of green tea leaf extract if it contains 98% polyphenols, 80% catechins, and 45% EGCG (epigallocatechin gallate).

Gianfredi V, et al. Green tea consumption and risk of breast cancer and recurrence- A systematic review and meta-analysis of observational studies. **Nutrients**. 2018 December;10(12):E1886.

Turmeric and Osteoarthritis Review (and More)

We know many things about therapeutic benefits of turmeric and the most abundant curcuminoid constituent, curcumin. A recent review article examines more closely the randomized, controlled trials (RCTs) of "curcumin" in the treatment of autoimmune and rheumatic diseases.

Using the methodology of searching the PubMed database for key words, a total of 32 RCTs met the inclusion criteria for this review of studies published between 2008 and 2018.

There were 16 RCTs and a total of 1,480 individuals using curcumin for osteoarthritis (OA). These 16 trials used doses of curcumin between 100-2000 mg/day for 6-32 weeks. Twelve were placebo-controlled, and four used positive controls, including non-steroidal anti-inflammatory drugs (NSAIDs) and the dietary supplements glucosamine hydrochloride (GH) and chondroitin sulfate (CS). The studies evaluated either curcuminoid extracts, a specific ratio of more than one curcuminoids or a combination of curcumin with Boswellia. Two of the studies only evaluated laboratory findings rather than clinical results such as pain, swelling, or mobility. Of the 14 RCTs that assessed clinical outcomes, 13 reported significant improvements in at least two areas. The average dose was 834.3 mg/day.

The most common improvements were increased walking distance and decreased Western Ontario and McMasters Osteoarthritis Index (WOMAC) score. One of the positive trials found that 1000 mg/day curcumin alone was not as effective as a combination of 950 mg/day curcumin plus 450 mg/day boswellic acid.

One study compared GH plus CS to 500 mg/day curcumin plus GH for 16 weeks and found significant clinical improvements in the curcumin group. In the three trials that used NSAIDS in comparison, two reported that curcumin effectiveness was similar to NSAIDS and one found it was superior.

Three of the five studies that measured serum levels of inflammatory markers had significant decreases with the curcumin.

This paper also reported on type 2 diabetes mellitus (T2DM); and as a brief summary here, curcumin did have anti-diabetic effects, improved glucose metabolism and insulin resistance, decreased key inflammatory markers and decreased progression to T2DM in those who were pre-diabetic. The authors conclude "the studies showed that curcumin supplementation possesses anti-diabetic effects and improves T2DM parameters in patients."

This review paper also reported on three placebo-controlled trials in patients with ulcerative colitis (UC). Two of the studies, which evaluated 2000 mg/day and 3000 mg/day curcumin, reported significant improvements in at least three clinical outcome measures. One study using a much lower dose of 450 mg/day curcumin for eight weeks reported no significant improvement.

The two small RCTs of rheumatoid arthritis and curcumin were reported. In one, 1000 mg/day curcumin for eight weeks improved disease activity score and pain levels but had no effect on laboratory markers while the other, using 1300 mg/day curcumin for two weeks, had no effect at all. One small study was evaluated in patients with lupus nephritis. At 1500 mg/day turmeric (66.3 mg/day curcumin) for 12 weeks, there was a significant decrease in proteinuria, systolic blood pressure, and hematuria.

Commentary*:* With this many positive trials on the benefits of curcumin in the treatment of OA, the comparable results to NSAIDS with fewer adverse events make it a first choice for relief of pain and swelling and improved function. The studies in pre-diabetics and T2DM are also encouraging, but longer-term studies would be helpful in understanding the true potential. Autoimmune illnesses such as RA and UC are very complex with serious consequences. While the curcumin research is small in these areas, a multi-faceted treatment program can easily include curcumin but not at the expense of other well thought out management and treatment options. Curcumin products very widely from simple curcumin powders/liquids/tinctures to those formulated with enhanced bioavailability methodologies. In time, we are likely to better understand how/when/in whom to select which curcumin formula and what dosage.

Yang M, Akbar U, Mohan C. Curcumin in autoimmune and rheumatic diseases. *Nutrients.* May 2019;11:1004. pii: E1004.

Ginger for Menstrual Cramps

Primary dysmenorrhea (aka menstrual cramps not caused by endometriosis or uterine fibroids or infections) is caused by increased prostaglandin leakage of the endometrium (lining of the uterus), during menses. The most common conventional treatment is a non-steroidal anti-inflammatory drugs (NSAIDS), which block an enzyme that causes the blockage of synthesis of the prostaglandins. Ginger is one such herb that has anti-spasmodic effects due to its ability to block cyclooxygenase as well as 5-lipoxygenase.

The current study was a randomized comparative cross-over clinical trial in 168 Iranian women aged 18-26. One group received Novafen (an NSAID) during the first menstrual cycle and ginger in the second, while the other group consumed ginger first, then Novafen. Women were given capsules containing either 200 mg of ground ginger or the commercially available Novafen. Women started taking capsules on the first day of menses when the menstrual pain started and took a capsule every six hours for a total of 48 hours.

All the women completed the trial with 48.8% experiencing grade II and 51.2% grade III dysmenorrhea. Both the treatments decreased the pain during the treatment period, especially during the first 24 hours. When taking Novafen, women reported a reduction in the mean pain score from 7.12 to 3.10 after the 48 hours. When taking ginger, the pain scores decreased from 7.6 to 2.69 after 48 hours. Satisfaction and bleeding were similar in both groups and the severity of symptoms before and after treatment were similar in both groups.

Commentary: In other studies, ginger has been shown to improve primary dysmenorrhea as well as heavy menstrual bleeding. One study compared ginger to mefenamic acid, another NSAID and ginger was shown to be as effective on pain relief.[1] Ginger has also had better results than placebo.[2] Ginger is safe and with minimal side effects and at least as effective as two other NSAIDS for acute relief of primary dysmenorrhea.

Rad H, et al. Effect of ginger and Novafen on menstrual pain: a cross-over trial. *Taiwanese J Ob/Gyn.* 2018;806-809.

Consider Saffron for Fibromyalgia

Fibromyalgia (FM) is considered a neurological disorder with chronic and widespread musculoskeletal pains. It can also be associated with mild to severe fatigue, anxiety, depression, sleep disturbances, hypersensitivities to light/sound/touch, digestive problems, headaches, and cognitive difficulties. More women than men have FM.

While we do not understand what causes fibromyalgia, it appears that it is multifactorial and not the same cause for every

➤

➤

patient, but includes genetics, infections with some illnesses triggering or aggravating fibromyalgia, and physical and/or emotional trauma/significant stressors.

It is considered neurological because there appears to be an abnormal increase in certain levels of select neurotransmitters in the brain that signal pain. In addition, the pain receptors in the brain of those with FM develop a pain memory and become more sensitive with a lower threshold to reacting to the pain signals.

Both conventional and natural medicine have yet to determine a clear cause and as yet to offer a reliable and successful treatment approach. Conventional treatment may include pain relievers and antidepressants. Duloxetine, aka Cymbalta, is an approved treatment for FM. It may help to reduce the pain and improve the fatigue and mood. Muscle relaxants and anti-inflammatories may offer some help along with medications such as gabapentin or pregabalin. Indeed, there is a need for expanded options as those in natural medicine are not sufficient either, such as vitamin D, magnesium, curcumin, ribose and others.

Human and animal studies indicate that saffron has antidepressant, antioxidant, and neuroprotective activity. As such, it may be a potential option for FM treatment, or at least part of a FM comprehensive treatment plan. The current randomized, double-blind, controlled trial compared the effects of saffron and duloxetine on symptoms in patients with FM.

Fifty-four patients with FM, ages 18-60 were enrolled in a trial in Iran. Patients were included if they had a diagnosis of FM according to the criteria set forth by the American College of Rheumatology and had pain scores >40 out of 100 using a Visual Analog Scale (VAS).

Patients were randomly assigned to take one capsule containing 30 mg duloxetine or one capsule containing 15 mg saffron extract daily during the first week. Patients then took two capsules of duloxetine or saffron daily during the second week and continued at that dose through a total of two months. Primary outcomes were changes in Hamilton Rating Scale for Depression score, Fibromyalgia Impact Questionnaire score, and Brief Pain Inventory pain score from baseline to eight weeks. Secondary outcomes were changes in VAS pain score, fatigue assessments, and Hospital Anxiety and Depression scores from baseline to eight weeks. Patients were instructed to avoid taking medications that could affect FM, during the study.

Mean scores for all outcome assessments improved after eight weeks in both the saffron and duloxetine groups and were not statistically significantly different from each other. There was no significant difference in the number of adverse events in either group.

Commentary: It is easy to get excited by saffron with recent studies in depression, ADHD in children, fibromyalgia, and PMS. The current study is certainly good preliminary evidence of a measurable level of improvement in symptoms of fibromyalgia with this dose of saffron. Saffron does have active constituents that have anti-inflammatory and antioxidant effects in the central nervous system and have been shown to increase levels of key neurotransmitters, including serotonin, norepinephrine, and dopamine. The current trial did lack a placebo arm, the study was a small number of individuals, and the study was short in duration. These would all be considered weaknesses of the study, but the study does lay important groundwork for saffron being part of a treatment strategy for those suffering from fibromyalgia.

Shakiba M, et al. Saffron (*Crocus sativus*) versus duloxetine for treatment of patients with fibromyalgia: A randomized double-blind clinical trial. *Avicenna J Phytomed*. November-December 2018;8(6):513-523.

Testosterone Therapy in Women – Safety and Efficacy

This systematic review and meta-analysis was done of randomized, controlled trials of testosterone therapy in women. The analysis focused on transdermal patches, releasing 300 mcg daily of testosterone or nontransdermal formulations at doses achieving similar blood levels at the patch. This dose of daily testosterone results in blood testosterone levels at the upper end of the premenopausal range.

Testosterone patches are not available in the US outside of research settings. The current testosterone-only products available to women in the US are compounded formulas of creams, capsules, injections, or troches. There is currently one generic non-compounded estrogen/testosterone product available in the US.

Of the 36 trials that were analyzed, there were 8,480 women participants; and most were 12-24 weeks in duration with the longest being two years.

Compared with placebo or menopausal estrogen with or without a progestogen, testosterone therapy significantly enhanced sexual function, including the frequency of sexual activity, libido, pleasure, arousal, orgasm, and self-image in postmenopausal women with low libido. Transdermal testosterone did not alter serum lipid values, but oral testosterone increased LDL-cholesterol, reduced total cholesterol, reduced HDL-cholesterol, and reduced triglycerides. Testosterone therapy as associated with weight gain and some women reported modest impact on acne and body hair growth.

Commentary: This meta-analysis does support the use of transdermal testosterone for menopausal women with low libido, but the trial was not long enough in duration to assess any effects on cardiovascular disease, breast cancer, or endometrial cancer. I consider myself very experienced with and educated about prescribing testosterone to peri and postmenopausal women. This requires being knowledgeable about not only effective doses of transdermal, oral and troche testosterone, but also safe doses in terms of minimal chance of nuisance side effects (mild acne, hair thinning, increased unwanted body hair) as well as grossly inappropriate doses for women who seek the benefits but not any phenotypical changes due to testosterone therapy. I have seen too many situations where pre and peri and postmenopausal women were being prescribed testosterone doses for the purpose of sexual dysfunction in particular, that I would consider inappropriate, if not actually unsafe.

Islam R, et al. Safety and efficacy of testosterone for women: A systematic review and meta-analysis of randomised controlled trial data. *Lancet Diabetes Endocrinol*. 2019 July 25 (e-pub).

References

1. Shirvani M, et al. The effect of mefenamic acid and ginger on pain reliefe in primary dysmenorrhea: a randomized clinical trial. *Arch Gyneco.l Obstet*. 2015;291(6):1277-81.
2. Rahnama P, et al. Effect of Zingiber officinale R. rhizomes (ginger) on pain relief in primary dysmenorrhea: a placebo randomized trial. *BMC Complement Altern Med*. 2012;12(1):1.

◆

supplementation with folinic acid (such as 1-2 mg per kg of body weight per day; maximum, 50 mg per day) frequently resulted in clinical improvement in children with autism spectrum disorders who had FRα autoantibodies, low CSF concentrations of 5-MTHF, or both.[10,11]

Folinic Acid Combined with Other Nutrients

Other factors thought to play a role in the pathogenesis of autism are increased oxidative stress and mitochondrial dysfunction. These abnormalities may result in part from deficiencies of antioxidant nutrients and nutrients that play a role in mitochondrial function. Many autistic children have nutritional deficiencies as a result of feeding problems, such as restricting their diet to a very narrow range of foods. Identifying and treating these deficiencies may improve outcomes beyond what can be achieved with folinic acid alone.

In a new study 82 autistic children (mean age, 4.4 years) underwent laboratory tests for FRα autoantibodies, as well as the levels of various vitamins, minerals, and coenzyme Q10.[12] Patients positive for FRα autoantibodies were treated with folinic acid (0.5-1.0 mg per kg per day). If no improvement was seen after six months, the dosage could be increased to 2 mg per kg per day, to a maximum of 50 mg per day. In addition, nutritional supplements were given if deficiencies were identified. Laboratory tests were repeated every three-to-four months, and the patients were treated for a total of two years. Eighty-four similar autistic children whose families did not agree to participate in this program served as controls. Outcomes were assessed by the change in the Childhood Autism Rating Scale (CARS) score. The CARS is a 15-item rating scale, with scores ranging from 15 to 60. A score below 30 indicates the absence of sufficient signs and symptoms to diagnose autism. Scores of 30 to 36.5 indicate mild-to-moderate autism, and scores of 37 to 60 indicate severe autism.

Seventy-six percent of the children were positive for FRα autoantibodies. Nutritional deficiencies that were identified included vitamin A (66% of patients), vitamin D (62%), folate (18%), iron (11%), selenium (9%), coenzyme Q10 (7%), zinc (5%), vitamin C (4%), and vitamin E (4%). In the group as whole, the mean CARS score improved from severe at baseline (41.3) to mild-to-moderate (34.4; $p < 0.0001$) after two years. Seventeen of 82 children (20.7%) achieved complete recovery (CARS score less than 30). The children who did not have FRα antibodies improved after correction of their nutritional deficiencies (18% of those children did receive folinic acid [0.5 mg per kg per day] to treat folate deficiency). In the children who were negative for FRα autoantibodies, the mean CARS score decreased from 42.1 at baseline to 33.9 after two years (a similar degree of improvement to that seen in children with FRα autoantibodies). Among the 84 patients in the control group, the mean baseline CARS score was similar in each of the age categories (1, 2, 3, 4, 5, or ≥ 6 years). This, according to the authors, suggests that autism severity does not decrease spontaneously as children get older. However, the authors assessed only baseline CARS scores in the control group and did not retest them after two years.

One could argue that this was not really a controlled trial because it did not compare the improvement in the treatment group with that in the control group. There might be fundamental differences between families who participate in a treatment program and those who decline to participate; and some of these differences might predict better outcomes. In addition, compliance with a treatment per se has been shown to result in beneficial effects, even if the treatment is a placebo.[13] However, while we might reasonably call this new study an uncontrolled trial, the results are still impressive. On average, children improved from severe to mild-to-moderate, and one-fifth of the children no longer fit the diagnostic criteria for autism. Of note, the study did not test for possible deficiencies of magnesium, riboflavin, and vitamin B3, all of which play a role in mitochondrial function. A more comprehensive approach might further increase the benefits reported in this study.

An internet search revealed that one commercial laboratory (Iliad Neurosciences, Inc.)[14] is offering the serum FRα autoantibody test for $295.

Alan R. Gaby, MD

References

1. Knivsberg AM, et al. Dietary intervention in autistic syndromes. *Brain Dysfunct*. 1990;3:315-327.
2. Lucarelli S, et al. Food allergy and infantile autism. *Panminerva Med*. 1995;37:137-141.
3. Ber A. Neutralization of phenolic (aromatic) food compounds in a holistic general practice. *J Orthomolec Psychiatry*. 1983;12:283-291.
4. Pennesi CM, Klein LC. Effectiveness of the gluten-free, casein-free diet for children diagnosed with autism spectrum disorder: based on parental report. *Nutr Neurosci*. 2012;15:85-91.
5. Whiteley P, et al. The ScanBrit randomised, controlled, single-blind study of a gluten- and casein-free dietary intervention for children with autism spectrum disorders. *Nutr Neurosci*. 2010;13:87-100.
6. Hsu CL, et al. The effects of a gluten and casein-free diet in children with autism: a case report. *Chang Gung Med J*. 2009;32:459-465.
7. Zioudrou C, et al. Opioid peptides derived from food proteins. The exorphins. *J Biol Chem*. 1979;254:2446-2449.
8. Knivsberg AM, et al. Reports on dietary intervention in autistic disorders. *Nutr Neurosci*. 2001;4:25-37.
9. Ramaekers VT, et al. Autoantibodies to folate receptors in the cerebral folate deficiency syndrome. *N Engl J Med*. 2005;352:1985-91.
10. Frye RE, et al. Cerebral folate receptor autoantibodies in autism spectrum disorder. *Mol Psychiatry*. 2013;18:369-81.
11. Ramaekers VT, et al. Folate receptor autoimmunity and cerebral folate deficiency in low-functioning autism with neurological deficits. *Neuropediatrics*. 2007;38:276-81.
12, Ramaekers VT, et al. Improving outcome in infantile autism with folate receptor autoimmunity and nutritional derangements: a self-controlled trial. *Autism Res Treat*. 2019;2019:7486431.
13. Petitti DB. Coronary heart disease and estrogen replacement therapy. Can compliance bias explain the results of observational studies? *Ann Epidemiol*. 1994;4:115-118.
14. iliadneuro.com. Accessed November 15, 2019.

◆

Nutritional Treatments for Autism

Autism is a developmental disorder that begins before the age of three years. Manifestations may include abnormalities of communication and social interaction; repetitive, restricted, and self-injurious behaviors; intellectual disability; and severely limited activities and interests. Autism is one of the more severe forms of a group of disorders known as autism spectrum disorders, which include pervasive developmental disorder and Asperger syndrome (a subset of pervasive developmental disorder). The cause of autism is not known, but abnormalities of cellular architecture in several areas of the brain, as well as various biochemical abnormalities, have been found in some patients. A growing body of evidence suggests that dietary modifications and nutritional supplements can be beneficial in the treatment of autism.

Food Allergy/Sensitivity

Numerous investigators have observed that food sensitivity is a contributing factor in some cases of autism.[1-6] Gluten and casein (a cow's milk protein) were by far the most commonly implicated offending substances, but other foods or other substances in certain foods (i.e. phenolics) were found to be involved as well. While some of the adverse reactions to foods in autistic children are probably true allergic reactions, some of the reactions to gluten and casein may be non-allergy-mediated. Peptides derived from the digestion of wheat gluten and casein have opioid activity,[7] and it has been suggested that these opioid peptides adversely affect the behavior of autistic children.[8]

Addressing food sensitivities, cortisol folate deficiency, and nutritional deficiencies have decreased autistic symptoms in some children.

Folinic Acid

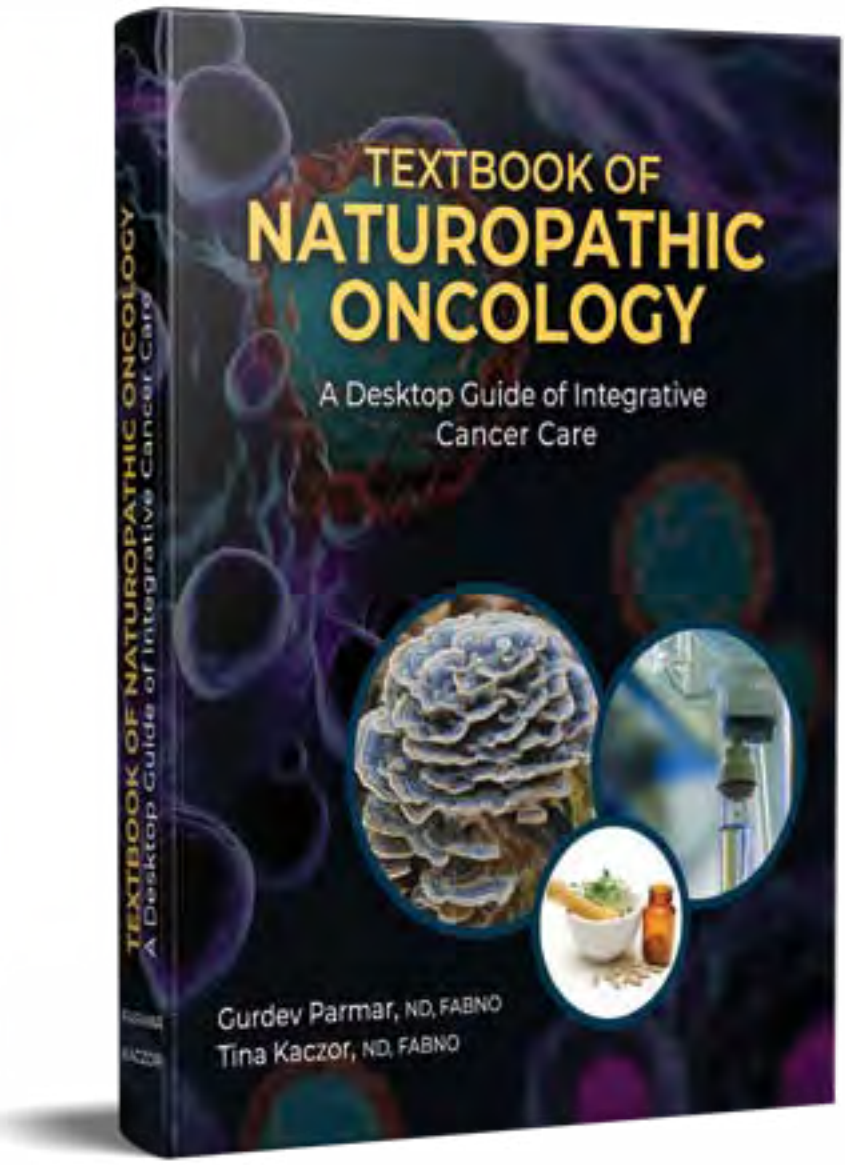
Cerebral folate deficiency is defined as any neuropsychiatric condition associated with low cerebrospinal fluid (CSF) levels of 5-methyltetrahydrofolate (5-MTHF; the active form of folate in CSF), in association with normal folate status and normal folate metabolism outside the central nervous system. Cerebral folate deficiency is common among children with autism spectrum disorders, and it appears to be caused in most cases by the production of autoantibodies that block the receptor involved in transporting folate across the blood-brain barrier (folate receptor alpha [FRα]). Folinic acid can bypass autoantibody-blocked folate receptors and enter the CSF by a different mechanism,[9] where it is converted to 5-MTHF. In uncontrolled trials,

continued on page 91 ➤

The Cancer Book is Done!

For the past six years I've watched from the sidelines as Dr. Gurdev Parmar and various colleagues have collaborated in writing a *Textbook of Naturopathic Oncology*. A year ago, Dr. Tina Kaczor, long time medical editor of the *Natural Medicine Journal*, joined their effort and with her help they have brought the project to completion. Knowing and respecting both of these practitioners, and especially having worked closely with Dr. Kaczor myself, I am looking forward to seeing their book. Rumor has it that it will be the definitive desktop reference on the subject. I look forward to reading and reviewing their work for a future *Townsend* issue. For more information: https://textbookofnaturopathiconcology.com

Jacob Schor, ND, FABNO



Editor-in-Chief:
Gurdev Parmar, ND, FABNO

Editor:
Tina Kaczor, ND, FABNO

Over 30 contributing Authors

"A masterpiece, a long-awaited comprehensive textbook which will establish its' importance in the years to come. The current textbook as well as its future editions will influence generations, and guide patients through the ever-growing field of integrative cancer diagnosis and treatment for truly individualized care."

Ralf Kleef, MD, Immunotherapy & Integrative Oncology, Vienna, Austria

"The Textbook of Naturopathic Oncology will certainly stand the test of time as one of this century's most important contributions to Integrative Oncology."

Lise Alschuler, ND, FABNO

To order your copy visit:

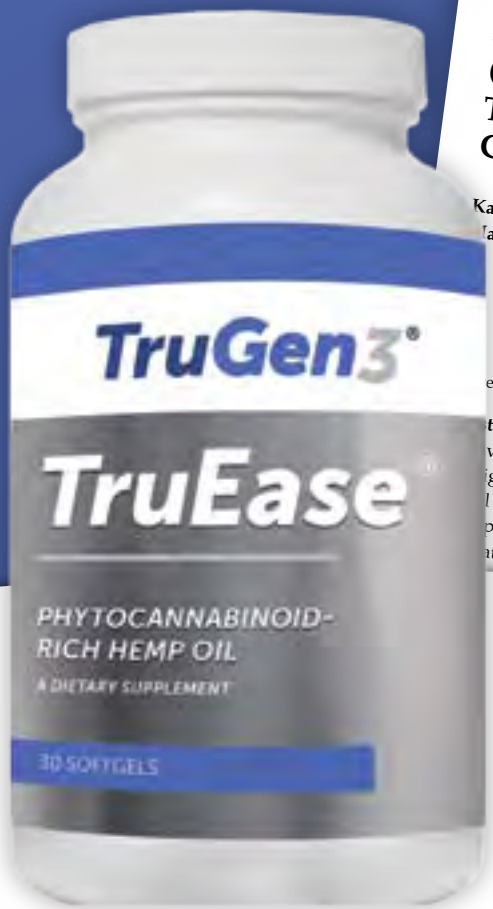
www.textbookofnaturopathiconcology.com

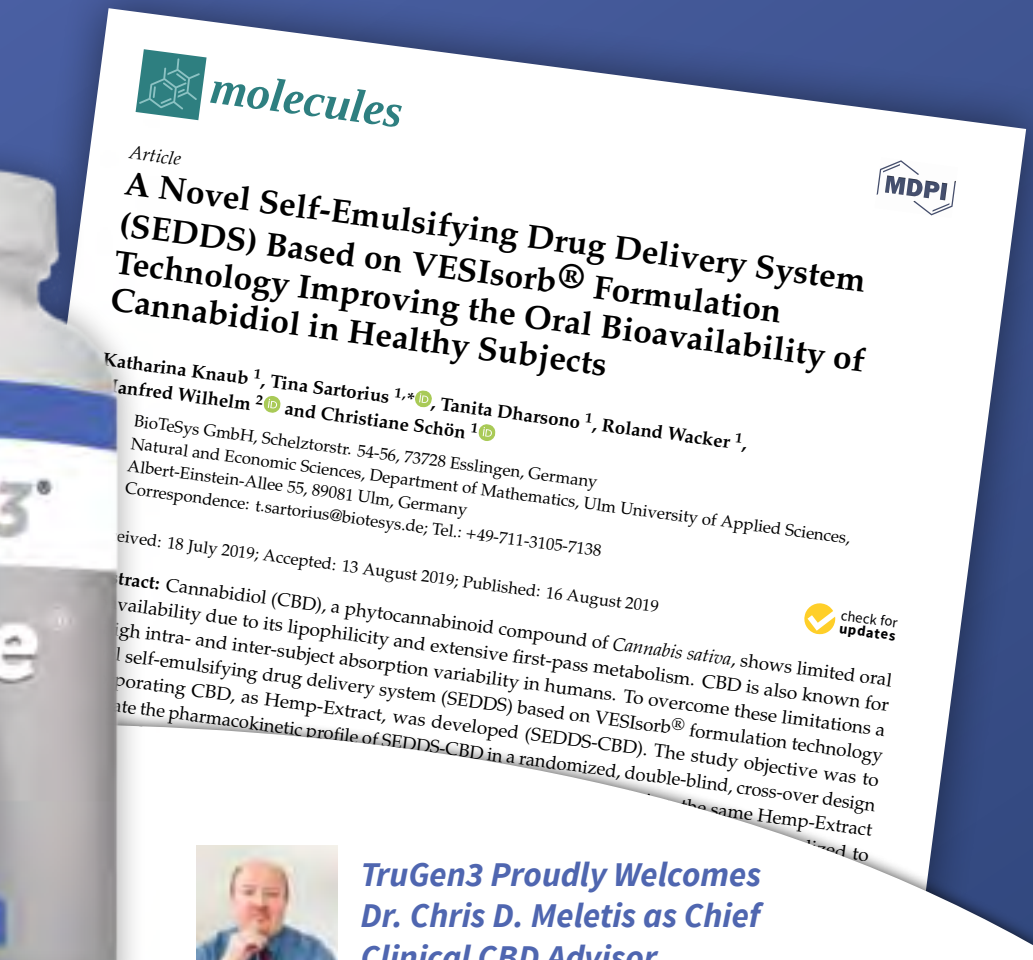
Also available on **Amazon** in hard copy or as a **Kindle book**

Truly the Best CBD...

Now Validated by a Breakthrough Clinical Study.

† This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.





molecules

Article

MDPI

A Novel Self-Emulsifying Drug Delivery System (SEDDS) Based on VESIsorb® Formulation Technology Improving the Oral Bioavailability of Cannabidiol in Healthy Subjects

Katharina Knaub [1], Tina Sartorius [1,*], Tanita Dharsono [1], Roland Wacker [1], Manfred Wilhelm [2] and Christiane Schön [1]

BioTeSys GmbH, Schelztorstr. 54-56, 73728 Esslingen, Germany
Natural and Economic Sciences, Department of Mathematics, Ulm University of Applied Sciences, Albert-Einstein-Allee 55, 89081 Ulm, Germany
Correspondence: t.sartorius@biotesys.de; Tel.: +49-711-3105-7138

eived: 18 July 2019; Accepted: 13 August 2019; Published: 16 August 2019

check for updates

tract: Cannabidiol (CBD), a phytocannabinoid compound of *Cannabis sativa*, shows limited oral vailability due to its lipophilicity and extensive first-pass metabolism. CBD is also known for gh intra- and inter-subject absorption variability in humans. To overcome these limitations a l self-emulsifying drug delivery system (SEDDS) based on VESIsorb® formulation technology porating CBD, as Hemp-Extract, was developed (SEDDS-CBD). The study objective was to te the pharmacokinetic profile of SEDDS-CBD in a randomized, double-blind, cross-over design the same Hemp-Extract

More than 4X the Bioavailability of Ordinary CBD products with MCT.†

TruEase® is truly today's Best-in-Class CBD product, produced under the highest quality and ethical standards, sold only through Health Care Professionals. **And now, TruEase® has been validated as the truly superior CBD product in a newly published Clinical Study: "A Novel Self-Emulsifying Drug Delivery System (SEDDS) Based on VESIsorb® Formulation Technology Improving the Oral Bioavailability of Cannabidiol in Healthy Subjects".** TruEase® uses patented VESIsorb® technology to provide **over 4X more bioavailability** than ordinary CBD products with MCT.† Order yours today.

TruGen3 Proudly Welcomes Dr. Chris D. Meletis as Chief Clinical CBD Advisor.

- **Receive direct access to Dr. Meletis for answers to CBD questions**
- VESIsorb® Technology for more than 4X bioavailability†
- Solvent-free Super Critical CO^2 extraction provides undetectable THC levels
- 25mg of CBD & 10mg of beta-caryophyllene

TruGen3®

Three Generations of Truth in Nutrition

www.trugen3.com 1-844-387-8436

Scan this QR code to read the complete Clinical Study!

www.trugen3.com/product/truease

Call or visit our website today for FREE SAMPLES and monthly CBD updates from Dr. Meletis